

The Constitution of Visual Consciousness

Edited by
Steven M. Miller

Advances in Consciousness Research

90



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The Constitution of Visual Consciousness

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Volume 90

The Constitution of Visual Consciousness. Lessons from Binocular Rivalry

Edited by Steven M. Miller

The Constitution of Visual Consciousness

Lessons from Binocular Rivalry

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Acknowledgments

In 1996, three years after graduating from medicine, I resolved to study the brain. I had been reading Edward Hundert's book *Philosophy, Psychiatry and Neuroscience: Three Approaches to the Mind*. For many years I had read books on philosophy of mind, psychology, and consciousness, and had been exposed to undergraduate neuroscience, psychology and psychiatry. My medical studies, grounded as they were in science, led me to believe that understanding the brain was critical to understanding the mind. However, I was equally aware that neuroscience and psychology could not do all the work. Philosophy was essential too, particularly on the issue of brain/mind relations. Hundert's interdisciplinary approach opened my eyes to the possibility of meaningfully exploring the nexus between science and philosophy in this context. The next book I read was Francis Crick's *The Astonishing Hypothesis*, which consolidated my decision to begin by focusing on the brain.

With no specific research plans, I approached John ('Jack') Pettigrew, an eminent Australian neuroscientist who had given lectures during my undergraduate years at the University of Queensland. Jack graciously offered to supervise me on one of two projects: neurochemistry-based studies on oxidative stress, or looking for a physiological switch between the two cerebral hemispheres. My plan at the time was to learn more about the brain in general, and to allow that study to inform my interest in the philosophy of mind and consciousness, so I promptly chose the hemisphere-switching project. Fortunately, Jack's plans for this work were not yet crystallized, thus providing an ideal environment for the bug of scientific hypothesis and discovery to bite me and take hold.

Within a few months, a conjunction of factors drove me to propose that binocular rivalry – the involuntary perceptual switching that occurs when the left and right eye each view a different image – might be a hemisphere-switching phenomenon. Though initially unconvinced, Jack capitulated to my enthusiasm for this idea. We thus had built, a crude headset with mirrors attached in front of each eye to induce rivalry. On the first day of experimenting with this headset, we found exactly what we were looking for, and more. I am especially grateful to Jack for the stimulating and accommodating environment provided by him, under his Directorship of the Vision, Touch and Hearing Research Centre.

In 2000, just prior to my departure from Jack's lab, I was writing a paper for a special issue on binocular rivalry for the now defunct journal, *Brain and Mind*. It was then that the idea underlying the present volume, and its forthcoming companion, emerged. Whilst detailing the various perception-dependent neural activities that had been identified during binocular rivalry, I realized that no matter how precise and detailed such understanding became, there would remain a problem for the scientific study of consciousness – that of distinguishing which of these neural correlates had anything to do with visual consciousness during rivalry, or in other words, which neural activities were actually constitutive of the visually conscious state.

Six years later, Matthew Kirkcaldie and Perminder Sachdev invited me to participate in a workshop on Neurophilosophy at the International Neuropsychiatry Association World Congress in Sydney. Several presentations from that workshop became papers for a special issue of *Acta Neuropsychiatrica*, edited by Gin Malhi. There I developed the correlation/constitution distinction problem and addressed some of the philosophical issues it entails. I was therefore, as I had originally hoped to do, exploring the nexus between the science and philosophy of consciousness (the result of which is this book and its companion). I am grateful to Matthew, Perminder and Gin, for the impetus to develop my interdisciplinary interests. It is also additionally pleasing to have Matthew contribute to the present volume, co-authoring a chapter with my long-time friend and neuroscience colleague, Anthony Hannan, who along with Matthew and I also presented at the Sydney workshop and wrote for the special issue of *Acta Neuropsychiatrica*.

I am indebted to several people who helped bring to life and to completion, the project of this book and its companion. Trung Ngo, who joined Jack's lab shortly after I did, and with whom I have worked closely now for over a decade, was an endless source of assistance and helpful discussion during development of the project and preparation of the book manuscripts. He is also responsible for the historical references and figures in my introductory chapter in this volume, and he cast his keen editorial eye over all of the contributions. Jakob Hohwy has also been a great sounding board for me since the project's inception. It was of course, invaluable for a neuroscientist who has a strong interest in philosophy to be able to discuss this project with a philosopher who has a strong interest in neuroscience.

I am grateful also to Maxim Stamenov, Chief Editor of *Advances in Consciousness Research*, who invited me to contribute to this series after attending my presentation at the 2010 annual meeting of the Association for the Scientific Study of Consciousness in Toronto. My dealings with Maxim since, and with staff at John Benjamins, have been a pleasure. I am of course, also particularly grateful

to the contributing authors in this and the companion volume for their stimulating papers, and for their willingness to review other authors' contributions.

Finally, I thank my family for their support and encouragement over many years, and for enabling me to follow my own path. Both books are dedicated to them.

Steven Miller
Melbourne
January, 2013

Visual consciousness and binocular rivalry

An introduction

Steven M. Miller

Monash University, Melbourne

Human vision is rich in content and experience. We perceive contours, colors, contrast, brightness, shapes, textures, objects, relations, depth, and motion. Upon all this we construct meaning, we involuntarily or voluntarily focus or deflect attention, and we can be either conscious, or unconscious, of presented visual information. For content of which we *are* visually conscious, there is a qualitative or experiential aspect. It is like something for us to perceive the color blue, for example, and on this basis, we are said to be phenomenally conscious of the color blue, or of blueness.

Visual consciousness is not usually an isolated perceptual experience. Blueness is experienced in conjunction with blue objects or scenes. The form, context, motion and meaning of these objects or scenes contribute to the overall phenomenal state. Along with the visual experience, a wide range of non-visual content is experienced in domains such as audition (the sound of waves lapping), olfaction (the smell of salt in the air), somatosensation (the touch of cool water), interoception (the sense of bodily relaxation), and affect (the feeling of happiness). Phenomenal consciousness is thus complex, multimodal and dynamic, and it readies us for action (or in the case of a blue seascape, for inaction).

Something in our brains constitutes the experience of blueness, and indeed the experience of all the phenomenal riches of a blue seascape. This book, and its forthcoming companion, is about exactly *what* constitutes phenomenal consciousness, and exactly *how* the science and philosophy of consciousness can approach this constitution question. The strategy is specific. This first book, written by scientists, lays the groundwork for the second by focusing on one domain – vision. Moreover, within this domain, the book focuses on one particular visual phenomenon – binocular rivalry – a detailed analysis of which speaks directly to the methodological problem of identifying the constitution of visual consciousness. The forthcoming companion volume turns from visual consciousness to phenomenal consciousness more generally, and is written by both scientists and philosophers.

Together, the two books address the nature of phenomenal consciousness and its study. Philosophers have long been interested in such questions. Indeed, these issues are fundamental concerns in the philosophy of mind. However, it has only been in more recent decades that scientists have been able to openly tackle the study of consciousness. Progress has been rapid and the scientific study of consciousness has flourished into a healthy, vibrant, interdisciplinary field of research (a fact attested to by the existence of this book series). Despite such progress, it is debatable to what degree scientists and philosophers meaningfully interact in this pursuit, as opposed to merely tolerating each other's presence, or merely straying into each other's field. It is my view that meaningful interdisciplinary interaction between scientists and philosophers is not only possible, but desirable. It is my hope that the second of these books will be evidence of this.

Before engaging in interdisciplinary discourse on the science and philosophy of consciousness, there is, as I have mentioned, groundwork to be done. Indeed, the reader's patience is required throughout this first volume, for it contains less explicit discussion of the study of consciousness than might be expected from the volume's title. Its contents are nonetheless critical to understanding the question of the constitution of consciousness, and to understanding at least part of an answer.

Two further introductory chapters lay foundations. Anthony Hannan and Matthew Kirkcaldie take on the difficult task of surveying the brain's constituents and organization at both the small and large scale, and the processes in which these constituents participate. We are led on an informative tour of how the brain is shaped by evolution and development and how its constituents, including genes, molecules, cells, neural circuits, and neural systems, are organized and function to produce human perception, cognition and behavior. The authors deftly navigate their multi-scale description of the brain, from gene to behavior, noting the extraordinary complexity of their subject. They point out that despite existing knowledge of how one level of constituent and process interacts with and influences another, reconciliation across different levels of description remains a major goal of present-day neuroscience.

Next, Nicholas Price takes us on another 'tour de force' of existing knowledge, providing intricate detail of the visual system's anatomy and physiology. Price's overview is built around four organizational principles and processing strategies: functional segregation and parallel processing; multiplexed neuronal response coding; multidirectional hierarchical functional processing; and vision as an active sense. The territory covered includes characterization of visual neuronal circuitry, the response properties of visual neurons, transformation of the retinal signal by cortical processing, the 'algorithmic' activity of visual neurons within circuits, the engagement of the subject in active elements of perceptual processing (including

the role of eye movements and attention), and how all this organization and function creates unified perception and reliable behavior. The reader, by the end of the chapter, will appreciate the breathtaking level of current understanding of the visual system's constituents, organization and processes, and the work that remains to be done to progress anatomical and physiological understanding even further.

Thereafter, the focus moves to the phenomenon of binocular rivalry. In so doing, this first book adopts an uncommon approach in collected volumes on vision and visual consciousness. Rather than addressing the topic by utilising a wide range of visual and attentional phenomena, and explicating what is known of neural mechanisms underlying these phenomena, this book instead focuses on just one visual phenomenon. Having stipulated this solitary target phenomenon of binocular rivalry, the aim is to disentangle it in great detail, by examining multiple methodological approaches to it, from multiple perspectives.

There are several reasons for this strategy. Binocular rivalry is a unique phenomenon in many respects. It has been studied for over two hundred years, requiring as it does, just the separation of each eye's presented image and sufficient image incongruence. This induces in the subject an alternating perception of each image every few seconds. In this curious way, the brain defaults, with relative equanimity, to the perceptual experience of each image in turn. It therefore resolves the sensory conflict by a process of alternate sampling, rather than mixing or superimposition. Take some time to experience and explore the phenomenon for yourself if you purchased with this volume, the recommended stereoscopic viewer (see the link on the John Benjamins website for this book – <http://benjamins.com/#catalog/books/aicr.90/main>). The images for use with the viewer are in Figure 1 to 4, and even the squares on the front cover of this book can be used to experience binocular rivalry.

With the viewer, note various aspects of the phenomenon in Figure 1 that will be discussed in detail in the chapters that follow, such as the basic alternation process, the clean and isolated visual states, the mixed states, the different types of transitions from one state to the other, and the rate of alternation. In Figure 2, note the synthesis of aspects of each eye's presented image into coherent rivaling images. There are many more aspects of rivalry that can be explored by the reader (and now perceptual experimenter) while progressing through this book and learning more of what is known about the phenomenon of binocular rivalry.

That and *how* the brain adopts the remarkable conflict resolution strategy of binocular rivalry, has justifiably intrigued investigators of the calibre of Helmholtz, Hering and Sherrington. Just *why* the brain developed this strategy remains unclear, though the phenomenon is perhaps reflective of fundamental and evolutionarily ancient principles of attentional processing. Indeed, it is by no means accidental that the brain employs a similar alternate sampling strategy even when



Figure 1. Conventional binocular rivalry. To view these gratings dichoptically (i.e., one to each eye), stand the stereoscopic viewer support panel in the center between the stimuli with the book face flat and level. Look directly down the viewer with both eyes and slowly move closer towards the lens panel until the black border around both gratings are fused. These alignment cues will help to determine your optimal viewing position for inducing reliable rivalry. Look through the left lens only to see the vertical grating, followed by the right lens only to see the horizontal grating, and then look with both eyes to observe the ensuing perceptual alternations. Note the periods of exclusive rivalry (i.e., only one image is visible); the rate of alternation between the two exclusive images; the predominance of one exclusive image over the other; periods of mixed, superimposed or unusual percepts; and the different types of transitions from one percept to the other.



Figure 2. Interocular-grouping (or multistable) binocular rivalry. In contrast to conventional binocular rivalry (Figure 1) where there is rivalry mainly between two conflicting images, these presented stimuli yield mainly *four* alternate percepts. Reported in 1928 by Emilio Díaz-Caneja (*Annales D'Oculistique*, 165:721–731), these stimuli show that observers not only perceive either of the presented images but also two other percepts comprised of elements from both eyes' images. Using the stereoscopic viewer as described above, these latter *coherent percepts* can be seen as either concentric circles or full horizontal lines, and demonstrate the brain's perceptual reorganization ability and the constructive nature of visual perception during rivalry.

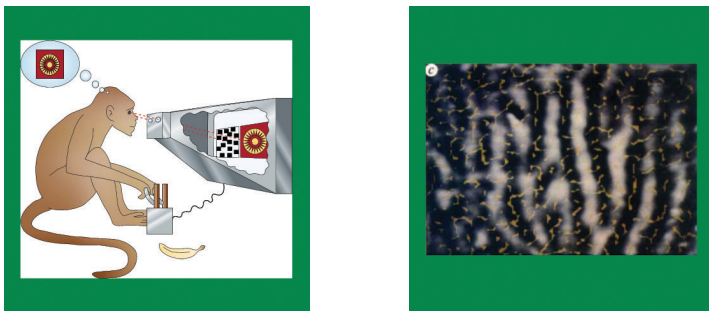


Figure 3. Binocular rivalry between complex images. Binocular rivalry can also readily occur between more complex images (commonly comprising house and face stimuli) than the line stimuli in Figure 1 and 2 above. The example shown here is of a macaque monkey image (left), which represents electrophysiological evidence for a high-level resolution of binocular rivalry, and an ocular dominance map from V1 (right; also from a macaque), which represents the low-level monocular channel competition model of the phenomenon. The perceptual alternations between these images not only demonstrate rivalry between complex stimuli, but also reflect rivaling high- and low-level interpretations of the phenomenon that have characterized its investigation. (Reprinted by permission from Macmillan Publishers Ltd: *Nat Rev Neurosci*, Blake & Logothetis, 3: 1–11, copyright 2002; *Nature*, Blasdel & Salama, 321: 579–585, copyright 1986.)

images in each eye are not incongruent, but rather involve ambiguous perspectives or interpretations. Many types of perceptual rivalry have now been reported and studied. Ambiguous images date to at least 300 B.C. (e.g., Euclid's reversible parallelepipeds noted by Wheatstone, 1838) and indeed even earlier, with reversible patterns apparent in late-Neolithic age pottery (Metzger, 1936/2006; *Laws of Seeing*, Cambridge, MA: MIT Press). Depicted in Figure 4 are the well-known Necker cube/rhomboid (1832) and Rubin's vase (1921), while Figure 5 shows much earlier examples of such ambiguous-figure rivalry from the 5th/6th and 17th Century, respectively.

New types of rivalry phenomena continue to be created and described (such as motion-induced blindness and continuous flash suppression). Evidence is accumulating that there is at least some degree of overlap in the neural mechanisms underlying binocular rivalry and various other forms of perceptual rivalry. Rivalry mechanisms have been the focus of intensive psychophysical, cognitive, computational, and neurophysiological investigation in the last two decades, and for many years prior in the case of psychophysics. The findings, for binocular rivalry at least, are summarized and reviewed in the chapters that follow. (A number of chapters also discuss related perceptual rivalry phenomena, but no chapters focus exclusively on these.)

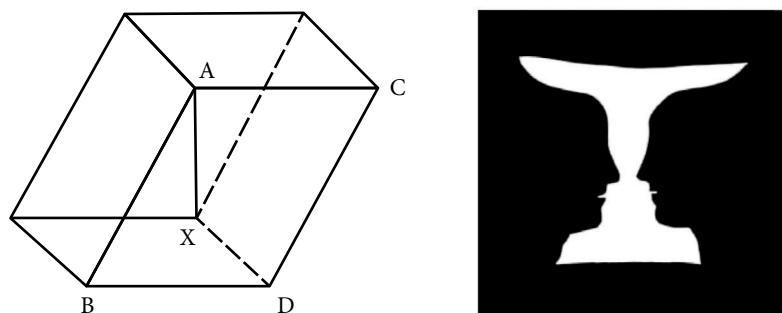


Figure 4. The Necker cube and Rubin's vase. The cube/rhomboid (left) is an *ambiguous* or *reversible* figure that alternates between two depth perspectives, in which the side delineated by A-B-D-C-A can be perceived as the front face towards the right or alternatively, as the base. This structure was first reported in 1832 by Louis Albert Necker, a crystallographer, who observed these involuntary perceptual changes in crystal engravings (*London and Edinburgh Philosophical Magazine and Journal of Science*, 1: 329–337). Indeed, it has been suggested that reference to the 'Necker rhomboid' and 'Wheatstone cube' is more fitting as these investigators first depicted and described reversals of depth in those respective ambiguous images (Wade, 1983, *Brewster and Wheatstone on vision*, London: Academic Press). On the right is Edgar Rubin's vase, a figure-ground type of ambiguous figure which perceptually alternates between two face profiles and a central white goblet (Rubin, 1921, *Visuell wahrgenommene Figuren*, Copenhagen: Gyldendalske). (The two ambiguous figures can also be viewed dichoptically with the stereoscopic viewer to observe multistable, four-percept alternations.)

The sheer curiosity that binocular rivalry engenders in all those who experience it is not what makes it of such immense interest to visual neuroscience and to the scientific study of consciousness. Rather, consider the following features of the phenomenon that justify claims of its utility, and that are detailed and expanded upon in the various chapters of this book. First, even setting aside non-visual phenomenal domains, visual scenes are incredibly complex and dynamic, and are therefore difficult to study even with modern neuroscientific methods. Binocular rivalry on the other hand, can be manipulated to involve the alternation of two relatively isolated visual states (by minimising, or excluding from analysis, the mixed or transitional states). Moreover, behavioral tracking of the isolated states and alternation dynamics (or of the mixed or transitional states, if this is the experimenter's interest – see below) is readily achievable by way of subject report, or even objectively through eye-movement recordings if the presented stimuli move in incongruent directions. This combination of relatively isolated visual states and readily reportable (or observable) state changes enables the investigator to track



Figure 5. Early examples of ambiguous-figure rivalry. On the top left is a 5th or 6th Century Roman mosaic consisting of multiple connected Necker-like structures, each comprising three adjoining sides. Each structure can be seen to perceptually alternate between two depth perspectives, either towards or from the page. The original color image was kindly provided by Nicholas Wade (see also Wade, 2012, *Gestalt Theory*, 34: 329–347). On the right is a 17th Century Islamic naval flag which depicts two face profiles, with the central vase-like image being an inverted representation of an Ottoman mosque (reprinted from Pion Ltd: Piccolino & Wade, 2006, *Perception*, 35: 1003–1006; original image provided by Nicholas Wade). On the bottom left, a close-up of the top of the flag shows the eyes of each profile are either side of the leaves, while the nose of each face forms the base of the vase and the mouths are closest to the central star.

a subject's visual trajectory in a manner that is not readily possible during natural viewing of visual scenes. With this capacity to reliably track dynamic visual trajectories, the path is open for investigators to seek correlations between neural processes and (rivaling) visual states. This path is also aided by the visual system being the best characterized and understood of all brain systems.

However, simply presenting physically alternating visual stimuli to a subject under normal viewing conditions, and thus mimicking the perceptions during binocular rivalry, would do exactly the same thing – provide a readily trackable and controlled visual trajectory with which to seek neural activity correlations. Binocular rivalry offers more than this. As is widely heralded in the literature, the phenomenon, and indeed all perceptual rivalry phenomena, offers the opportunity

to dissociate neural activity that correlates with (dynamic) perception, from that which correlates with (stable) stimulus presentation. The scientific study of consciousness of course particularly values identification of the former, i.e., of *perception-dependent* neural activity. Identification of perception-dependent neural correlates of consciousness during binocular rivalry was a major finding and topic of discussion in consciousness research in the late 1990s. The data discussed involved both single-unit electrophysiology in awake, behaving macaque monkeys (see also Figure 3) and indirect measures of neural processing with brain-imaging techniques in humans. The field has continued to expand the now impressive list of neural correlates of consciousness during rivalry, with the newest perception-dependent correlate reported this year.

In addition, the phenomenon of rivalry is able to be probed with multiple methodologies in both animals and humans. Methods such as single-unit and local field potential electrophysiology, electroencephalography (EEG) and event-related potential recording, magnetoencephalography (MEG), various brain-imaging techniques, and transcranial magnetic stimulation (TMS) can all be applied to study rivalry, furthering knowledge of underlying neural mechanisms. Moreover, binocular rivalry offers the investigator a host of opportunities to reliably manipulate the phenomenon and its dynamics, through alteration of stimulus factors (exogenous factors, such as contrast or stimulus context), and subject factors (endogenous factors, such as administering pharmacological agents and voluntary attentional control). These manipulations and their effects on the dynamics of rivalry offer additional means of teasing apart neural mechanisms of rivalry and its modulation. Further investigative opportunities offered by the phenomenon include its links to other well-studied phenomena within cognitive neuroscience such as attention, memory and affect, as well as recently emerged avenues such as genetic and molecular aspects of rivalry dynamics.

The unique ability of binocular rivalry to enable identification of neural correlates of consciousness has justified the many claims of its utility in consciousness research. However, the purpose of this book and its companion is to delve even further into the implications for consciousness science of all this correlate-finding. It is my view that no amount of correlate-finding alone will lead to an understanding of the constitution of visual consciousness, and that this distinction – the correlation/constitution distinction – exemplified most clearly by contemporary findings from binocular rivalry research, presents a very real challenge for the science of consciousness (see Miller, 2001, Binocular rivalry and the cerebral hemispheres: With a note on the correlates and constitution of visual consciousness, *Brain and Mind*, 2: 119–149; Miller, 2007, On the correlation/constitution distinction problem (and other hard problems) in the scientific study of consciousness, *Acta Neuropsychiatrica*, 19: 159–176). It is also a distinction

that carries the potential for new approaches in the philosophy of mind (much of which is concerned with the philosophy of phenomenal consciousness), thus enabling a two-way interdisciplinary discourse: science informs the philosophy of consciousness and philosophy informs the science of consciousness. These books seek to improve understanding of the correlation/constitution distinction problem, to present it as exemplified by findings from binocular rivalry research, to suggest approaches to dealing with it, and to address its philosophical and theoretical implications.

Beyond these lofty goals, it is also timely for there to appear a collected volume on the state of binocular rivalry research. The last such edited volume, *Binocular rivalry* (2005, MIT Press), was that by David Alais and Randolph Blake. There exists also, the recently updated review of binocular rivalry in Ian Howard and Brian Rogers' *Perceiving in depth: Vol. 2, Stereoscopic vision* (2012, OUP), the original version of which served as my own introduction to the field in the mid-late 1990s.¹ Furthermore, there have been journal special issues on rivalry, including those in *Brain and Mind* (2001, Vol 2, Iss 1), *Philosophical Transactions of the Royal Society of London B: Biological Sciences* (2012, Vol 367, Iss 1591, 'Multistability in perception: Binding sensory modalities'), and *Frontiers in Human Neuroscience* (2012, 'Binocular rivalry: A gateway to consciousness'). The resurgence of interest in binocular rivalry and multistable perception over the past two decades is also reflected by the number of publications on the topic in the highest ranked international journals and the frequency of dedicated rivalry symposia at scientific conferences. This resurgence has concurrently driven interest in consciousness research, as has been discussed above. The papers in the present volume not only serve to update the reader on progress in binocular rivalry research, but also to take a multi-perspective view on the phenomenon and its study, pitched at both initiated and uninitiated readers.

Nicholas Wade and Trung Ngo introduce the phenomenon of binocular rivalry by providing an historical overview of its study. They start by documenting observations of the phenomenon made in the 16th Century and onwards, well before those made by Wheatstone and Helmholtz. The authors go on to discuss how examination of binocular rivalry stemmed from early inquiry into binocular vision and binocular combination, with Descartes' theory of brain pathways for processing retinal disparity provoking his contemporaries into observing binocular rivalry. Wade and Ngo next outline the advent of experimental methods for examining perception, such as the invention of the stereoscope, which transformed rivalry studies, including the work of Wheatstone, Helmholtz and Panum.

1. During production of the current volume, sadly Ian Howard died.

They also discuss philosophical traditions that contextualized the advances in rivalry research, as well as how early notions of attention and consciousness were applied to rivalry.

The psychophysical properties of binocular rivalry are then reviewed by Jan Brascamp and Daniel Baker, who start by introducing the reader to the notion of psychophysics. They then distinguish two classes of binocular rivalry psychophysics. According to this division, the first aims to understand the phenomenon itself while the second is concerned with another benefit of binocular rivalry for the study of visual consciousness – a means to prevent visual input from accessing consciousness, enabling examination of just what is processed of the *unconscious*, suppressed stimulus and by which neural activities. Thus Brascamp and Baker overview the large and growing list of properties of binocular rivalry, with respect to both dominance and suppression phases, from what is now more than 100 years of psychophysical research. They end their survey with a caution, noting that correlated neural activity during binocular rivalry may be specific to this phenomenon, rather than to visual consciousness per se.

Next, Richard Thomson and Paul Fitzgerald detour from the focus on rivalry to look more closely at some of the common methods applied to its study, including non-invasive EEG and MEG, the stimulation/disruption technique of TMS, and brain-imaging techniques such as structural magnetic resonance imaging, diffusion tensor imaging and functional magnetic resonance imaging (fMRI). They provide an overview of technical elements of these various methodologies, including the advantages and disadvantages with each, and discuss current thinking on what physiological processes determine the measured signals (including modeling approaches to source localization). Examples of applications of the technologies are provided, including some in the context of binocular rivalry. The chapter provides important background for later chapters on EEG, MEG, TMS, and fMRI studies of rivalry, and concludes by discussing future methodological focus points (such as opportunities for combining techniques).

Frank Sengpiel then introduces the method of invasive single-cell and multi-channel electrophysiology and reviews studies of these methods in the settings of interocular suppression and binocular rivalry. This is done with reference to the five dogmas from Barlow's 'neuron doctrine of perceptual psychology', that were formulated to explain the relationship between neuronal firing and subjective perception. The review also provides historical context for the electrophysiological study of rivalry within the neurophysiological milieu of the second half of the 20th Century. Sengpiel discusses the initial electrophysiological work conducted in anesthetized cats and progresses to studies of awake, behaving macaque monkeys, outlining the various regions in the visual processing

hierarchy that demonstrate neuronal signals of stimulus dominance or suppression. Sengpiel also addresses the discordance between electrophysiological and brain-imaging data, as well as issues of temporal correlation (synchrony) of neuronal firing, feedback from higher brain regions and the need for micro-stimulation studies of rivalry.

Thereafter, Philipp Sterzer reviews how the various non-invasive methods discussed by Thomson and Fitzgerald have been specifically applied in the context of binocular rivalry (and other rivalry types). The chapter outlines findings from EEG, MEG, fMRI and TMS studies of rivalry, and, like the chapter by Sengpiel, analyses potential reasons for discordant results obtained with different methodologies. Sterzer's discussion of this literature is structured around processing of the suppressed stimulus (as in the chapter by Brascamp & Baker), and also a further benefit of binocular rivalry for the study of visual consciousness: that it highlights the *constructive* nature of perception. In this regard, Sterzer considers analysis of neural activity relative to rivalry transitions as being highly informative. The chapter ends by discussing the notion of multi-level processing during rivalry and the emerging, albeit conflicting, data on the mechanistic role of parietal and frontal brain regions.

Trung Ngo, Wendy Barsdell, Phillip Law and I then review a specific model of rivalry that emerged from the first application of brain stimulation techniques to the phenomenon. Ngo et al. describe the interhemispheric switch (IHS) model, its intellectual genesis, and the caloric vestibular stimulation (CVS) and TMS data on which this model is based. In addition, they review findings from subsequent CVS and TMS studies, noting the latter have focused on modulation of rivalry rate. The authors then take up the issue of rivalry rate and describe the serendipitous finding made during investigation of the IHS model, that this is significantly slower in subjects with the psychiatric condition, bipolar disorder. They go on to describe the current investigation of rivalry rate as a potential diagnostic aid and endophenotype in clinical psychiatry, the genetic contribution to individual variation in rivalry rate, and opportunities for probing genetic, molecular and neurophysiological aspects of rivalry using a recently described *Drosophila* (fruit fly) model.

A return to psychophysical aspects of binocular rivalry then follows, with David Bressler, Rachel Denison and Michael Silver discussing these from the perspective of high-level modulations of the phenomenon. They outline the role of stimulus and observer factors in determining perceptual selection, dominance and suppression during rivalry. On stimulus factors, the authors discuss how stimulus configuration – the arrangement and grouping properties of stimulus elements – influences perception during rivalry. They go on to detail the role of the visual context of presented stimuli, with respect to both spatial context

(non-rivaling surrounding stimuli) and temporal context (preceding stimuli, including what they term 'predictive context'). On observer factors, Bressler et al. review studies of the influence of attention and volition on perception during rivalry, as well as the influence of the neurochemical state of the subject, from relatively stable genetic and molecular elements to dynamic, pharmacological modulation.

Hugh Wilson then describes the computational approach to binocular rivalry and adopts a strategy that focuses on decision processing in resolving sensory conflict. Computational modeling is introduced and applied to binocular rivalry and its role in drawing together multiple levels of description of brain processing is outlined. The modeling is also discussed in the context of various neurophysiological and psychophysical aspects of binocular rivalry. Thereafter, Wilson aims to show that rivalry models can generalize to inform understanding of the neural basis of deliberation. Cooperative and especially competitive processes, including feedback processes, both within neural networks and with their inputs, are highlighted as critical aspects of conscious deliberation that also characterize the proposed generalized rivalry model. The model aims to describe low- and high-level (especially prefrontal) contributions to rivalry and to decision-making, incorporating emotion and memory functions and global workspace theory.

Finally, Chris Klink, Richard van Wezel and Raymond van Ee explore the future of binocular rivalry research. They divide approaches to studying rivalry into three categories: using the phenomenon to study perception and consciousness, disentangling mechanisms of the phenomenon and their relation to other aspects of binocular vision (such as binocular fusion and stereopsis), and interacting with (modulating) the phenomenon. In describing these approaches, the authors draw on current and developing technologies to illustrate the gains made, and those still to be made, in binocular rivalry research. Their discussion includes techniques already encountered in the volume, such as fMRI, EEG, MEG, TMS, microstimulation, genetics, and computational modeling, but also introduces new methodologies such as near-infrared spectroscopy and photostimulation. The authors outline the exciting opportunities for applying existing and developing techniques in combination (as discussed also by Thomson & Fitzgerald), to achieve a detailed understanding of binocular rivalry, binocular vision and visual consciousness.

Upon reaching the end of this first book, the reader will have traversed the landscape of existing knowledge on the human brain's constituents, organization and processes, on the visual system in even more detail, on common techniques used in modern human neuroscience, and on the phenomenon of binocular

rivalry in exquisite detail. At that point the reader might wonder what has been learned of the constitution of visual consciousness and how the lessons learned can be utilized in approaching the correlation/constitution distinction problem. However, to properly understand these questions, examination is required of just what is meant by 'consciousness', 'correlation' and 'constitution'. It is not until the forthcoming companion volume that such issues will be addressed explicitly. Nonetheless, the reader of this volume will have come to appreciate the extraordinary phenomenon of binocular rivalry, the depth and breadth of the science and theory it has generated and will continue to generate, and the utility of rivalry for the rapidly developing scientific study of consciousness.

Constituents, organization and processes of the human brain

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The human brain is an extraordinarily complex biological system underpinning cognition and experience. This complexity is evident at all levels, from genetics to molecular, cellular, network and systems constituents. This article provides an overview of these constituents, their organization and the processes in which they are engaged. We discuss the shaping influences of development and evolution, and describe the brain's structure and function at several levels: cellular features, the organization of neurons into functional systems, the gross anatomy of the nervous system and the specific structural and functional properties of the cerebral cortex. There is considerable evidence that cortical activity – though not all cortical activity – is correlated with conscious experiences, but exactly which activities constitute consciousness is unclear.

Introduction

The human brain is the most complex system known, a kilogram-and-a-half of neural tissue which embodies everything we think, feel and do. The young daughter of one of the authors recently punned, “Which organ can’t you *live* without? Your *liver!*” – but in a world of major organ, face and hand transplants, the one truly irreplaceable component is the brain. Its store of experience, memory and knowledge defines the self, makes the world comprehensible and is at the core of conscious being. If we are to even attempt to understand the constitution of conscious experience, or *any* higher order cognitive process, we must first appreciate the structural and functional complexity of the brain. In this chapter we survey the constituents and organization of the human brain, providing a conceptual framework for the more complex theoretical and philosophical arguments put forward in the forthcoming companion volume.

Appreciating the complexity of the human brain, and the factors which produce that complexity, requires understanding from a variety of perspectives. In

this chapter we discuss major principles and ideas which have shaped our understanding of the properties of nervous systems, providing a biological viewpoint and a descriptive lexicon for readers of this volume and its companion. Phylogeny, ontogeny, cellular components, organization and anatomy are considered independently by necessity, because reconciling these domains remains the goal of neuroscience. The order in which they are presented is arbitrary, and does not imply that some are more fundamental than others; instead, they are often considered simultaneously when understanding neural function.

Phylogeny

Evolution is the definitive conceptual framework for interpreting the structure and function of biological systems, and the human brain is no exception. Our anthropomorphic instinct is to place *Homo sapiens* at the pinnacle of evolution, but we are really a twig on one branch of an extraordinarily complex tree. On this branch we find our closest relatives, the great apes, and beside us chimpanzees, the closest extant species. Although the vast majority of our genetic makeup is identical to these near relatives, our brains have achieved extraordinary cognitive abilities which far outstrip any ape. This apparent contradiction has remained a central problem in neuroscience.

It is widely accepted that our brains are made from essentially the same components as those of other mammals (e.g., DeFelipe, 2011), and thus far neuroscience has found no uniquely human anatomy or physiology which corresponds to exceptional mental abilities (but see Allman et al., 2010). Comparisons between human brains and those of other animals have been made for decades, but it is surprisingly difficult to decide exactly what should be measured. The familiar doctrine that our brains are far larger than expected for our body size turns out to be exaggerated by comparisons with relatively unrelated mammals, and there is no *prima facie* reason that the ratio of brain weight to body weight should be much more significant than the number of neurons, for example. The degree of observed discrepancy is heavily skewed by the choice of measurement, as well as the fact that the scaling principles which govern these properties vary considerably between different orders of mammals. The most conservative view to take is that primates in general have efficiently constructed, neuron-packed brains, of which ours is the largest example (Azevedo et al., 2009;erculano-Houzel, 2009).

Regardless of their exact underpinnings, our abilities have evolved rapidly compared to parallel primate lineages, and dozens of theories have sought to explain this singular development. The observation that our ancestral brain reached its present size long before modern civilization or culture may provide

some insight into the affective, cognitive and motor functions it evolved to subserve, or the factors which permitted its rapid expansion. Bipedalism, social cognition and communication in hunter-gatherer cultures, an omnivorous diet including cooked food, sexual selection, and many other factors have been suggested as drivers of the evolution of the human brain and its functional capacities (e.g., Allman, 2000; Barrett & Henzi, 2005; Kirkcaldie & Kitchener, 2007; Shultz & Dunbar, 2010).

Although many of these drivers favor behavioral sophistication, the options for achieving that capability are constrained by the structure of the nervous system itself – as Allman (2000) observes, reworking the function of the brain must be achieved by augmentation, adaptation and modification, so that every generation possesses an efficient and capable nervous system rather than a less useful intermediate stage toward a greater capability. In this context, some components of the CNS are more easily adapted to new functions without compromise to existing efficiencies (e.g., Clark, Mitra, & Wang, 2001). Our mammalian brain consists of component parts whose layout and function is closely equivalent to shrews, whales and elephants, for example (e.g., Krubitzer & Hunt, 2009), and like all mammals we have a six-layered cerebral cortex (or *neocortex*). The cortex, whose characteristic folded texture covers most of the visible outer surface of the forebrain, is an analytical structure which adds sophistication and integration to simpler behavioral control and reflexes – and its rapid, augmentative development in humans and other species suggests that it is ideally suited to radical evolutionary change without disruption of core nervous system functions (see Kirkcaldie & Kitchener, 2007). Furthermore, the abilities and functions of the cortex are closely tied with conscious experience.

In keeping with this argument, we may usefully ask whether higher order cognitive processes such as consciousness were also favored by evolutionary forces (Miller, 2007; see chapter by Panksepp in forthcoming companion volume). For example, consciousness might have conferred selection advantages by improving behavioral planning – correlating working memory with attentional processes – or integrating emotional experiences with cognition to add depth, dimension and relevance to memories. However, it might simply be that some degree of consciousness is an epiphenomenon of complex brains, and that the elaboration of the human brain has given us an elaborate consciousness as a byproduct of growth.

Ontogeny

Although the complexities of human developmental processes are beyond the scope of our chapter, it is not possible to meaningfully describe the brain without sketching the principles by which its structure arises. These processes explain why

we have brains with these specific structural and functional qualities, and how these qualities relate to our unique abilities. These qualities may in turn suggest a basis for higher order cognitive processes, including consciousness (Hannan, 2007).

At the individual level, the key determinant of brain properties is ontogeny – in biology, the collective term for developmental processes which generate the adult organism, and the level at which genes have their most direct effect on neural structure. This decisive influence is determined at conception, when a unique human genome is generated in an ovum whose internal environment, a strong influence on subsequent development, is likewise unique. This genome, via the complex coding and regulatory sequences of DNA, shapes and directs the extraordinary developmental program followed by human embryos.

After fertilization, a complex cascade of molecular and cellular events rapidly generates a multicellular embryo, each cell inheriting the same genome with an additional epigenetic “mark-up” that specifies increasingly detailed patterning information. The brain begins as skin: at early stages the embryo’s outer layer folds inward to form the neural tube and the neural crest, and the embryonic nervous system begins to be specified. Cells divide at different rates in different regions of the tube, forming the structures of the forebrain and hindbrain as a series of swellings, and exerting patterning and growth-regulating effects on their neighbors – see Sanes, Reh and Harris (2012) for a comprehensive overview. By birth, most cells and organs of the body have been generated and organized into functional assemblies such as tissues and organs, and for most of the body postnatal development is merely growth, sexual maturation and aging. However, for the central nervous system, gestation is merely the first chapter of a far more elaborate development, sculpted by environment, experience and feedback from emerging sensory, cognitive and motor functions.

Functions of the nervous system are largely defined by the connections between cells, which develop in stages. During embryonic development, each of our hundred billion neurons extends receptive and communicative filaments, called dendrites and axons, under the influence of secreted signals and marker proteins found on the surface of other neurons and bodily cells (see Kolodkin & Tessier-Lavigne, 2011, for an introduction). This guided, exploratory growth produces arrangements of staggering complexity and finesse – for example, a sensory neuron in the spinal cord may extend a fiber to contact a patch of skin on a specific toe, traveling past billions of irrelevant cells until it finds its goal, while simultaneously guiding a fiber up the spinal cord through a complex routing system to make connections in the same cluster as fibers from other parts of the same toe. This extraordinary feat of guidance is achieved by equipping the growing tip with receptors sensitive to standardized signaling molecules secreted throughout the body. Under genetic control which depends on their birth location, neurons equip their growth cones with

receptors attracted to some molecules, repelled by others and indifferent to those not relevant to their purposes (Dent, Gupton, & Gertler, 2011). This key principle of developmental organization has only been appreciated and explored in the last few decades, and fundamental discoveries are still being made.

After birth, the nervous system capitalizes on this rich structural order by honing it into the most effective control system it can be, growing and winnowing cells and connections on the basis of their utility and efficiency. This process of plasticity persists in various forms throughout life, underpinning rapid accommodations to changing conditions as well as more permanent connections which allow memories to persist for decades. In general, the scope of plasticity diminishes as we pass through childhood, adolescence and adulthood, locking our life's experience into the fabric of neural connectivity.

Cellular constituents

More than a century ago, histologists studying the nervous system began to realize that its densely matted meshwork of fibers, nuclei and protoplasm is composed of an astronomical number of individual cells. These cells' finely wrought shapes and incredibly long processes were unlike any others previously observed; in fact much of the early debate about the structure of the nervous system arose from the inadequacies of standard histochemical techniques to penetrate its structural complexity (Figure 1; Golgi, 1901; Ramón y Cajal, 1901). Even the doyen of cellular neuroanatomists, Santiago Ramón y Cajal, had to resort to studies of developing brains to gain a foothold on their mature complexity (DeFelipe & Jones, 1988). The adult human brain contains up to 200 billion cells: 80–100 billion *neurons* and as many more *glia* (Azevedo et al., 2009), seamlessly coupled into a dense fabric of electrochemical communication and regulation. Individual neurons exhibit wonderful structural and functional sophistication, with up to 200,000 synapses on dendrites, and axon branches teased and extended into filigree shapes extending for hundreds of centimetres in some cases. Across the entire brain, quadrillions of synapses connect billions of neurons in vast information-processing networks.

In the brain, the three main glial types are *astrocytes*, *oligodendrocytes* and *microglia*; the latter act as sentinels of the immune system and aggressively police the extracellular environment. Astrocytes envelop and couple with neuron cell bodies and dendrites, providing food and a regulated environment, as well as signaling between themselves. Oligodendrocytes perform similar roles for axons, some of which they bind in spirals of fatty myelin, consolidating and speeding signaling. Although originally regarded as mere 'glue' holding neurons together, glial cells have received far more attention and recognition by neuroscience in the

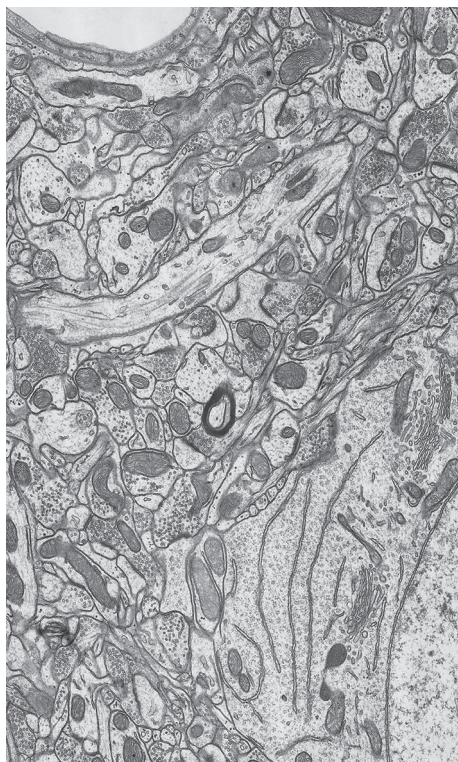


Figure 1. Viewed by an electron microscope, the complexity of a tiny sliver of mouse neocortex about 6×10 microns is apparent. At top left, the open space of a capillary is surrounded by structures of the blood-brain barrier. Part of a dendrite crosses the section plane diagonally in the middle of the picture, and the nucleus of a neuron surrounded by cellular manufacturing apparatus is visible at bottom right. Darker ovals with internal lines are mitochondria, the energy factories of all cells. The dark ring near the center is a multi-layered coating of myelin around an axon. Lastly, this image contains about 50 synapses, recognizable as clusters of tiny circular neurotransmitter packets beside a dark smudge in the membrane, which contains the receptors on the post-synaptic side. A single cubic millimetre of cortex has been estimated to contain a total of four and a half kilometres of axons and dendrites (Braitenberg & Schüz, 1998). Scanning transmission electron micrograph by kind permission of Dr Graham Knott, École Polytechnique Fédérale de Lausanne.

last two decades (Kettenmann & Verkhratsky, 2008). Intricate neuronal-glial and glial-glial interactions alter neural communication, information processing and plasticity, and most interactions between neurons are mediated or overseen by glial partners. They complement neuronal processing: neuronal events are rapid, isolated, specific and evanescent, whereas glial activity is slow, integrative and

modulates large populations of neurons chemically and metabolically. Although these functions are of critical importance to neural processing, they are not yet deeply understood and we will not deal with them further. Other cell types in the brain, such as ependymal and vascular cells, will not be discussed, as they are not easily linked to the cognitive processes that are the core subject of this book and its companion volume.

Neurons are unique in a number of ways. Their structure is usually described in functional terms (Figure 2): a branching tree of *dendrites* collect influences which converge on the *soma*, the location of the nucleus and most of the cellular machinery. Signals leave the neuron via the *axon*, a specialized cellular extension which transmits activity reliably over long distances, branching and rebranching to innervate the appropriate recipients, be they muscles, glands or other neurons. Neurons have excitable membranes which, via molecular tools that manipulate charged ions, can rapidly fire activity across the neuronal surface, thereby integrating influences and transmitting signals to interconnected neurons. In typical neural activity, dendrites receive synaptic input from other neurons, and transmit the resultant signals to the cell body (soma) where an ‘integrate and fire’ process sparks an action potential along the axon, exciting all the branches and terminals it supplies. At the terminals, the arrival of the action potential causes signaling molecules (neurotransmitters) to be released at *synapses*, coupling sites with other cells. The influence felt by the post-synaptic cell may be excitatory, inhibitory, modulatory or biochemical (leading to structural alteration, changes in gene expression or new patterns of activity), depending on the neurotransmitter and the receptors employed. A thorough overview of these fundamental neuronal properties is provided by Kandel, Schwartz and Jessell’s (2000) authoritative text.

Neurons in the human brain exhibit impressive diversity in structure and function. One of the core distinctions is between excitatory and inhibitory neurons, also referred to as principal neurons and interneurons. Principal neurons release the neurotransmitter glutamate from their synapses when they fire, typically inducing excitatory depolarization of the postsynaptic cell. Interneurons generally release the neurotransmitter GABA (γ -aminobutyric acid) which restores the resting potential on the postsynaptic side, blocking excitation. This “bread and butter” neurotransmission tends to deal with factual information such as the location and type of a stimulus, or exactly which part of the body to move. Another suite of neurotransmitters – noradrenaline, dopamine, serotonin, acetylcholine, histamine and others – qualitatively alter processing in the brain; it should be noted that in the peripheral nervous system, acetylcholine and noradrenaline are also used to directly activate the muscles and glands of the body and organs. These modulatory neurotransmitters shift the circuits of the brain into different modes or patterns – for example, sleeping versus waking, or the vigilant state of panic.

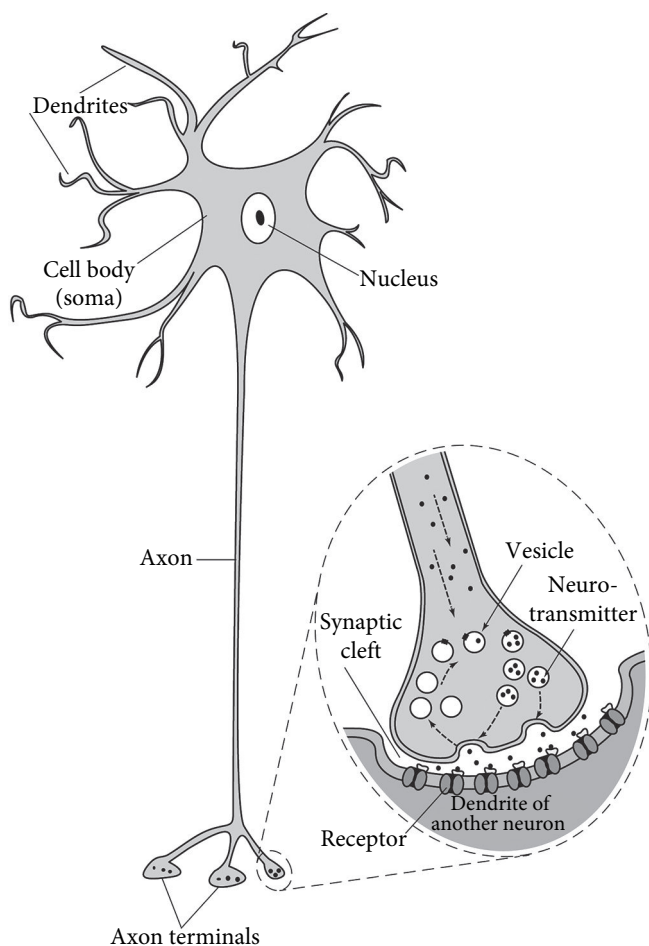


Figure 2. Diagram of an average neuron and one of its synapses. Dendrites – cellular extensions which receive communications from other neurons – converge on the cell body (or soma). The nucleus acts as the regulatory center for gene expression and manufacturing processes in the cell body, from which proteins are transported to the dendrites and axon. The axon extends from the soma to send activity to other neurons or cells. At its far ends, packaged bundles of chemical signals are released into synapses, where they can activate receptors on another cell and influence its activity. Adapted from figures in Watson et al. (2010).

Dopamine may also be seen as the currency of the brain's value system, being closely associated with reward, pleasure and the criteria by which connections are favored. For a more detailed, but still descriptive, overview of neuron function in the brain, see Watson, Kirkcaldie and Paxinos (2010).

Organization of neural circuitry

During postnatal development and plasticity, neurons form and refine their synaptic connections with other neurons to create neural circuits and systems (see Nieuwenhuys, 1994, for an overview). The following chapter of this book (Price, this volume) provides excellent examples of circuits constituting the visual system: although they mediate key features of visual processing, their core function depends on properties shared by neural circuits throughout the brain, such as a balance of excitatory and inhibitory synapses. With individual neurons potentially receiving many thousands of excitatory and inhibitory synapses, the information processing capacity of an interconnected microcircuit is immense: neurons continuously weigh the influence of membrane signals from these inputs to modulate their action potential firing rates, which can range from less than once a second to hundreds of Hertz. These microsecond-precise responses are made against a background of polyrhythmic activity, in which large groups of cells lock together in temporary resonance, favoring inputs which harmonize with their activity and filtering out others. Dynamic processes allow rapid adjustments to reconfigure cortical circuits on the fly, which can prefigure longer term physical plasticity (Calford, 2002). Temporary groupings of cells can extend across large areas or involve just a few hundred neurons, depending on the requirements of the task, and are hypothesized to correlate with attention-related activity (e.g., Jensen, Kaiser, & Lachaux, 2007).

The most intensely studied microcircuits, and those most relevant to many cognitive processes, are those of the cerebral cortex. Within the six layers of human neocortex, numbered from the surface inward, microcircuits act to group activity in columnar arrangements. Incoming information can be received, for example, on layer 4 granular neurons, followed by rapid transduction to pyramidal neurons in other layers of the column, lateral transfer to other columns (local or across the hemispheres) and specific subcortical targets. Within such columns, complex inhibitory neurons sculpt and modulate the activity of the excitatory neurons, producing highly intricate, elaborative networks of information processing. In the cerebral cortex, these microcircuits are often quite functionally similar to each other, so that most groupings of cortical neurons perform similar functions on the inputs they receive. The real power of cortical processing is the exuberant interconnection between circuits, so that inputs are propagated and transformed as they spread across the cortical surface, described by Braitenberg and Schüz (1998) as a “mixing device”. This rich local connectivity between circuits is provided by neurons of the outer layers of the cortex, which are particularly well developed in humans (DeFelipe, 2011). The thoroughness with which the cortex elaborates its activity implies that simply enlarging the size of the cortical sheet

has produced more complex, novel analysis in human brains, by enabling more widely intermixed, spreading patterns.

Structural and functional organization

Although most neurons are fundamentally similar, developmental processes group them into discrete structures whose function depends on the connections they receive, and the targets of their output. This grouping and clustering enables organized bundling of connections, and allows us to describe the nervous system at large scales – i.e., neuroanatomy. The basis of neuroanatomy is the observation and classification of these relationships, whether by naked-eye differences in *gross anatomy* (the appearance and form of neural tissue) or by *histology*, the sectioning and staining of tissue to reveal individual neurons and glia. Neuroanatomy provides a basis for *neurophysiology* (functional descriptions of the nervous system), because anatomy is strongly influenced by the functional connections between neurons. Although neuroanatomy and neurophysiology are closely intertwined and inform each other, dividing the nervous system into discrete functional units may imply a hierarchy of organization which is misleading and inappropriately reductive in some cases. Regardless, the vocabulary of neuroanatomy is essential in discussing the nervous system, and so this section will introduce the basic terminology. For overviews, see Swanson (2011) and Watson et al. (2010).

The functional layout of the human brain and spinal cord follows exactly the same plan as those of other mammals (Swanson, 2000; Figure 3), and although certain aspects are specific to humans, we differ most in the size and relative proportion of our nervous system components. Schematically, the central nervous system is a *neuraxis* (nerve trunk) running along the *dorsal* (back) surface of the body. Sensory *receptors* (via *afferent fibers*) feed axons in to the neuraxis, from which *motor* neurons send *efferent* fibers to activate muscles and glands, triggering movement and the regulation of bodily processes such as blood flow.

For most of its length the neuraxis is called the *spinal cord*. This deceptively simple structure receives sensory information from the skin and organs, and organizes and controls movement on large scales. Many patterned activities such as walking and jumping depend entirely on intricately connected networks in the spinal cord, which sequence limb movements and adjust to challenges such as uneven surfaces and injuries; only quite general input from the brain is required for the spinal cord to achieve sophisticated actions.

At the *rostral* (head) end of the spinal cord, where it joins the *brain*, the neuraxis thickens with extra cells, bundled into dense clusters called *nuclei* (not to

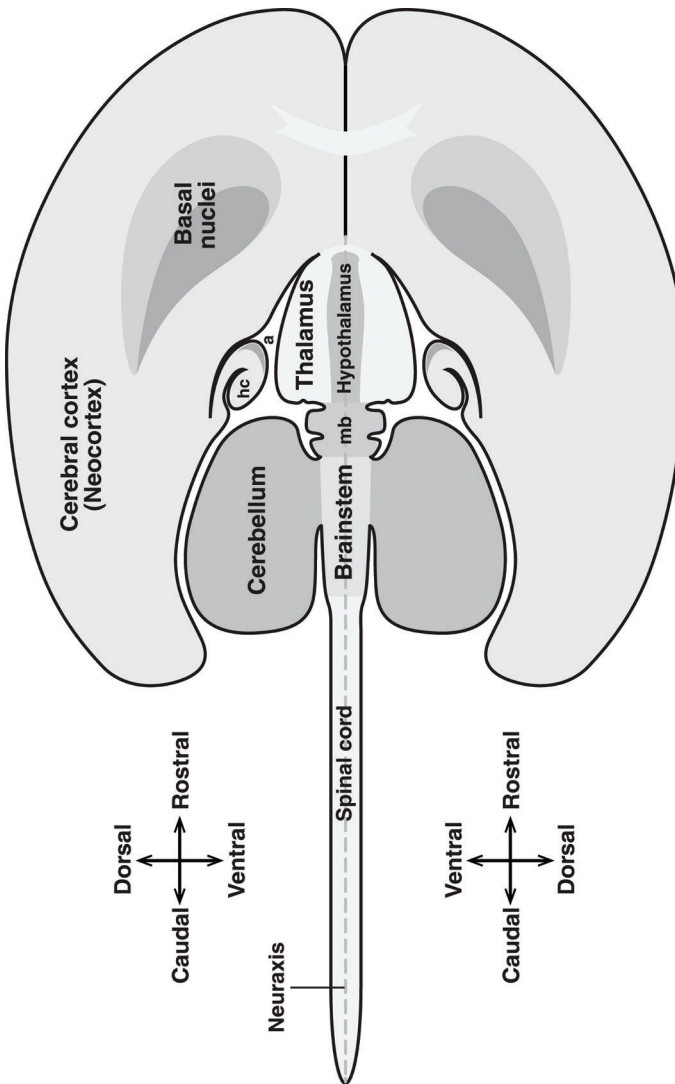


Figure 3. A flat-map of the human nervous system shows simplified relationships between the major structures. The neuraxis runs horizontally along the middle of the diagram, and the structures of the brain are shown as if split down the midline and laid symmetrically either side of it. Abbreviations: mb, midbrain; hc, hippocampus; a, amygdala (shaded at tip of hippocampus). Original diagram, based on a concept by Swanson (2000).

be confused with the nucleus inside each cell). These nuclei handle sensory and motor traffic between the brain and spinal cord, as well as inputs and outputs for the specialized structures of the head, and regulation of vital functions such as breathing and blood pressure; the *vagus nerve*, a large *cranial nerve*, extends from these nuclei down the neck to convey sensation and control signals for most organs of the body cavity. The complex and tightly packed cone of nuclei and fiber bundles at the head of the spinal cord is called the *medulla*, the *caudal* (tail) end of the brainstem. Moving rostrally, the nuclei increase in size and complexity, handling sensation and movement of the face, mouth, tongue and inner ears through cranial nerves. Many of the sensory fibers communicating to the brain send side branches to an apple-sized, tightly packed mass of layered cells on the dorsal surface, the *cerebellum*, whose minuscule granule cells number more than half of the neurons in the body. The best known functions of the cerebellum are for correcting movement errors and adjusting movement to cope with changes in posture, balance and acceleration, an astonishingly complex task which evidently requires a vast, interconnected network of processing neurons.

Rostral to the brainstem is the *midbrain*, from which cranial nerves related to eye movement emerge. These are driven in part by complex integrating centers for visual and auditory stimuli, the *colliculi*, which orient and guide our heads toward novelty and away from threatening stimuli. Rostral to the midbrain, we find the *diencephalon*, with the egg-sized *thalamus* occupying the central core of the forebrain. Its function is tightly coupled with the *neocortex*, supplying it with sensory information and boosting its activity into action. Ventral to the thalamus is the *hypothalamus*, a small but highly significant group of integrating nuclei which monitor the vital signs and requirements of the entire body, and organize physiological and behavioral responses to deal with hunger, thirst, reproductive needs, the cycles of sleep and waking and many other essentials. Arising near the hypothalamus and curving up, over and outward, the bundles of the *fornix* and the *septum* lead to the rolled-up *hippocampus* and the nut-shaped *amygdala*. The amygdala is an organising center for the exciting, novel and dangerous, signaling situations of great behavioral importance. The hippocampus integrates activity from across the forebrain, knitting the threads of experience into a loose cloth of recent events and familiar places, which may have a lasting impact on memory if they are considered important.

Finally, at the rostral extreme of the neuraxis, the cerebral cortex sweeps forward, up and over the forebrain, extending outward and forward at its far end in a shape like ram's horns, but thickened and covered by a folded sheet of neurons and glia. The most recent development in mammalian brain evolution, this neocortex is the most conspicuously overdeveloped structure of the human brain.

Cerebral cortex

The neocortex is the brain structure most closely connected with conscious experience: altered states of consciousness are accompanied by marked changes in cortical activity (e.g., Steriade, 2000), and direct stimulation of cortical activity can repeatably induce conscious experiences (e.g., Penfield & Rasmussen, 1950). The neocortex is also called *isocortex* because of its uniform structure – across the entire sheet, remarkably little variation in its cellular makeup and arrangements can be discerned without special analysis. Despite this uniformity of appearance, a century of observation and testing of cortical damage and stimulation pioneered by Broca, Wernicke, Luria, Penfield, Sperry, Gazzaniga, and others has firmly established that subregions of the cortical sheet have distinct functional specializations, whose arrangement is quite consistent between individuals (Figure 4; for more reading see Gazzaniga, 1989; 2005; Luria, 1966; Penfield & Rasmussen, 1950; Ramachandran & Blakeslee, 1998). These functions may be general, such as the organized representation of a sensory input system, or so specific that damage may cleanly excise single abilities like face recognition from an otherwise normal behavioral repertoire.

Each hemisphere can be divided into *frontal*, *parietal*, *occipital*, *temporal* and *insular* lobes (Figure 4) on the basis of anatomical landmarks, but this is only a coarse indication of the functional arrangement. The frontal lobe organizes behavior, the occipital lobe processes vision, the insula deals with taste and visceral sensation, the temporal lobe audition and memory, and the parietal lobe processes somatosensory inputs and integrates them with other senses. Each of the sensory systems is processed by a hierarchy of cortical regions, beginning with a “primary” map of the sensory structure (e.g., skin or retina), surrounded by successively more integrative representations of the events happening in the primary representation. For example, auditory input is represented in the primary auditory cortex and then analyzed by surrounding cortical regions, one of which (Wernicke’s area) is adept at recognising speech-related patterns. Conversely, the frontal regions represent possible movements and behaviors in a gradient running from general and abstract notions in the prefrontal regions, through increasingly specific plans for sequences and types of movement, coalescing in specific directives for body parts and muscles in the primary motor cortex at the border with the parietal lobe. Uniquely in the nervous system, the abstract representations of the cortex allow interaction between different sensory modalities, so that they influence each other and give rise to more complex perceptual events with multimodal properties. In the parietal cortex, converging analyses of vision, touch, position and hearing produce a multisensory representation of space, a body-centered map which acts as a reference for our mental world, and a framework for describing orientation

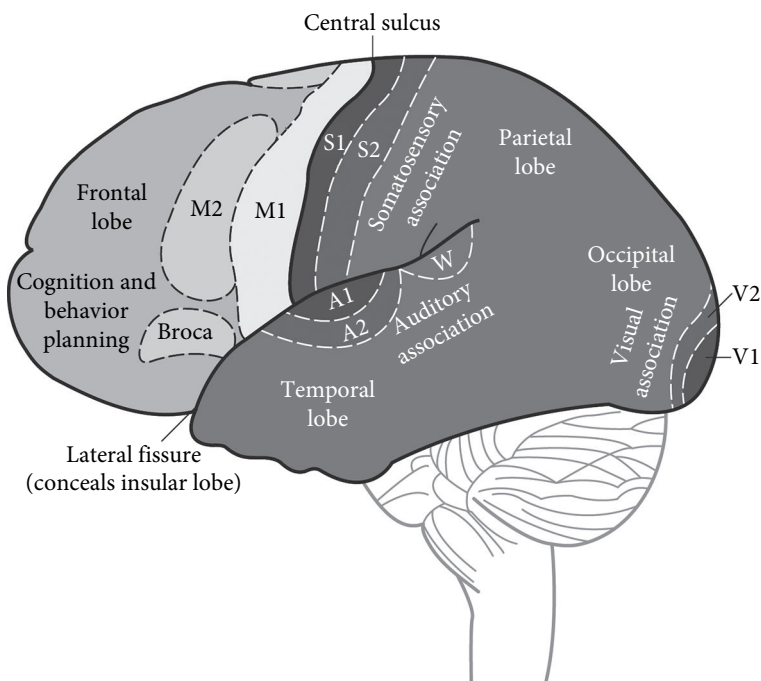


Figure 4. Basic arrangement of the functions of the neocortex. Lighter and darker shading indicate the main functional division between motor and sensory functions. Forward of the central sulcus, the frontal lobe plans, organizes and executes behavior. Behind the central sulcus, the parietal, occipital and temporal lobes analyze somatosensory, visual and auditory inputs, respectively; inside the lateral fissure, the insular lobe integrates sensation and control of the viscera. Primary sensory maps (S1, V1, A1) are surrounded by secondary sensory analysis (S2, V2, A2) and association areas which further interpret sensory events. In motor function, the specific activities specified by primary motor cortex (M1) are sequenced and specified by prefrontal and secondary motor (M2) areas. Broca's area organizes speech and writing for communication; Wernicke's area (W) recognizes spoken communication from auditory analysis. Below the cortex, the cerebellum and brainstem are indicated in lighter outlines. Adapted from figures in Watson et al. (2010).

and movement. Our actions are specified as representations of spatial targets in this posterior parietal area, providing a goal and referent for movement systems tasked with moving to or interacting with that point in space. Thus, the sensory and motor control systems are tied to a common frame of reference, and damage in this region has devastating effects on the mental representation of space. Specific areas including prefrontal cortex and the hippocampus have been implicated in working memory and sustained attention (e.g., Poch & Campo, 2012),

which may be regarded as critical hallmarks of conscious experience. Temporal lobe structures including the hippocampus are associated with formation of long-term declarative memories, but we know that such memory traces may also be stored in a distributed subset of networks that were activated during the original experience (e.g., Penfield & Rasmussen, 1950).

We have mentioned that a great deal of CNS development occurs postnatally; this is particularly true of the cerebral cortex, which at the time of birth is almost a blank slate. Although essentially all cortical neurons are generated *in utero*, their connections are rudimentary, and the cortex depends heavily on experience to determine structural arrangements. Sensory representations are shaped by incoming activity, and reflect the qualities of the inputs received – for example, an optical defect in one eye will result in the cortex ignoring the low-quality input from that retina, even if the retina is entirely normal and faithfully reports a blurred image (Knudsen, 2004). Once experience has sculpted these representations into coherent and sensible patterns, the process of extracting the meaning of sensory inputs can begin. The term “meaning” is used lightly here, but the rules which produce “meaningful” patterns of connectivity literally determine the structure of our conscious minds, by building the functions performed by analytical parts of the cortex. Whereas the primary representations of sensory receptors and motor actuators are easily described by physiology, they are not available to consciousness – except perhaps in altered forms of consciousness such as those exhibited by “savants”, as suggested by Snyder (2009). Instead, the conscious mind traffics in downstream, more abstract representations of these primary stimuli and outputs – the same representations which are enabled by developmental processes favoring “meaningful” connectivity.

The unequivocal, and generally consistent, relationship between focal cortical damage (or stimulation) and qualitative changes in mental function strongly implies that cortical activity is intimately involved in the specific qualities of our conscious experience (e.g., Ramachandran & Blakeslee, 1998). Thus, the plasticity criteria which shape those cortical functions appear to be directly responsible for the nature of our mental experience. This raises a subtle problem: how can processes which shape plasticity at individual connections, ensure that the resultant network produces usefully integrated functions? The clear implication is that the usefulness of a cortical representation must exert an influence on the smaller-scale guidance of plasticity between individual cells, or at individual synapses – otherwise no coherent representation would emerge. It may be that a kind of homeostatic process acts on short-term synaptic plasticity, which would naturally decay when “overwritten” by subsequent activity, unless reinforced by contributing to larger scales of organization. In this way, billions of individual short-term

plasticity events may accumulate into patterns of connection which persist for years or even decades.

The ability to selectively preserve changes which contribute to organized activity would seem to be a fundamental requirement for building complex but useful nervous systems, in which case it would not be unique to humans. It seems likely that global plasticity criteria, such as coherence and minimization of unnecessary activity, would already be well established rules across evolutionary history, particularly in a metabolically expensive tissue such as the brain (e.g., Fedrigo et al., 2011). It is clear, however, that even in individuals, multiple criterion sets determine cortical organization: for example, the left and right hemispheres use equivalent inputs to generate qualitatively different representations of the world, as observed in patients with separated hemispheres (Gazzaniga, 2005).

If we use similar plasticity rules to other mammals, our mental representations are a product of our particular sensory systems exerting a patterning effect on a cortical sheet which self-optimizes for coherent representation. At first glance this suggests a passive role for cortical development, which depends on interaction with the environment and not necessarily on consciousness. However in a conscious animal, “coherence” or “meaning” might be judged by the sense made of current inputs, compared to that of previous experience – yielding an optimal, general-purpose analysis which is likely to be useful in commonly encountered situations. The emotion- and reward-dependent process that selects which experiences to add to the stored knowledge of the cortex would also be critical to this evaluation. Such an integration with previous analysis is another instance in which the continuity of conscious experience might be advantageous in building a better brain, and may be why consciousness is so closely tied with cortical activity: the self-determined intrinsic structuring we describe seems like a plausible way that the essentially homogeneous cortex could be customized for such a diverse array of purposes. Whisker processing, echolocation, pack hunting and gossip are all neocortical functions in different mammal species.

Therefore, studying the guiding principles by which a cortical representation is judged “useful”, and the way that evaluation might be used to shape the function of cortical representations, is probably the most direct route to understanding how cortical activity underpins a conscious experience.

Molecular constituents

As we have mentioned, conception generates a unique genome to guide development and cellular functions. Beyond the genome, every cell houses a mind-boggling array of molecules – not only DNA, but hundreds of thousands of configurations of RNAs, proteins, sugars, lipids and other molecules, many of which interact in obvious or subtle ways. Faced with the teeming complexity of cellular biochemistry, the mind recoils and seeks a simpler, more ordered level of description from which to understand brain function. Unfortunately, none really exists.

Perhaps the most significant difference between human-designed engineering and biological systems is that the latter lack a fundamental hierarchy. For example, in electronics, the quantum properties of semiconductors are significant at the fabrication level of design, but once they are part of a transistor, their “flavor” disappears: it is possible to build exactly the same microprocessor using different semiconductor types operating at different voltages, or to power computers of equivalent function using batteries or mains electricity. Humans design engineered systems at whichever level of description is suitable, and ignore larger and smaller scales: one can optimize the arithmetic processing of a CPU (central processing unit) without considering transistor properties, and in such a way that it will not affect higher level software. By contrast, natural selection acts on alterations at *any* level, from a trivial genetic substitution to high-level functional reorganization. Anything which affects survival and reproduction is significant.

The result is a brain whose qualities depend on every level of influence: genetic makeup, the regulation of gene expression, the routing and trafficking of gene transcripts, protein translation, the interaction of proteins, cellular transport, membrane properties, cellular signaling, contact between cells, neurotransmitter recycling – the list is endless. A minor change in a gene sequence which slightly perturbs the electrical properties of a membrane channel may cause epilepsy, abolishing consciousness in system-wide episodes of disorder (Bouthour et al., 2012). There is no privileged level of description for the brain, to which its other properties are secondary. Instead, it requires a holistic understanding which is quite alien to reductionist, hierarchical paradigms of engineering design.

Also unlike designed systems, the higher order complexity of the nervous system has to be achieved using changes to the sequence and regulation of genes – as if a new computer had to be derived by substituting different atoms in the semiconductors from which its components were made. The ability to redesign by genetic variation relies on a powerful, hidden level of order in biology: stable communities of genes which interact and form self-regulating systems with a high

probability of producing a viable organism, even when genes are shuffled or occasionally mutated. Genes are selected and preserved both for their own merits and for their contribution to the stability of the community, providing a strongly self-regulating environment which is tolerant of a range of eccentricities in gene function. This buffered environment allows genetic variations to accumulate without significantly compromising function, until by chance they may combine in a new individual to interact in some unexpected way.

A substantial proportion of our genes are expressed in the nervous system, suggesting that neurons and glia are sustained by an even greater molecular complexity than other cell types. Neurons in particular have unique molecular requirements. During development, neuronal precursors must migrate (often over large distances), differentiate and form rich synaptic connectivity with other neuronal populations. Mature neurons must maintain large numbers of synapses which themselves exhibit exquisite experience-dependent molecular heterogeneity. Thus, individual neuronal populations can be identified according to expression of specific ion channels, neurotransmitter receptor subtypes, synaptic signaling components, etc. (e.g., Petilla Interneuron Nomenclature Group, 1998). Individual synapses are known to contain hundreds of distinct proteins, as well as RNA transcripts and other molecules. The tremendous complexity at the level of proteomes (the total protein complement of an individual cell or tissue), is further complicated when the diverse array of functional non-coding RNAs are taken into account. And finally, the genome of each neuron is not static: it can be altered via epigenetic modifications, such as long-term molecular changes associated with experience-dependent gene expression, synaptic plasticity and learning and memory.

Conclusions

Although these short treatments offer some of the flavor of bioscience perspectives on the brain, we make no claims of privileged understanding. As we have noted throughout, deeper knowledge of brain constituents brings greater complexity rather than simplification, which makes neuroscience feel like a losing battle at times. Future investigators will no doubt conclude that our understanding of the human brain in the early 21st century was primitive indeed, because we are now only at the beginning of functionally mapping the brain's constituents at molecular, cellular, network and systems levels.

Despite such ignorance, the immense challenges ahead make the field an exhilarating one in which to be involved. A dazzling array of novel technical approaches, which continue to be refined and expanded, have exposed neural correlates for a

wide variety of brain functions – although conscious experience remains the most tantalising and elusive. From the other end of the scale, increasing knowledge of brain development and evolution offer key perspectives on the fundamental structure of mammal brains, the criteria by which they organize themselves, and perhaps eventually the mechanistic basis of higher order functions.

Although the traditional concepts of neuroscience may eventually prove inadequate to the task of describing the constitution of consciousness, for now they are the best framework that science has for such discussions. We hope that this ‘Cook’s tour’ of the human brain has provided a glimpse of the enormity of the task at hand. In order to fully explain consciousness, a future framework will need to comprehensively integrate theoretical and experimental data at multiple levels, including molecules, cells, circuits and systems. This represents one of the great scientific challenges of the 21st century.

References

- Allman, J. M. (2000). *Evolving brains*. New York: W. H. Freeman.
- Allman, J. M., Tetreault, N. A., Hakeem, A. Y., Manaye, K. F., Semendeferi, K., Erwin, J. M. et al. (2010). The von Economo neurons in frontoinsular and anterior cingulate cortex in great apes and humans. *Brain Structure and Function*, 214(5–6), 495–517.
- Azevedo, F. A. C., Carvalho, L. R. B., Grinberg, L. T., Farfel, J. M., Ferretti, R. E. L., Leite, R. E. P. et al. (2009). Equal numbers of neuronal and nonneuronal cells make the human brain an isometrically scaled-up primate brain. *Journal of Comparative Neurology*, 513(5), 532–541.
- Barrett, L., & Henzi, P. (2005). The social nature of primate cognition. *Proceedings of the Royal Society of London Series B: Biological Sciences*, 272(1575), 1865–1875.
- Bouthour, W., Leroy, F., Emmanuelli, C., Carnaud, M., Dahan, M., Poncer, J. C. et al. (2012). A human mutation in *gabrg2* associated with generalized epilepsy alters the membrane dynamics of GABA_A receptors. *Cerebral Cortex*, 22(7), 1542–1553.
- Braitenberg, V., & Schüz, A. (1998). *Cortex: Statistics and geometry of neuronal connectivity* (2nd ed.). Berlin: Springer.
- Calford, M. B. (2002). Dynamic representational plasticity in sensory cortex. *Neuroscience*, 111(4), 709–738.
- Clark, D. A., Mitra, P. P., & Wang, S. S. (2001). Scalable architecture in mammalian brains. *Nature*, 411(6834), 189–193.
- DeFelipe, J. (2011). The evolution of the brain, the human nature of cortical circuits, and intellectual creativity. *Frontiers in Neuroanatomy*, 5, 29. doi: 10.3389/fnana.2011.00029
- DeFelipe, J., & Jones, E. G. (1988). *Cajal on the cerebral cortex*. New York: Oxford University Press.
- Dent, E. W., Gupton, S. L., & Gertler, F. B. (2011). The growth cone cytoskeleton in axon outgrowth and guidance. *Cold Spring Harbor Perspectives in Biology*, 3(3). doi:10.1101/cshperspect.a001800
- Fedrigo, O., Pfefferle, A. D., Babbitt, C. C., Haygood, R., Wall, C. E., & Wray, G. A. (2011). A potential role for glucose transporters in the evolution of human brain size. *Brain, Behavior and Evolution*, 78(4), 315–326.

- Gazzaniga, M. S. (1989). Organization of the human brain. *Science*, 245(4921), 947–952.
- Gazzaniga, M. S. (2005). Forty-five years of split-brain research and still going strong. *Nature Reviews Neuroscience*, 6(8), 653–659.
- Golgi, C. (1901). The neuron doctrine: Theory and facts. *Nobel lectures: Physiology or medicine*, 1921, 189–217.
- Hannan, A. J. (2007). Brain phylogeny, ontogeny and dysfunction: Integrating evolutionary, developmental and clinical perspectives in cognitive neuroscience. *Acta Neuropsychiatrica*, 19(3), 149–158.
- Herculano-Houzel, S. (2009). The human brain in numbers: A linearly scaled-up primate brain. *Frontiers in Human Neuroscience*, 3, 31. doi: 10.3389/neuro.09.031.2009
- Jensen, O., Kaiser, J., & Lachaux, J.-P. (2007). Human gamma-frequency oscillations associated with attention and memory. *Trends in Neurosciences*, 30(7), 317–324.
- Kandel, E. R., Schwartz, J. H., & Jessell, T. M. (2000). *Principles of neural science* (4th ed.). New York: McGraw-Hill Medical.
- Kettenmann, H., & Verkhratsky, A. (2008). Neuroglia: The 150 years after. *Trends in Neurosciences*, 31(12), 653–659.
- Kirkcaldie, M. T. K., & Kitchener, P. D. (2007). When brains expand: Mind and the evolution of cortex. *Acta Neuropsychiatrica*, 19(3), 139–148.
- Knudsen, E. I. (2004). Sensitive periods in the development of the brain and behavior. *Journal of Cognitive Neuroscience*, 16(8), 1412–1425.
- Kolodkin, A. L., & Tessier-Lavigne, M. (2011). Mechanisms and molecules of neuronal wiring: A primer. *Cold Spring Harbor Perspectives in Biology*, 3(6). doi: 10.1101/cshperspect.a001727
- Krubitzer, L., & Hunt, D. L. (2009). Captured in the net of space and time: Understanding cortical field evolution. In J. H. Kaas (Ed.), *Evolutionary neuroscience* (pp. 545–568). San Diego: Academic Press.
- Luria, A. R. (1966). *Higher cortical functions in man*. London: Tavistock.
- Miller, S. M. (2007). On the correlation/constitution distinction problem (and other hard problems) in the scientific study of consciousness. *Acta Neuropsychiatrica*, 19(3), 159–176.
- Nieuwenhuys, R. (1994). The neocortex. An overview of its evolutionary development, structural organization and synaptology. *Anatomy and Embryology*, 190(4), 307–337.
- Penfield, W., & Rasmussen, T. (1950). *The cerebral cortex of man: A clinical study of localization*. Boston, MA: Little, Brown.
- Petilla Interneuron Nomenclature Group, Ascoli, G. A., Alonso-Nanclares, L., Anderson, S. A., Barrionuevo, G., Benavides-Piccionne, R., Burkhalter, A. et al. (2008). Petilla terminology: Nomenclature of features of GABAergic interneurons of the cerebral cortex. *Nature Reviews Neuroscience*, 9(7), 557–568.
- Poch, C., & Campo, P. (2012). Neocortical-hippocampal dynamics of working memory in healthy and diseased brain states based on functional connectivity. *Frontiers in Human Neuroscience*, 6, 36. doi: 10.3389/fnhum.2012.00036
- Ramachandran, V. S., & Blakeslee, S. (1998). *Phantoms in the brain: Probing the mysteries of the human mind*. New York: William Morrow and Company, Inc.
- Ramón y Cajal, S. (1901). The structure and connexions of neurons. *Nobel lectures: Physiology or medicine*, 1921, 220–253.
- Sanes, D. H., Reh, T. A., & Harris, W. A. (2012). *Development of the nervous system* (3rd ed.). San Diego: Academic Press.

- Shultz, S., & Dunbar, R. (2010). Encephalization is not a universal macroevolutionary phenomenon in mammals but is associated with sociality. *Proceedings of the National Academy of Sciences USA*, 107(50), 21582–21586.
- Snyder, A. (2009). Explaining and inducing savant skills: Privileged access to lower level, less-processed information. *Philosophical Transactions of the Royal Society of London B: Biological Sciences*, 364(1522), 1399–1405.
- Steriade, M. (2000). Corticothalamic resonance, states of vigilance and mentation. *Neuroscience*, 101(2), 243–276.
- Swanson, L. W. (2000). What is the brain? *Trends in Neurosciences*, 23(11), 519–527.
- Swanson, L. W. (2011). *Brain architecture: Understanding the basic plan* (2nd ed.). New York: Oxford University Press.
- Watson, C. R., Kirkcaldie, M. T. K., & Paxinos, G. (2010). *The brain: An introduction to functional neuroanatomy*. San Diego: Academic Press.

Overview of visual system structure and function

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The fundamental role of the visual system is to analyze properties such as form, color and motion in the environment, facilitating the generation of behaviors conducive to survival. A (happy) outcome of these computations is that humans are endowed with conscious visual perception. Despite the complexity of processing in the visual system, we experience a single, unified and continuous percept. This review describes the general anatomy and physiology of the primate visual system, emphasizing four organizational principles and processing strategies that ultimately inform perception and behavior: information processing is functionally segregated; information is encoded in a multiplexed manner; information is hierarchically processed, dependent on feedback and feedforward connectivity; vision is an active sense, with perception and eye movements tightly integrated.

1. Introduction

A major aim of sensory neuroscience is to explain the neuronal basis of conscious experience. That is, to describe how our subjective experiences and perception of the world can arise from the circuitry, activity and interactions of the millions of neurons in the dozens of brain regions. Elucidating these neuronal mechanisms is a massive undertaking, and requires a multifarious approach that accounts for the anatomy, physiological responsivity, and ultimately the function of neural circuits. To begin with, a “map” of the neural circuits is required. This is an anatomical description of the local and global pattern of connections both within and between brain regions, the specific connections between different neuron types, and the direction of information flow. Next, a characterization of response properties is required. This accounts for the specific stimuli which activate a single neuron, and the general stimulus attributes (e.g., color, motion, form) that are represented in the activity of a brain region. A common observation is that structure and function

within brain regions are intimately related; anatomical connections between neurons are not simply random, but can account for much of the function that the neurons subserve. Finally, a quantitative description of the “algorithms” executed by the brain is required. This explains how the activity of populations of neurons within specific circuits completely underlies both perception and behavior.

Humans, like all primates, are highly visual animals and at least 20% of the brain is partially or exclusively devoted to some form of visual processing. We focus here exclusively on the primate visual system, with many of the results drawn from studies in macaque monkeys, which have a similar low level visual system to humans. These visual areas are well described, and the patterns of anatomical connectivity between them are mostly well characterized. Further, we know a lot about the nuts and bolts of visual processing – how features in the visual world are extracted and represented in the electrical activity of neurons in the eye, thalamus and cortex. This makes vision an excellent sense to study in order to more generally appreciate how perception arises from neural activity in the brain. The perceptual and behavioral tasks that the visual system supports are many and varied: based on features such as color, shape, depth and position, it enables recognition, categorization and identification of complex objects such as faces and animals. Based on position and motion information, it enables object localization and tracking, navigation, trajectory estimation and interaction with moving objects. This diversity of stimulus properties and behaviors all arise from the initial transformation of light signals into a spatial and temporal pattern of electrical signals by the retina, and hints at the anatomical segregation that occurs later in the visual processing hierarchy to support the diverse range of visual functions.

Here, I describe the general anatomy and physiology of the primate visual system, with an emphasis on four organizational principles and processing strategies that ultimately inform perception and behavior. First, visual processing is functionally segregated, with different stimulus attributes (e.g., orientation, color, speed of motion) processed in parallel. This parallel processing occurs at multiple spatial scales, from distinct layers, columns and compartments within defined brain regions, through to simultaneous processing across whole brain regions. Second, neural responses are affected by multiple stimulus attributes and thus a neuron’s firing rate simultaneously encodes information about these stimulus attributes in a multiplexed manner. Information about a specific attribute can therefore only be decoded from the distribution of activity across a neuronal population. Third, visual processing is not a sequential set of computations, but depends on a network of feed-forward, lateral and feed-back connections that form a functional processing hierarchy. Finally, vision is an active sense, and perception is both influenced by, and depends on, eye movements, expectation and task demands.

Correspondingly, this review is divided into four sections, which follow the way the visual world is sequentially transformed and represented by the visual system. In the first, we explore the close link between the anatomical and functional segregation evident in the parallel processing from retina to cortex. Next, we address how primary visual cortex (V1) transforms the retinal signal and the range of stimulus features that are simultaneously represented in cortical neuronal activity. In the third section, the network of dozens of extra-striate visual areas is introduced, focusing on how they form a functional processing hierarchy that supports both perception and action. Finally, we describe how eye movements, expectations and task demands influence and interact with visual perception, highlighting that vision is an active sense.

2. From retina to cortex

2.1 Parallel processing in the retina

Vision begins in the retina, where rod and cone photoreceptors transduce the spatial and temporal pattern of light from the environment into a spatial and temporal pattern of electrical activity. Although the world is perceived as three-dimensional, the photoreceptors in each eye are arranged as a two-dimensional surface. This is a clear demonstration that many perceptually obvious features are not actually present in the retinal representation of the world and must be generated, or extracted from the retinal signal. The ease of access to the retina, its elegant structure and its clear functional role have made it the focus of study since the earliest anatomists (Ramón y Cajal, 1893). Thus, the circuitry, morphology and function associated with most cell types within the retina are well characterized; there is a unidirectional flow of information from photoreceptors via bipolar cells to the retinal ganglion cells (RGC) and the spatial and temporal receptive field of each bipolar cell and RGC is shaped by lateral connections involving horizontal cells and amacrine cells.

Importantly, the output of the retina is not a single spatiotemporal transformation of the visual scene. Rather, there are at least 12 parallel processing pathways within the primate retina, each culminating in a unique class of RGC, which convey information about specific attributes of the scene (Dacey, 2000, 2004; Field & Chichilnisky, 2007; Masland, 2001). These RGC differ in their spatial size, temporal fidelity, luminance and wavelength sensitivity and are described in more detail in the next section. Although there are multiple types of ganglion cells, their associated pathways are neither entirely redundant, nor entirely independent. For example, a single photoreceptor may project to both On- and Off- bipolar

cells, which are therefore depolarized or hyperpolarized by luminance increments. These parallel circuits are retained via On-and Off- RGC, which respond preferentially to luminance increments and luminance decrements, respectively. The common photoreceptor input means that even though the ganglion cells are sensitive to different features in a scene, their responses are correlated (Field et al., 2010; Greschner et al., 2011).

The concept of a “receptive field” was initially used to describe the spatial region in which the presence of a stimulus altered the activity of a neuron (Hartline, 1938; Kuffler, 1953). A more complete receptive field description accounts for the spatial and temporal properties of stimuli that modulate a neuron’s activity, allowing the response to a stimulus of arbitrary position, size, timing and color to be predicted. Thus the concept of a receptive field is relevant and applied throughout the visual system. In the retina, receptive fields can be predicted from a neuron’s anatomical structure – its inputs and dendritic field. A ganglion cell has a receptive field center associated with direct inputs from bipolar cells and a receptive field surround defined by lateral inhibition from horizontal cells and amacrine cells. Thus, an RGC receptive field is typically modeled by two concentric patches, which are antagonistic in how they activate the ganglion cell. In addition to spatial structure, RGC responses depend on the wavelength of the incident light. Humans are typically trichromats, having three cone classes maximally sensitive to short, medium and long wavelengths, with peaks near 415, 530 and 560 nm in the range of blue, green and red, respectively (Dartnall, Bowmaker, & Mollon, 1983). Thus, depending on the relative strength of inputs from each cone class to receptive field center and surround, RGC are able to compute local differences in light intensity or color (Figure 1b).

Ganglion cells in the fovea have small dendritic arbors and their receptive field center may comprise inputs from just a single cone via a single bipolar cell. Conversely, in the peripheral retina, ganglion cells have large receptive fields, receiving convergent inputs from thousands of adjacent photoreceptors (Dacey & Petersen, 1992). Anatomically, this means that moving from the central fovea to the periphery there is an increase in the size of a ganglion cell’s dendritic arbor and decrease in the density of cell bodies (Figure 1a). Functionally, increasing eccentricity is associated with an increase in receptive field size and a decrease in visual acuity. The high density of RGC in the central fovea and the low cone-RGC convergence ratio support the high acuity vision that is used for object recognition, reading and tasks that require sensitivity to high spatial frequencies.

The majority of RGC types and approximately 90% of the total population of ~1.5 million RGC project to the lateral geniculate nucleus (LGN) in the thalamus (Perry, Oehler, & Cowey, 1984). This projection is presumably responsible for most conscious visual perception, but the precise role of each RGC type remains

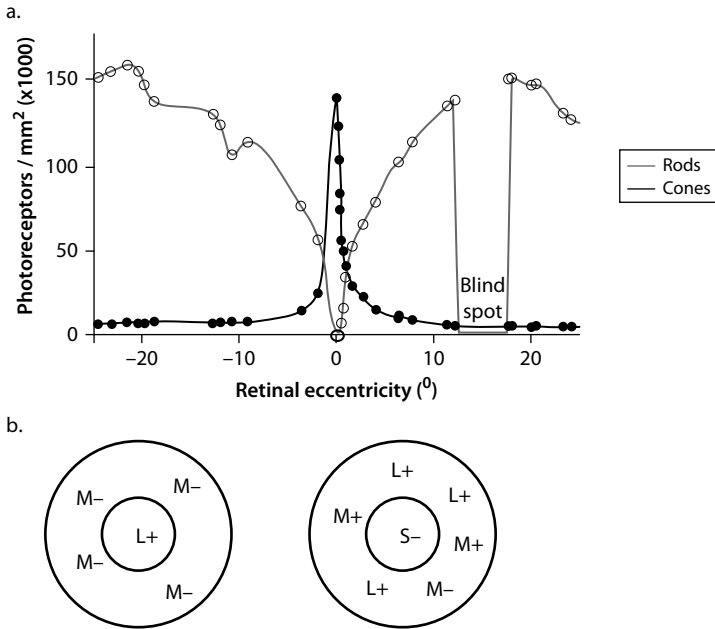


Figure 1. (a) Density of rod and cone photoreceptors as a function of retinal eccentricity in the human retina (data from Osterberg, 1935). In the nasal portion of the retina, just above the horizontal meridian, the axons of the RGC exit the retina and there are no photoreceptors, producing the $\sim 5^\circ$ blind spot centered at $\sim 15^\circ$ eccentricity. (b) Center-surround spatial receptive fields of two typical RGC, indicating whether inputs are excitatory (+) or inhibitory (–) and arise from Short, Medium or Long wavelength sensitive cones. The cell on the left is excited by red light in its receptive field center and inhibited by green light in its surround. The cell on the right is inhibited by blue light in its center and excited by yellow light (red + green) in its center. Such cells are absent in the central fovea because there are no blue cones there, and rare elsewhere because of the paucity of blue-off pathways.

unclear. Six other targets of retinal projections have been identified: the accessory optic system, the pretectal area, the superior colliculus (SC), the medial region of the inferior pulvinar, the pregeniculate nucleus and the suprachiasmatic nucleus. Broadly speaking, these regions play roles in controlling ocular reflexes, eye movements and regulating circadian rhythms. While the SC and pulvinar are known to be important for oculomotor control and visual perception, they will not be discussed further (Chalupa, 1977). Recently there has been great interest in the approximately 2% of RGC that contain melanopsin and are intrinsically photosensitive even in the absence of rod or cone photoreceptor input (Dacey et al., 2005).

These neurons are likely to primarily contribute to regulating circadian rhythms, and their sluggish responses suggest that they may not be important for image-forming or conscious vision. While recent reports suggest these intrinsically photosensitive RGC may support image forming vision in humans lacking rods and cones (Zaidi et al., 2007), the primary retinal pathway involved in conscious visual perception is the projection to the thalamic LGN.

2.2 Transforming the retinal signal

Of the dozen or so RGC types, three in particular are well characterized and display clear anatomical segregation in their pathway from retina, through LGN, to the primary visual cortex. These are the midget, parasol and bistratified ganglion cells, which project in parallel to the parvocellular, magnocellular and koniocellular layers in the LGN. This segregation is preserved in the earliest stage of cortical processing, as the parvo- and magnocellular layers of the LGN target distinct sublaminae in layer 4 of V1. Further, the fingerprints of these 3 pathways are evident throughout the visual system. Before describing the properties of each pathway, there are a few features common to all LGN receptive fields, which inherit their primary response properties from the retina. First, LGN receptive fields are exclusively monocular, with inputs from the two eyes systematically alternating across the 6 layers of the LGN (Figure 2). Second, they do not show strong orientation selectivity, but may show orientation biases due to asymmetric spatial pooling of retinal inputs. Third, as in the retina, the majority of neurons show center-surround opponency. For On-center cells, this means that illumination of the receptive field center leads to an increased firing rate and illumination of the surround reduces the firing rate. For Off-center cells, this pattern is reversed. Therefore, there is antagonism between stimuli that activate the center and surround, such that diffuse, uniform illumination does not significantly activate most cells. This highlights the importance of identifying spatial discontinuities in illumination, which are associated with edges and corners.

The LGN is also more than just a relay station for information transfer between retina and cortex. Thalamic afferents can be characterized either as drivers (the minority) or modulators based on whether they provide feed-forward sensory inputs or modify these inputs (Sherman & Guillery, 2006). Critically, less than 10% of inputs to the LGN are of retinal origin, clearly demonstrating the importance of cortical feedback and local inhibitory connectivity in determining the signals that ultimately project from the LGN to the cortex (Van Horn, Erisir, & Sherman, 2000). The precise role of this extensive feedback remains unclear, but it suggests that signals along the feedforward retina-thalamo-cortical pathway can easily be

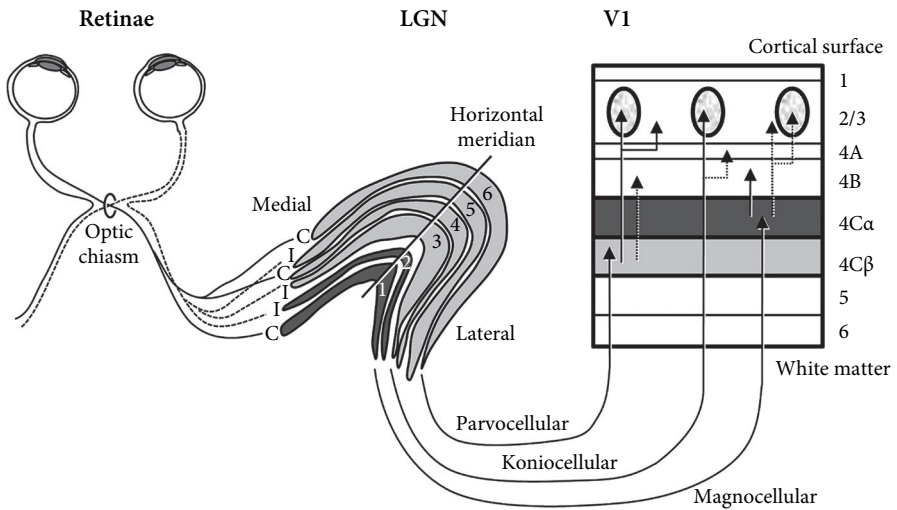


Figure 2. Parallel retino-geniculo-cortical pathways. Information from each eye undergoes a partial decussation such that the left visual field is processed by the right LGN (as shown). The LGN is a 6 layered structure, with each layer receiving stereotyped innervation from specific RGC classes in either the ipsilateral or contralateral eye. Parasol RGC project to the magnocellular Layers 1 and 2 of the LGN, midget RGC project to the parvocellular layers 3–6 and bistratified RGC project to the intermediate koniocellular layers. Inputs from the two eyes alternate such that layers 1, 4 and 6 receive information from the contralateral eye, and layers 2, 3 and 5 receive information from the ipsilateral eye. The M, P and K layers of the LGN primarily project to V1 layers 4Cα, 4Cβ and the layer 2/3 blobs, respectively. Thalamo-cortical connections that are weaker, or that have been identified more recently are shown as dotted lines.

modified by cortical feedback (Sillito, Cudeiro, & Jones, 2006), with the feedback likely to play a role in amplifying and tightening the tuning of LGN responses (Alitto & Usrey, 2003).

Midget and parasol RGC have relatively small dendritic arbors and high cell densities compared to other cell types, and their over-representation accounts for why they are the most well-studied retinal cell types. Midget cells selectively project to the dorsal, parvocellular layers (3–6) of the LGN and constitute approximately 70% of the total retino-thalamic projection (Dacey, 2004; Dacey & Petersen, 1992; Masland, 2001). The parvocellular (P) cells of the LGN relay information to layers 4Cβ and 6 of V1. As their name suggests, they have small cell bodies and small dendritic arbors, accounting for their small spatial receptive fields. In the central fovea, they receive inputs from just a single cone, thus

preserving the maximum possible visual acuity given the photoreceptor spacing. This conveys high spatial frequency sensitivity, or the ability to resolve fine spatial features. However, midget cells have sluggish responses and slow conduction velocities, accounting for their low temporal frequency sensitivity. Importantly, the majority of midget cells carry color-opponent signals, with their receptive field centers receiving excitatory inputs from just 1 or 2 cone types.

Parasol cells constitute approximately 10% of the retinal projection to the LGN. Their thalamic and cortical projections, anatomical features and visual sensitivity are complementary to those of midget cells, suggesting that they subserve different functional roles. Parasol cells predominantly project to the magnocellular layers (1–2) of the LGN, and information is subsequently relayed by the M cells to layers 4C α and 6 of V1. Compared with midget cells, parasol cells have larger cell bodies and more extensive dendritic arbors, which manifest functionally as larger spatial receptive fields. They have higher contrast sensitivity, lower spatial frequency sensitivity and faster conduction velocities subserving high temporal frequency sensitivity. This is the first clue that they may contribute to motion processing. They are “color-blind” with broadband spectral sensitivity because they receive inputs from all cone types.

A third common RGC type are the bistratified cells, which account for approximately 8% of the projection to the LGN. The targets of these cells are less clear than for the midget and parasol cells, however, they project predominantly to the intercalated koniocellular layers between the more clearly defined magno- and parvocellular layers. These K cells in the LGN may be distinguished neurochemically; in adult monkeys, three proteins are expressed exclusively in K cells, but not in M or P cells (Fukuda, Saito, Yamamoto, & Tanaka, 1994; Hendry & Reid, 2000; Hendry & Yoshioka, 1994). The distinguishing physiological feature of bistratified ganglion cells is their blue-yellow color opponent signal, and their eventual cortical target is the cytochrome oxidase rich “blobs” in the supragranular layers 2/3 of V1 (discussed below), highlighting their important role in color vision.

The segregation of sensory information in the visual system is clear from the earliest levels. There are parallel circuits evident within the retina, which project to distinct layers within the LGN. Moreover, this segregation is preserved in the thalamic projections to V1 and to a lesser degree, areas beyond V1. Within the retina, the different ganglion cell types have complementary anatomy (e.g., the spread of their dendritic field, cell body size and density), contributing to their different functional sensitivity (e.g., their spatial receptive field, spatial frequency tuning and spectral sensitivity). In the next section, we explore how these parallel pathways are both preserved and intermixed within V1, and how this affects visual information flow throughout cortex.

3. Parallel and multiplexed processing within early visual cortex

The sensory representation of the visual world that initially reaches the cortex must be transformed into a form that subserves visual perception or visually guided motor behaviors. Visual processing in the cortex involves a distributed hierarchy of specialized areas, which are both interdependent and parallel. In the macaque monkey, at least 30 distinct visual processing regions have been identified, with around 50% of the cerebral cortex playing some role in visual processing. In humans, similar processing regions have been described, with approximately 20–30% of the cortex playing a role in aspects of vision (Felleman & Van Essen, 1991; Tootell, Dale, Sereno, & Malach, 1996; Tootell, Tsao, & Vanduffel, 2003). Distinct visual areas were first defined anatomically, based on their cytoarchitecture (Brodmann, 1909/2006), myelination (Flechsig, 1901) or anatomical connectivity (Felleman & Van Essen, 1991). Functional distinctions between areas can also be made based on retinotopic organization within an area or functional receptive field properties. Thus there are 4 independent criteria that can be used to distinguish cortical areas: cyto- and myeloarchitectonic organization, connectivity pattern, retinotopic organization, and functional properties. Unfortunately, few regions have been precisely defined with both anatomical and functional approaches and most studies can only address one or a few of the four criteria. Thus there remains controversy over the anatomical boundaries and functional role of many of the more specialized brain areas in the processing hierarchy. These problems may be partly addressed by the technique of functional magnetic resonance imaging (fMRI) studies in macaques and especially fMRI-guided electrophysiology (Brewer, Press, Logothetis, & Wandell, 2002; Goense & Logothetis, 2008; Tsao, Freiwald, Tootell, & Livingstone, 2006).

3.1 Functional clustering in V1

Across the approximately 1350 mm² surface area of V1 in the macaque, there are systematic relationships between the receptive field properties of adjacent neurons, reflecting a high degree of functional clustering. Neurons are organized retinotopically, such that adjacent neurons have receptive fields that encode adjacent portions of the visual field, although there is local scatter in the precise position and size of each receptive field (Sincich, Adams, & Horton, 2003). Importantly, the surface area of cortex does not uniformly represent the visual field as there is an over-representation of the fovea and receptive field sizes scale with eccentricity such that a neuron's RF width is less than one-tenth the eccentricity of the RF center (Daniel & Whitteridge, 1961; Orban, Kennedy, & Bullier, 1986).

The earliest studies in V1 showed that the majority of neurons have elongated receptive fields, and are thus selective for both the orientation and position of lines and bars (Hubel & Wiesel, 1962). Neurons in the same vertical column of cells prefer very similar orientations, but systematic changes are observed in neurons' preferred orientations as electrodes are advanced parallel to the cortex. From these electrophysiological experiments it was theorized that orientation columns had a regular repeating organization. This organization was not directly observed until the advent of optical imaging, which allowed the orientation preferences of a populations of neurons to be simultaneously observed, highlighting the pinwheel-like arrangement of preferred orientations across the cortical surface (Blasdel & Salama, 1986; Bonhoeffer & Grinvald, 1991) (Figure 3a, b).

V1 is the first region to show binocular processing as it receives convergent inputs from both eyes (inputs from each eye remain spatially and functionally separated across the layers of the LGN). Neurons in the input layer 4C are monocular, and in humans, there are columns of neurons approximately 1 mm width that all receive inputs from the same eye. These ocular dominance columns are ~0.5 mm wide in macaque. Thus, moving horizontally through layer 4C, the transition from left- to right-eye preferring neurons can be quite abrupt, switching in as little as 50 μm (LeVay, Connolly, Houde, & Van Essen, 1985; Malach, Amir, Harel, & Grinvald, 1993; Wiesel & Hubel, 1974). In superficial layers the transitions are more gradual, with many neurons responding to inputs from both eyes, however, there is an alternating pattern of ocular dominance evident across cortex, such that neurons preferentially respond to inputs from the left or right eye (Figure 3c). A fourth clustering is aligned with the center of ocular dominance columns, comprising spatially alternating domains of high color- and orientation-selectivity (Livingstone & Hubel, 1984; Lu & Roe, 2008). These color domains correspond to the cytochrome-rich "blobs".

The spatial clustering of neurons with similar function may not be necessary for supporting normal visual function, and may simply reflect the optimization of development mechanisms. For example, rodents lack the pinwheel organization of orientation columns (Ohki, Chung, Ch'ng, Kara, & Reid, 2005), and squirrel monkeys normally lack ocular dominance columns (Livingstone, 1996). However, spatial clustering offers a simple mechanism to implement post-decision feedback, or top-down modulation of neurons with similar tuning properties, which could be the basis of spatial or feature attention. Further, neurons with similar orientation preference and co-axial receptive fields show preferential lateral connections, suggesting that clustering plays a functional role (Bosking, Zhang, Schofield, & Fitzpatrick, 1997; Malach et al., 1993).

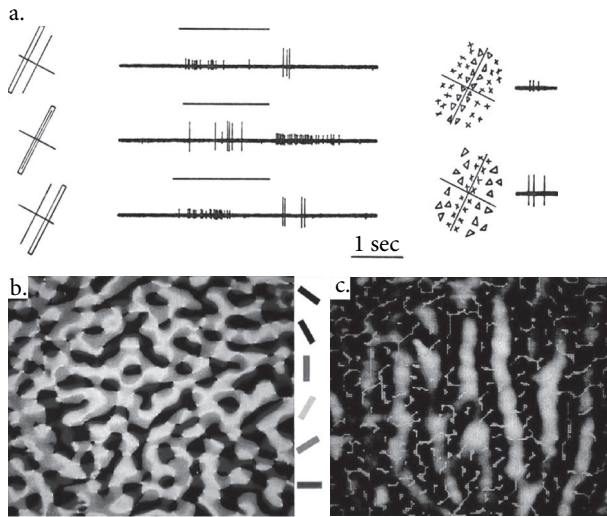


Figure 3. (a) Simultaneous recordings from two adjacent V1 simple cells (Hubel & Wiesel, 1962). On the left, the location of a $0.25 \times 2.5^\circ$ slit of light is shown for 3 different stimulus locations. The recorded extracellular activity is shown in the central column, with the light slit presented during the period indicated by the horizontal line above each recording. The neuron with the smaller action potential (top right) is inhibited by the oriented light slit presented in the center of its receptive field (triangles in receptive field maps in the right column). The neuron with the larger action potential (lower right) is excited by the stimulus in the center of its receptive field. The neurons have identical preferred orientations. Gray-scale maps of preferred orientation (b) and ocular dominance (c) across a 6×7 mm region of the V1 cortical surface in a macaque monkey (Blasdel & Salama, 1986). Adjacent columns of neurons have similar preferred orientations and orientation varies smoothly across the cortical surface (b). Preferred eye is similar for adjacent columns of neurons, but can change rapidly (c). (Panel a. reprinted by permission from Wiley: *J Physiol*, Hubel & Wiesel, 160: 106–154, copyright 1962. Panels b. and c. reprinted by permission from Macmillan Publishers Ltd: *Nature*, Blasdel & Slama, 321: 579–585, copyright 1986.)

3.2 Receptive field properties in V1

The earliest description of V1 receptive fields focused on the spatial organization of subregions sensitive to luminance increments (ON subregions) and decrements (OFF subregions). From this, it became clear that there are two main classes of spatial receptive fields: simple cells have elongated, but spatially separate ON and OFF subregions (Figure 3a), thus they are optimally stimulated by bars with

specific orientations and spatial locations within their receptive fields (Hubel & Wiesel, 1962). Complex cells also have elongated receptive fields, but show spatially overlapping ON and OFF subregions. Thus they are sensitive to orientation, but insensitive to spatial location within their receptive field.

In addition to tuning for spatial position, orientation and ocular dominance, V1 neurons are tuned for direction, spatial frequency and temporal frequency. In cats and ferrets, there is spatial clustering for these features (Shmuel & Grinvald, 1996; Shoham, Hubener, Schulze, Grinvald, & Bonhoeffer, 1997; Weliky, Bosking, & Fitzpatrick, 1996) and direction columns have been observed in marmoset V1 (Roe, Fritsches, & Pettigrew, 2005). However, clustering for temporal and spatial frequency is weak in other primates and has not been observed in macaques (Purushothaman, Khaytin, & Casagrande, 2009). Some V1 neurons are selective for color, and while it was initially proposed that neurons were highly tuned for either color or orientation, there is now converging evidence that neurons may be highly selective for both color and orientation (Conway et al., 2010).

Neurons in V1 are influenced by spatial and temporal context, most clearly demonstrated by their extraclassical receptive fields: neurons have a “classical” spatial receptive field in which stimuli can directly evoke action potentials and a surrounding “extraclassical” receptive field, which cannot directly drive action potentials, but can potently modulate responses to stimuli in the classical receptive field (Allman, Miezin, & McGuinness, 1985). Extra-retinal, or factors not directly relating to visual stimulation, such as task demands and spatial attention also modulate the responses to stimuli in the classical receptive field (McAdams & Maunsell, 1999). Thus it is clear that each V1 neuron is not optimized to contribute to the perception of a singular property. Rather, information encoding is multiplexed such that a neuron’s response is primarily determined by stimulus attributes such as position, size, color and orientation, but the response to these attributes is further modulated by context and task.

3.3 Anatomy of pathways through V1 and V2

A prevailing view of primary visual cortex is that the distinct magno-, parvo- and koniocellular input pathways from the LGN serve unique functional roles in processing form, color, motion and depth, and therefore there is little intermixing between these pathways both within and beyond V1. This tripartite theory was propounded by Livingstone and Hubel based on an astute synthesis of psychophysical, physiological and anatomical studies, but it preceded an understanding of the koniocellular pathway or knowledge of the fine anatomical connectivity within V1 (Livingstone & Hubel, 1988). More recent descriptions of circuitry

within V1 suggest that the functional segregation evident at the input synapses is partially (but not completely) lost by the level of the second synapse.

Gross level structures in V1 and V2 can be defined based on the distribution of the mitochondrial enzyme cytochrome oxidase (CO). The density of CO within a layer correlates with the strength of inputs from the LGN, thus layers 2/3, 4A, 4C α , 4C β and 6 stain most strongly. In superficial layers 2/3 of V1, moving parallel to the cortical surface, alternating regions of dense and light CO are evident, referred to as blobs and interblobs, or patches and interpatches. Blobs are approximately 200 μm wide, separated by 500 μm and spatially co-localized with ocular dominance columns (Hendrickson, Wilson, & Ogren, 1978; Horton, 1984; Horton & Hedley-Whyte, 1984; Horton & Hubel, 1981). In V2, alternating thick, thin and pale CO stripes are evident.

Refinements of the initial tripartite model of segregated processing pathways from retina to V2 via LGN and V1 proposed that the magno- and parvo-cellular layers of the LGN projected to layer 4C α and 4C β in V1, while the koniocellular layers project to the blobs in layers 2/3. After further internal processing, independent outputs arise from layer 4B, the blobs and interblobs, projecting to the thick, thin and pale CO stripes in V2 (Livingstone & Hubel, 1983, 1987). Importantly, segregation of parvo- and magno- inputs throughout V1 is not complete, as selective inactivation of either the parvocellular or magnocellular layers in the LGN leads only to a reduction in the responses of V1 neurons (Malpeli, Schiller, & Colby, 1981; Nealey & Maunsell, 1994). Recent technical developments such as laser photostimulation for uncaging of glutamate, 2-photon imaging, multi-synapse tracing using rabies virus and precise targeting of tracer injections to different CO compartments in V1 and V2 have allowed precise revisions of the tripartite model. Neurons of magno- and parvocellular origin in 4C α and 4C β respectively, have been shown to subsequently project to both blobs and interblobs in layer 2/3, demonstrating intermingling of the M and P pathways (Lachica, Beck, & Casagrande, 1992; Yabuta & Callaway, 1998). Similar intermixing is evident in layer 4B of V1, where pyramidal projection neurons are now known to receive parvocellular and possible koniocellular inputs, in addition to the well-established magnocellular projection from 4C α (Yabuta, Sawatari, & Callaway, 2001). Thin stripes in V2 receive inputs from both interblobs and blobs (Xiao & Felleman, 2004) and V1 columns aligned with interblobs project to both thick and pale stripes (Sincich & Horton, 2002). The intermixing of magno-, parvo- and koniocellular pathways does not preclude functional specialization, as the magnocellular-dominated pathway, through layer 4B and the thick stripes in V2 contributes predominantly to motion processing, whereas the parvo- and koniocellular dominated pathways contribute to form and color processing. However, intermixing does argue against simple functional segregation

based purely on retinal inputs. Taken together, these results suggest two dominant pathways from V1 to V2: columns aligned with blobs project to thin stripes while interblob columns project to pale and thick stripes (Nassi & Callaway, 2009; Sincich & Horton, 2002, 2005).

4. Beyond striate cortex

After initial processing in V1 and V2, visual information is processed by a hierarchy of cortical areas to achieve specific behavioral and perceptual goals (Figure 4). The transfer of information along the hierarchy is not unidirectional; rather, reciprocal connectivity is evident between the majority of connected areas, indicating that ongoing processing occurs simultaneously in areas throughout the hierarchy. The directionality of the reciprocal connections can be defined based on the layer-specificity of input and output projections. Forward projections tend to originate in supragranular layers (2/3) and project to layer 4, whereas feedback projections originate in supragranular layers and to a lesser degree the infragranular layers (5/6), and project to layers other than layer 4 (Rockland & Pandya, 1979). Based on these rules, visual areas can be arranged into a processing hierarchy that contains over ten levels (Felleman & Van Essen, 1991; Maunsell & van Essen, 1983a). Further, processing appears to be initially divided into two streams with limited cross-talk, with convergence at two high-order areas; the anterior superior temporal polysensory area (STPa) and the dorsolateral prefrontal cortex (DLPFC) which includes area 46 (Young, 1992). Note that this is a clearly cortico-centric view of the visual system; even though sub-cortical areas such as the SC and pulvinar have long been known to play important roles in visual perception and oculomotor control (Chalupa, 1977; Kaas & Lyon, 2007), their organization and function are less clear than that of the cortex, and will not be reviewed here.

Traditionally, it has been difficult to directly compare results from animal models, which are typically obtained with invasive anatomical or electrophysiological techniques, with non-invasive imaging results from humans. Recently, however, functional imaging studies in both alert and anesthetized macaques (Brewer et al., 2002; Goense & Logothetis, 2008) and electrophysiological recordings or stimulation in human patients, who have subdural or intracranial electrodes placed to monitor epilepsy seizure foci (Crick, Koch, Kreiman, & Fried, 2004; Murphey, Maunsell, Beauchamp, & Yoshor, 2009) have begun to unify the findings in monkey and man. This should allow the identification of homologous regions, which derive from brain areas in a common ancestor, even though through evolution, changes in precise structure, function and location may have occurred (Orban, Van Essen, & Vanduffel, 2004). Currently, of the ~30 visual areas

elaborated in the macaque, only those areas that are low in the processing hierarchy show clear homology in humans: V1, V2, V3 and MT. The homology of higher order areas, notably those associated with object and face processing, is less clear, partly because of a large expansion in the human parietal and temporal lobes in comparison with macaques and partly because of functional differences. Thus, we will focus below on the better-characterized processing hierarchy in the macaque brain, under the assumption that while the precise brain regions may not be the same in man and monkey, the general principles of organization remain the same.

4.1 Two streams of cortical visual processing

Although the magno-, parvo- and koniocellular neurons in LGN represent three parallel processing pathways from retina to V1, these signals are intermixed within V1 and there are only two clear parallel pathways or streams through the rest of the cortical hierarchy. The original proposal for functional segregation between the two streams was based on anatomical evidence and lesion experiments in macaques (Ungerleider & Mishkin, 1982). The dorsal stream, originating in MT and proceeding into the parietal lobe, was thought to be concerned with the perception of spatial relationships and object localization – a perceptual “where” pathway. Projections to MT originate in layer 4B of V1 and the thick stripes in V2, thus they are magnocellular-dominated and the inputs are tuned for direction and disparity. As discussed further below, the dorsal stream may actually comprise two substreams, devoted to different aspects of motion processing (Pitzalis et al., 2010; Rizzolatti & Matelli, 2003). The ventral stream, originating in V4 and targeting the inferotemporal cortex (IT), was thought to be involved in the identification and recognition of objects – a perceptual “what” pathway. This pathway is dominated by parvo- and koniocellular projections to V4 from the thin and pale stripes of V2 which are primarily selective for orientation and color. Importantly, there is considerable cross-talk between areas in the dorsal and ventral streams and also between cortical and subcortical areas. This is evident from early in the hierarchy as the pattern of connectivity between V4 and MT is not consistent with standard feedback or feedforward connections (Maunsell & van Essen, 1983a; Rockland & Pandya, 1979; Ungerleider, Galkin, Desimone, & Gattass, 2008).

Notably, the proposed distinct perceptual roles for the dorsal and ventral streams remain controversial. While the “what” versus “where” distinction is supported by the properties of neurons obtained in electrophysiological recordings in areas along each anatomically defined stream, an alternative perspective argues that the streams contribute primarily to visual processing for guiding actions and movements, and visual processing supporting perception (Goodale & Milner, 1992). Whereas the distinction between the “what versus where” streams reflects

how neuronal activity represents the world and how the signals might be transformed to support perception of different aspects of the world (Ungerleider & Mishkin, 1982), dividing the streams according to vision for “action versus perception” reflects how signals are transformed to achieve different objectives and to interact with the world (Goodale & Milner, 1992; Milner & Goodale, 2008).

A further complication comes from network analysis of cortical interconnectivity, which suggests that while there is a clear hierarchical structure in visual sensory areas, with two well-defined streams with limited cross-talk, a precise and unique hierarchy of areas cannot be defined (Hilgetag, O'Neill, & Young, 1996, 2000; Young, 1992). Further, because we have a single unified percept of the world, it does not make sense to have two independent streams that independently support perception of form and motion. Therefore, it has been proposed that a high-order convergence of the two streams must occur, putatively in area 46 and STPa (Young, 1992).

4.2 The dorsal stream

Broadly speaking, areas in the dorsal stream contain motion-sensitive neurons and are involved in visual analysis of biological motion and actions, complex motion analysis for extracting heading direction and guiding locomotion, controlling pursuit eye movements, target selection for arm and eye movements and allocating spatial attention (Andersen, Asanuma, Essick, & Siegel, 1990; Andersen, Snyder, Bradley, & Xing, 1997; Blatt, Andersen, & Stoner, 1990; Cohen & Andersen, 2002; Jellema & Perrett, 2003; Siegel & Read, 1997).

Recently, converging anatomical and physiological evidence has suggested that V1 sends direct projections to two areas in the dorsal stream; MT and V6. Thus, the dorsal stream may be subdivided into dorsolateral (ventro-dorsal) and dorsomedial (dorso-dorsal) streams, originating in MT and V6, respectively (Rizzolatti & Matelli, 2003). In new-world primates, the dorsomedial area (DM) is the apparent homolog of V6 in humans and old-world primates (Pitzalis et al., 2006; Rosa & Tweeddale, 2001). V6 appears specialized for motion analysis (Fattori, Pitzalis, & Galletti, 2009; Pitzalis et al., 2010), however, the neurons are not strongly direction-selective and tend to respond to motion in both directions along a preferred axis (Lui, Bourne, & Rosa, 2006). V6 contains a retinotopic map, but unlike surrounding areas, it lacks an emphasis on the central visual field. Further, it is sensitive to the motion of stimuli across large regions of the visual field, failing to show strong center-surround antagonism. This has led to the suggestion that it is functionally involved in distinguishing object and self-motion, guiding movements, or action understanding (Lui et al., 2006; Pitzalis et al., 2010; Rizzolatti & Matelli, 2003).

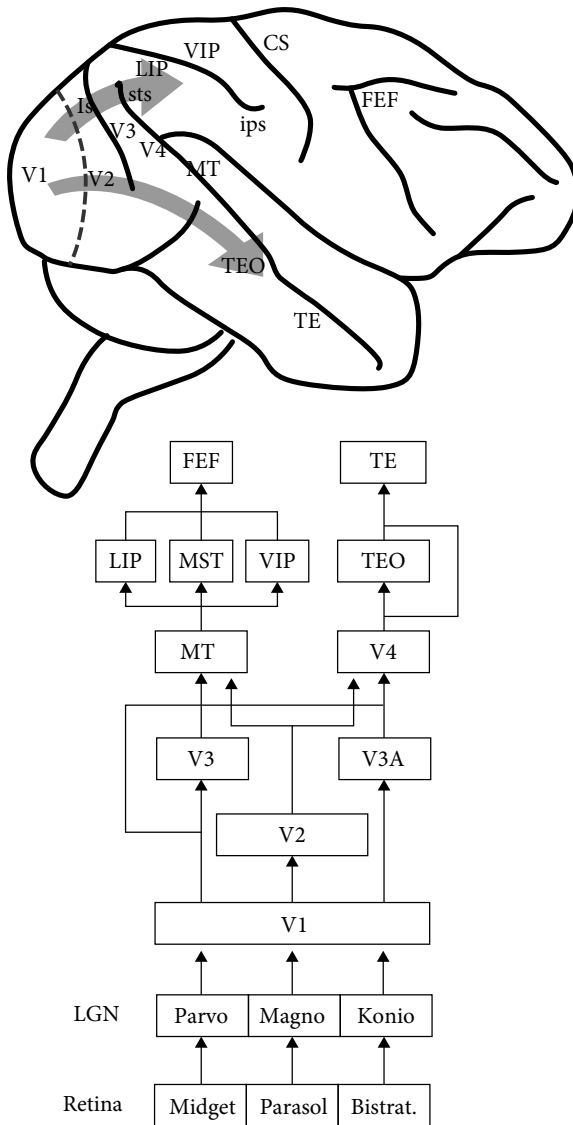


Figure 4. Functional hierarchy of cortical visual areas in the macaque showing feed-forward connectivity. Only areas discussed in this review have been indicated, but many other areas and connections exist (Felleman & Van Essen, 1991). Gray arrows indicate dorsal and ventral streams of information flow. Dorsal stream areas: MT – middle temporal area; MST – medial superior temporal area; LIP – lateral intraparietal area; VIP – ventral intraparietal area; FEF – frontal eye fields. Ventral stream areas: TEO – temporal-occipital area; TE – temporal area. Sulci: ls – lunate sulcus; sts – superior temporal sulcus; ips – intraparietal sulcus; cs – central sulcus

The dorsolateral stream has been attacked with a multitude of techniques including anatomy, electrophysiological recordings, microstimulation, reversible inactivation and lesion studies; therefore, its physiological properties and functional role are better understood than those of the dorsomedial stream. As the gateway to the dorsolateral stream, area MT has been closely associated with the representation and perception of the direction, speed and depth of visual motion – critical properties for spatial localization and visuomotor interactions. MT lesions cause deficits in motion perception (Newsome & Pare, 1988) and individual neurons in MT are tuned for direction, speed and binocular disparity (Maunsell & Van Essen, 1983b, 1983c). Notably, when monkeys view stimuli that are either perceptually bistable (Bradley, Chang, & Andersen, 1998; Dodd, Krug, Cumming, & Parker, 2001; Krug, Cumming, & Parker, 2004) or ambiguous (Britten, Newsome, Shadlen, Celebrini, & Movshon, 1996; Liu & Newsome, 2005; Uka & DeAngelis, 2006), the spiking rates of MT neurons correlates with stimulus perception. This indicates that decision related activity is evident in an ostensibly sensory area, although it remains unclear if this activity is causal in generating decisions, or due to attention or post-decision feedback. Strong support for a causal relationship comes from studies that have used electrical microstimulation to bias motion perception towards the preferred direction or disparity of neurons clustered near the microelectrode tip (DeAngelis, Cumming, & Newsome, 1998; Salzman, Britten, & Newsome, 1990).

Beyond MT, there is no widely-agreed upon anatomical classification of the number or nature of regions within the dorsal stream (Felleman & Van Essen, 1991; Galletti, Fattori, Gamberini, & Kutz, 1999; Lewis & Van Essen, 2000a; Nelissen, Vanduffel, & Orban, 2006; Seltzer & Pandya, 1986; Ungerleider & Desimone, 1986). In a recent, highly compartmented description of the dorsal stream, seven areas are at hierarchical levels equal to or higher than MT/MST in the dorsal stream: area 7a, the dorsal and ventral lateral intraparietal areas (LIPd and LIPv), the ventral and medial intraparietal areas (VIP and MIP) the medial-dorsal parietal area (MDP or V6a) and the dorsal prelunate area (DP) (Lewis & Van Essen, 2000b). However, a range of partitioning schemes exist, with competing terminology because of differences in criteria for defining regions. Further, it has been difficult to precisely assign functional roles to all the areas that have been anatomically defined. The two most common approaches to defining function have been the examination of neural responses (using fMRI or electrophysiology) during passive viewing of a range of stimuli, or comparison of neuronal and perceptual performance during constrained psychophysical tasks. This has been fruitful for areas such as dorsal MST, which incorporates visual, vestibular and eye movement information and contains neurons sensitive to complex motion patterns such as expansion or rotation. The basic receptive field properties and

correlation between neuronal activity and choices in psychophysical tasks have led to the suggestion that MSTd is critical for determining heading direction (Gu, Angelaki, & Deangelis, 2008; Gu, DeAngelis, & Angelaki, 2007).

Beyond MT, areas in the dorsal stream are characterized by having larger receptive fields and less clearly defined retinotopy. However, the visual stimuli or behavioral tasks relevant to these areas are less clear, and sensory driven activity in these areas may only make sense in the context of a behaviorally relevant task. Thus, an ethological approach that takes into account the requirements that the monkey has for its visual system will likely be required to elucidate the functional response properties of the anatomically defined higher-order areas (Orban, 2008).

4.3 The ventral stream

Processing throughout the ventral stream culminates in IT neurons that are selective for the two- and three-dimensional structure of complex objects, including faces and body parts (Desimone, Albright, Gross, & Bruce, 1984; Gross, Rocha-Miranda, & Bender, 1972; Tanaka, 1996). It remains unclear how these representations are formed, and what attributes the neurons are encoding. A prevailing theory is that objects can be described in terms of “primitives” or their constituent parts, with single neurons encoding different primitives (Biederman, 1987). Thus, a starting point is to demonstrate neuronal tuning for a range of primitives. By analogy with processing in the dorsal stream, the stimulus primitives that selectively activate neurons in V1 (position, orientation, spatial frequency, temporal frequency) or MT (position, direction, speed, disparity) are well established. However, the image of a single object is infinitely variable due to changes in viewing angle, illumination and size, and there are many ways to parameterize object features, thus establishing the primitives for the ventral stream has proven elusive.

The object features encoded in low levels of the ventral stream are relatively intuitive. Processing of form begins in V1, where neurons are sensitive to luminance boundaries and show tuning for both orientation and spatial frequency. Indeed, neurons in V1, V2 and V4 show similar orientation and spatial frequency tuning (Hegde & Van Essen, 2007). Oriented lines give the first level of structure required for defining object boundaries. In V4, neurons encode more complex features such as curvature and it has been demonstrated that neural response of the V4 population carry sufficient information to completely represent the curvature associated with all possible 2D object boundaries (Pasupathy & Connor, 2002). Importantly, receptive fields in V4 are larger than those in V1 and they encode relative, not absolute, position within their receptive fields (Gallant, Braun, & Van

Essen, 1993; Pasupathy & Connor, 1999, 2001). Encoding of relative position is critical for generating robust position invariance – i.e., it is the shape of an object and its spatial relationship with other objects that matters, not its absolute position in the retinal image.

Beyond V4, object processing is evident throughout the posterior bank of the superior temporal sulcus (STS) in the temporal lobe, but there are no widely agreed upon boundaries between areas. As in the dorsal stream, these problems arise because there is no definitive way to use cyto- and myeloarchitecture, connectivity and functional response properties to define areas in a single animal. The simplest scheme describes the progression of information from V4 to temporo-occipital cortex (TEO), with both areas projecting to TE (Desimone, Fleming, & Gross, 1980; Distler, Boussaoud, Desimone, & Ungerleider, 1993). Other studies describe the information flow from posterior, through central, to anterior IT (PIT, CIT and AIT) (Felleman & Van Essen, 1991). While the final stages of processing within both schemes (TE and AIT) are agreed upon, V4A, part of the V4 complex (Shipp & Zeki, 1995) likely includes both PIT (Felleman & Van Essen, 1991) and the posterior part of TEO (Boussaoud, Desimone, & Ungerleider, 1991; Zeki, 1996).

Neurons in TE have no retinotopic organization and their receptive fields may span the entire visual field. Thus they extend the position invariance found in the small receptive fields of V4 to cover all possible object locations. Further, their responses are relatively invariant for stimulus size and orientation in the frontoparallel plane (Ito, Tamura, Fujita, & Tanaka, 1995; Tanaka, 1996; Tanaka, Saito, Fukada, & Moriya, 1991). Reflecting the columnar organization evident in earlier visual areas, neurons in TE display a columnar organization, with adjacent cells responsive to similar object features (Fujita, Tanaka, Ito, & Cheng, 1992). It is likely that objects are then represented by the combination of both active and inactive columns (Tsunoda, Yamane, Nishizaki, & Tanifuji, 2001), and active and inactive neurons within each column (Tanaka, 2003). Diverse methods are currently being applied to understand object coding in IT (Kourtzi & Connor, 2011). These include adaptive methods, in which visual stimuli are progressively modified based on neuronal responses to those stimuli, in an attempt to learn how to better parameterize object structure (Fujita et al., 1992; Yamane, Carlson, Bowman, Wang, & Connor, 2008). Objects can also be defined based on their membership of categories such as faces, body parts, chairs, tools or fruit, thus neuronal tuning for category can be studied. Finally, because object understanding depends on learning and experience, the development of neural tuning over time is being studied to understand the dynamic nature of object representations.

Two specific stimulus sets relevant to the ventral stream warrant special mention: color stimuli and faces. Beginning in V1 blobs and the thin stripes of V2, color-sensitive neurons appear clustered in specialized modules throughout the ventral stream (Livingstone & Hubel, 1984; Lu & Roe, 2008). Subsequently, luminance-invariant, hue-selective neurons are clustered in “globes” a few millimeters across throughout the posterior inferotemporal cortex (V4, PITd and posterior TEO) and area TE (Conway, Moeller, & Tsao, 2007). The close proximity, but segregation of object-selective and color-selective neurons in TE suggests that they serve a common perceptual goal and that color information makes an important contribution to object perception. Neurons responsive to face features were first identified in macaque electrophysiology experiments (Bruce, Desimone, & Gross, 1981; Gross et al., 1972; Perrett, Hietanen, Oram, & Benson, 1992). However, their clustering was not demonstrated until fMRI-guided electrophysiology experiments, which identified three face patches in TE that have stronger responses to faces than non-face objects, and which show parametric tuning for face features (Tsao, Freiwald, Knutsen, Mandeville, & Tootell, 2003; Tsao et al., 2006). This is an example of both categorical coding (e.g., faces versus non-faces) and object parameterization (e.g., neurons are tuned for parameters such as eye separation and face aspect ratio). Similar face selective regions have been identified in humans, but the homology of the macaque and human areas is not yet clear (Tsao, Moeller, & Freiwald, 2008).

4.4 Cortical confluences

Despite the multitude of cortical processing areas devoted to vision, humans perceive a single, continuous and unified percept. This might suggest that there is competition between areas, with processing in only one area able to reach perceptual awareness at any point in time. However, sensation and perception are integrated across sensory domains (e.g., we can localize an object using visual, auditory and somatosensory information), clearly requiring a confluence of information processing from areas at the top of the hierarchy in the dorsal and ventral streams. This convergence should allow sensory information to inform both perception and behavior and is evident in STS and DLPFC.

The upper bank of STS in macaques, which incorporates the polysensory area STP, includes neurons that are responsive to visual, auditory and somatosensory stimuli, even under anesthesia (Bruce et al., 1981; Dahl, Logothetis, & Kayser, 2009; Hikosaka, Iwai, Saito, & Tanaka, 1988). Similar multisensory responsivity has been inferred in humans (Beauchamp, Yasar, Frye, & Ro, 2008) and in both cases, stronger responses are evoked by moving stimuli. The upper STS is

connected with sensory cortices, but also with prefrontal areas 9 and 46 (Seltzer & Pandya, 1978, 1989, 1994), conferring upon it the ability to integrate multi-sensory information and use this to guide complex, cognitive behaviors. Current theories about the role of this multisensory integration include processing the sight and sound of biological motion (Barracough, Xiao, Baker, Oram, & Perrett, 2005; Beauchamp, Lee, Haxby, & Martin, 2002), speech processing and understanding social and behavioral cues (Allison, Puce, & McCarthy, 2000; Hein & Knight, 2008).

The anatomical connections and structural localization of DLPFC are well studied in both macaques and humans (Barbas & Pandya, 1989; Petrides & Pandya, 1999; Walker, 1940), however, the further localization of divisions within DLPFC remain contested between studies and species. Under the most restricted definition, DLPFC includes Brodmann areas 9 and 46. Critically, both dorsal and ventral visual streams in addition to auditory and somatosensory cortices project directly to DLPFC, in particular area 46. Further, area 46 within DLPFC is interconnected with the supplementary, pre-supplementary and premotor cortices, and also with the cerebellum and SC. Thus, area 46 is ideally placed to modulate motor behaviors based on a broad range of incoming sensory evidence. Functionally, activity of subsets of neurons in DLPFC seems to support any and every sensory or cognitive task that has been investigated, and the localization of specific functions has proved elusive. What over-arching principles can then be defined? While initially implicated in working memory (Goldman-Rakic, 1988), DLPFC is broadly involved with the executive control of behavior, regulating voluntary and planned motor acts (Tanji & Hoshi, 2008). It supports rule-based and goal-directed behavior by feedback to sensory and motor areas, biasing action selection toward the most favorable sensori-motor transformation and helping to organize the temporal structure of new and complex behaviors (Miller & Cohen, 2001). Activity in DLPFC is thus thought to represent the goals and rules of behavior, with this activity maintained and modified over time. The neurons do not directly enact the sensori-motor or input-output relationship, but modify the activity of neurons in lower areas to achieve the desired behavior and guide decision making.

4.5 Response timing

One prediction of a purely feed-forward hierarchy is that response latencies associated with the onset of a visual stimulus should show an orderly increase throughout the hierarchy as information progresses from area to area. For example, because there is an anatomically defined progression from V1 via V2 to MT, we might expect latencies in V2 to be intermediate between those of V1 and MT.

This is not seen, as most V2 neurons have longer latencies than those found in MT (Figure 5). In fact, a cortical area's level in the hierarchy is a poor predictor of neuronal latencies – the distribution of latencies in the frontal eye fields (FEF) is only a few milliseconds longer than those in MT and MST, despite FEF being at a much higher level in the processing hierarchy. In contrast, V4 has median latencies approximately 30 ms longer than MT, even though they are at the same level in the processing hierarchy (Schmolesky et al., 1998).

A better predictor of neuronal latency is the stream in which an area is located – latencies in the parvocellular-dominated ventral stream are considerably longer than those in the magno-dominated dorsal stream (Nowak & Bullier, 1997; Nowak, Munk, Girard, & Bullier, 1995). This distinction is evident from the level of the thalamus; in LGN of anesthetized macaques, the 25th–75th percentiles of latencies are non-overlapping between magno cells (31–34 ms) and parvo cells (44–56 ms) (Schmolesky et al., 1998) (Figure 5). Further, in V1 and V2, the latency distribution of orientation selective neurons is shorter than that of non-orientation selective neurons and color selective neurons have longer latencies than non-color tuned neurons (Nowak et al., 1995). These latency differences have two clear anatomical correlates. First, there are higher levels of myelination in the dorsal stream, particularly in the inputs to MT, which was initially defined anatomically for its dense pattern of myelination (Van Essen, Maunsell, & Bixby, 1981). Second, the dorsal stream contains higher densities of neurofilament protein, which regulates axonal diameter and therefore conduction velocities (Hof et al., 1996). It is also possible that the accelerated processing in the dorsal stream may arise simply because of the preponderance of lateral connectivity within dorsal compared to ventral stream areas (Hilgetag et al., 2000). This lateral, or monosynaptic, connectivity with an area facilitates rapid transfer of information up the hierarchy because incoming signals terminate in the same cortical layers from which the efferent fibers originate.

The functional rationale for such large differences in latency may arise from the proposed different roles of the dorsal and ventral streams in supporting vision for visuomotor interactions and perception, respectively. Arguably, objects and faces do not need to be rapidly perceived, and accuracy or the generation of appropriate behavior is not significantly impaired by an extra few milliseconds of processing delay. In contrast, visually-guided interactions with objects, especially with moving objects, require rapid sensory processing in order to generate accurate behaviors such as eye movements and hand reaches.

Processing demands along the dorsal and ventral streams cannot entirely account for the latency differences between areas; this is especially highlighted by the overlap between FEF and MT latencies. This demonstrates that the view of simple feed-forward hierarchical organization within a stream is incorrect, or

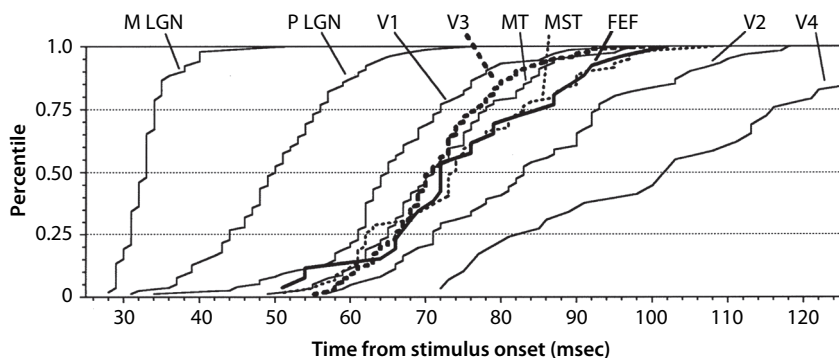


Figure 5. Cumulative distributions of visual-flash evoked onset response latencies in the magnocellular and parvocellular layers of the LGN and various cortical areas. (Reprinted by permission from the American Physiological Society: *J Neurophysiol*, Schmolesky et al., 79: 3272–3278, copyright 1998.)

at best, incomplete. Rather, significant processing must occur in parallel across areas, requiring simultaneous feedforward and feedback flow of information, or cortico-thalamo-cortical links (Sherman & Guillery, 2006). This may additionally require information flow from retina to higher order areas that doesn't strictly follow the hierarchy, as must occur in blindsight and when lesions impair the function of specific areas (Gilaie-Dotan, Perry, Bonneh, Malach, & Bentin, 2009; Stoerig & Cowey, 1997).

5. Active vision

Since the work of Yarbus (1967) it has been clear that vision is an active sense, and that eye movements play a critical role in how we perceive and interact with the world. Further, how our brain represents visual information depends on more than just the retinal inputs as a range of extra-retinal influences such as attention, expectations and task demands shape activity throughout the visual system. In this section, we explore the implications of eye movements and extra-retinal influences on visual perception.

5.1 Why move the eyes?

The visual world is not represented in the brain as a series of photographs nor as a video stream – rather, we interact and explore the visual world using eye movements, much as we explore the contours of an object with our fingers. The reason

for this is clear from the retinal structure – from the fovea to the retinal periphery, the cone photoreceptor density decreases and the convergence ratio of cones to ganglion cells increases. In combination, this means that visual acuity declines precipitously from central to peripheral retina (Osterberg, 1935). Therefore, if a task requires high spatial frequency sensitivity, the object of interest should be within the central 1° of the fovea and should be as close to stationary as possible within this region as even slow drifts on the order of $5^\circ/\text{s}$ lead to blurring and loss of acuity.

To support the highest acuity vision requires keeping the eyes as still as possible, minimizing motion blur and allowing the fixation of points of interest within the scene. Importantly, the eyes are never completely stationary as slow drifts, microsaccades and tremor continually occur, with displacements of less than 1° and speeds of $<100^\circ/\text{s}$ (Martinez-Conde, Macknik, & Hubel, 2004; Yarbus, 1967). The functional importance and role of these “fixational eye movements” is still under debate, but it is clear that they can be beneficial. If an image is perfectly stabilized on the retina it fades after a few seconds, but returns as soon as a small displacement is allowed (Riggs, Ratliff, Cornsweet, & Cornsweet, 1953). This is likely due to it being metabolically expensive to continually signal the presence of an unchanging stimulus, thus adaptation of the photoreceptors may help conserve energy by only signaling stimulus changes.

5.2 Selection and control of saccades

Fixation locations during free viewing of a scene are heavily dependent on both the task and the spatial properties of the scene (Yarbus, 1967). Bottom-up information related to scene statistics such as the presence of high spatial frequencies, edges, corners, and high local contrast can help generate a salience map that represents what is important and informative in a scene. However, it would not be optimal to stubbornly fixate the single most salient point in a scene, or continually return to the same point. Rather, the eyes must fixate the point in the scene that is best for meeting the spatio-temporal demands of the current task – this requires integrating top-down information based on working memory, the constraints of the current task and attentional demands, with the continually changing bottom-up visual information obtained with each refixation (Hayhoe & Ballard, 2005; Henderson, 2003; Koch & Ullman, 1985). Thus, visual perception and cognition interact closely with eye movement planning and execution.

Saccades share with smooth pursuit a common goal of placing or stabilizing the retinal image of target objects at the fovea, whether that target object is stationary or moving. Therefore, it is not surprising that the two types of eye movement have overlapping control circuitry involving a distributed network of cortical

and subcortical areas (Krauzlis, 2005; Munoz, 2002; Pierrot-Deseilligny, Milea, & Muri, 2004; Sparks, 2002; Thier & Ilg, 2005). In the cortex, saccade planning and target selection involves the dorsal stream, especially the lateral intraparietal area (LIP), FEF and supplementary eye fields, and DLPFC. Subcortically, the basal ganglia, SC, cerebellum and a range of brainstem regions are involved in controlling saccades.

5.3 Implications of saccadic eye movements for studies of perception

While maintaining prolonged fixation on a single stationary point may be normal behavior in a laboratory setting, it is a highly unnatural way of gaining information about the visual world. Rather, the planning and execution of eye movements are intimately linked with visual perception and cognition. Further, the control of eye movements and spatial attention may involve similar neural mechanisms, demonstrating the importance of considering eye movements when studying perception.

Dozens of saccades are made each minute, and during normal viewing the eyes remain open if the saccade amplitude is small. Thus, most saccades are associated with whole-field image motion lasting tens of milliseconds. To prevent the disconcerting percept of the entire world moving, peri-saccadic perception is suppressed, evident as marked reductions in contrast sensitivity (Diamond, Ross, & Morrone, 2000) and image motion sensitivity (Allison, Schumacher, Sadr, & Herpers, 2010). This suppression may be linked to the perceptual compression of both space and time during saccades (Binda, Cicchini, Burr, & Morrone, 2009; Morrone, Ross, & Burr, 2005). Importantly, soon after a saccade ends, the ability to detect certain stimuli is enhanced (Burr & Morrone, 1996; Wittenberg, Bremmer, & Wachtler, 2008), as is the ability to track moving scenes (Ibbotson, Price, Crowder, Ono, & Mustari, 2007). Collectively, these saccade-related modulations in visual information flow must be predominantly extra-retinal in origin because they are evident before the onset of eye movements and do not occur simply because of the rapid image motion generated by saccades. This implies that an efference copy of the motor command is used to modulate sensory processing, likely involving a pathway through the SC and FEF (Sommer & Wurtz, 2002).

Saccades interact with the perception of rivalrous stimuli, in which different stimuli are presented to the two eyes (binocular rivalry) or a single stimulus can be perceived in multiple ways (perceptual rivalry, as in the Necker cube and many Escher paintings). However, it is not clear whether this is due to an extra-retinal signal associated with the eye movements themselves, or simply due to the image change produced by saccades. While selective attention to different

stimuli has long been known to modulate, but not completely control, perceptual alternations during rivalry (Helmholtz, 1910), saccades exert different effects. For example, saccade frequency increases prior to binocular rivalry flips, but decreases after perceptual rivalry flips (van Dam & van Ee, 2006). Further, saccade or stimulus-jump induced changes in ocular dominance depend on the eye of dominance before the saccade or stimulus motion (Kalisvaart, Rampersad, & Goossens, 2011). Thus, it may be that saccades actively regulate the flow of visual information, helping to maintain perceptual stability and continuity (Ross & Ma-Wyatt, 2004).

During maintained fixation, the rate of microsaccades is modulated by attention and alertness (Martinez-Conde et al., 2004) and microsaccades have been shown to overcome visual fading during fixation (Martinez-Conde, Macknik, Troncoso, & Dyar, 2006) and motion-induced blindness (Hsieh & Tse, 2009). Normally we are unaware of the retinal motion associated with microsaccades, although this motion can be visualized by exploiting adaptation effects, as in the Enigma illusion (Troncoso, Macknik, Otero-Millan, & Martinez-Conde, 2008). This suggests that just as an extraretinal signal supports saccadic suppression, similar suppression occurs during microsaccades, allowing motion during microsaccades to be discounted at a sub-conscious level. This can actually interfere with the detection of genuine, short-duration motion that occurs around the time of a microsaccade (Herrington et al., 2009).

5.4 Attention and expectations

While fixating one object, it is possible to selectively attend to other spatial locations, and to move this locus of attention around the visual field (Posner, 1980). Selective spatial attention enhances reaction times and the detection and discrimination of stimuli at the attended location, at the expense of impaired perception at other regions of the visual field (Bashinski & Bacharach, 1980; Shepherd, Findlay, & Hockey, 1986). Similarly, task performance is enhanced at the location of planned saccades, suggesting that selective spatial attention may recruit similar neural circuitry to that involved in eye movement generation (Corbetta et al., 1998; Moore, Armstrong, & Fallah, 2003; Rizzolatti, Riggio, Dascola, & Umiltà, 1987). Thus, while spatial attention and eye movement planning and execution can be controlled independently (Juan, Shorter-Jacobi, & Schall, 2004), saccade planning can have significant consequences on the spatial locus of attention, and attending to non-foveal spatial regions can affect subsequent saccade generation or may require suppressing saccades (Corbetta, 1998; Guitton, Bachtel, & Douglas, 1985; Thompson, Biscoe, & Sato, 2005).

Attention can assist perceptual processing by favoring the representation of one stimulus over another. This may be achieved through normalization mechanisms that change the gain of a neuron's response depending on the stimulus conditions, task demands and viewer's attentional strategy (Lee & Maunsell, 2009; Reynolds & Heeger, 2009). While attention can favor the representation of one stimulus over another, perception still requires knowing the range of stimuli that might possibly exist. Much recent work has focused on the idea that the role of perceptual processes in the brain is to choose the most likely stimuli from a range of possibilities, given the constraints of both noisy stimuli and noisy neuronal representations of those stimuli (Friston, 2005; Ma, Beck, & Pouget, 2008). A Bayesian framework has been adopted to explain this process, suggesting that perception depends not just on the probability that a given stimulus evokes a given pattern of neuronal activity but also on the probability of that stimulus occurring or existing in the world. These stimulus probabilities, or "priors" represent our beliefs and expectations about the range of possible stimuli and our confidence or uncertainty about those beliefs (Ma, Beck, Latham, & Pouget, 2006; Ma et al., 2008). These priors cannot be hard-coded in the brain, but must be established and modified through exposure to the world, adaptation and learning.

6. Conclusions

A critical role of the visual system is to extract information from the visual world in order to guide decision making and generate appropriate behaviors. While the network of brain regions that contribute to this task, especially at the "front-end" of the system, are relatively well established, much remains to be learned about the connectivity and computational processing performed within and between these regions. Here we have focused on four functional and organizational principles evident in the visual system.

First, the processing of sensory information is *anatomically and functionally segregated*. This parallel processing is ubiquitous and evident at multiple levels and spatial scales. Segregation begins in the retina, with over a dozen parallel circuits corresponding to different RGC types, and is evident in the projections through LGN to cortex, which feature independent magno-, parvo- and koniocellular pathways with different spatiotemporal sensitivity and different cell types. Further, in V1 and V2, there are anatomically distinct layers or compartments that have unique patterns of inputs and outputs, and which appear to be specialized for processing different stimulus attributes such as color, depth or form. At a higher level, there are dozens of anatomically and functionally defined cortical

and subcortical visual regions that are broadly interconnected, but narrowly specialized for processing different attributes properties such as heading direction, faces or objects.

Second, information processing is multiplexed, so that single neurons simultaneously carry information about multiple stimulus attributes. Further, sensory neurons are sensitive to a range of any stimulus quality. For example, the output of retinal photoreceptors depends on the wavelength, intensity and spatial position of incident light. Similarly, the firing rate of single neurons in MT depends on the position, direction, speed and disparity of moving stimuli. Specific stimulus properties such as position or direction may therefore only be extracted from the responses of a population of neurons, not a single neuron.

Third, feed-forward, lateral and feed-back connectivity between areas is critical for information processing. Visual information is not passed sequentially from retina to thalamus to cortex, with progressively more complex stimulus features extracted by areas higher in the processing hierarchy. In contrast, the number and strength of feedback connections often outweighs that of feedforward connections, and even though cortical areas are specialized for processing specific attributes, they are highly interconnected.

Fourth, visual perception is an active and continually refined process. We move our eyes to search a scene or track a moving object, and we can selectively attend to specific spatial locations or stimulus properties. Further, what we perceive depends not only on the stimulus, but what we expect or believe the stimulus might be. Thus perception is a continuous, ongoing process, which depends not just on the external environment, but also on our interactions with the environment.

Despite the complexity and segregation evident in the visual system, we experience a single, continuous percept: instantly able to see a moving object and perceive its redness, its roundness and its trajectory. Thus, motion, form and color are unified into a global percept. Decades of study of the anatomy and physiology of the visual system have provided a framework for understanding how different regions of the brain are connected and represent attributes of the visual world. Future work will provide a clearer description of how this information is bound together across areas, in order to create stable neural representations that support reliable perception and behavior.

References

- Alitto, H. J., & Usrey, W. M. (2003). Corticothalamic feedback and sensory processing. *Current Opinion in Neurobiology*, 13(4), 440–445.
- Allison, R. S., Schumacher, J., Sadr, S., & Herpers, R. (2010). Apparent motion during saccadic suppression periods. *Experimental Brain Research*, 202(1), 155–169.
- Allison, T., Puce, A., & McCarthy, G. (2000). Social perception from visual cues: Role of the STS region. *Trends in Cognitive Sciences*, 4(7), 267–278.
- Allman, J., Miezin, F., & McGuinness, E. (1985). Stimulus specific responses from beyond the classical receptive field: Neurophysiological mechanisms for local-global comparisons in visual neurons. *Annual Review of Neuroscience*, 8, 407–430.
- Andersen, R. A., Asanuma, C., Essick, G., & Siegel, R. M. (1990). Corticocortical connections of anatomically and physiologically defined subdivisions within the inferior parietal lobule. *Journal of Comparative Neurology*, 296(1), 65–113.
- Andersen, R. A., Snyder, L. H., Bradley, D. C., & Xing, J. (1997). Multimodal representation of space in the posterior parietal cortex and its use in planning movements. *Annual Review of Neuroscience*, 20, 303–330.
- Barbas, H., & Pandya, D. N. (1989). Architecture and intrinsic connections of the prefrontal cortex in the rhesus monkey. *Journal of Comparative Neurology*, 286(3), 353–375.
- Barraclough, N. E., Xiao, D., Baker, C. I., Oram, M. W., & Perrett, D. I. (2005). Integration of visual and auditory information by superior temporal sulcus neurons responsive to the sight of actions. *Journal of Cognitive Neuroscience*, 17(3), 377–391.
- Bashinski, H. S., & Bacharach, V. R. (1980). Enhancement of perceptual sensitivity as the result of selectively attending to spatial locations. *Perception & Psychophysics*, 28(3), 241–248.
- Beauchamp, M. S., Lee, K. E., Haxby, J. V., & Martin, A. (2002). Parallel visual motion processing streams for manipulable objects and human movements. *Neuron*, 34(1), 149–159.
- Beauchamp, M. S., Yasar, N. E., Frye, R. E., & Ro, T. (2008). Touch, sound and vision in human superior temporal sulcus. *Neuroimage*, 41(3), 1011–1020.
- Biederman, I. (1987). Recognition-by-components: A theory of human image understanding. *Psychological Review*, 94(2), 115–147.
- Binda, P., Cicchini, G. M., Burr, D. C., & Morrone, M. C. (2009). Spatiotemporal distortions of visual perception at the time of saccades. *Journal of Neuroscience*, 29(42), 13147–13157.
- Blasdel, G. G., & Salama, G. (1986). Voltage-sensitive dyes reveal a modular organization in monkey striate cortex. *Nature*, 321(6070), 579–585.
- Blatt, G. J., Andersen, R. A., & Stoner, G. R. (1990). Visual receptive field organization and cortico-cortical connections of the lateral intraparietal area (area LIP) in the macaque. *Journal of Comparative Neurology*, 299(4), 421–445.
- Bonhoeffer, T., & Grinvald, A. (1991). Iso-orientation domains in cat visual cortex are arranged in pinwheel-like patterns. *Nature*, 353(6343), 429–431.
- Bosking, W. H., Zhang, Y., Schofield, B., & Fitzpatrick, D. (1997). Orientation selectivity and the arrangement of horizontal connections in tree shrew striate cortex. *Journal of Neuroscience*, 17(6), 2112–2127.
- Boussaoud, D., Desimone, R., & Ungerleider, L. G. (1991). Visual topography of area TEO in the macaque. *Journal of Comparative Neurology*, 306(4), 554–575.
- Bradley, D. C., Chang, G. C., & Andersen, R. A. (1998). Encoding of three-dimensional structure-from-motion by primate area MT neurons. *Nature*, 392(6677), 714–717.

- Brewer, A. A., Press, W. A., Logothetis, N. K., & Wandell, B. A. (2002). Visual areas in macaque cortex measured using functional magnetic resonance imaging. *Journal of Neuroscience*, 22(23), 10416–10426.
- Britten, K. H., Newsome, W. T., Shadlen, M. N., Celebrini, S., & Movshon, J. A. (1996). A relationship between behavioral choice and the visual responses of neurons in macaque MT. *Visual Neuroscience*, 13(1), 87–100.
- Brodmann, K. (1909/2006). *Brodmann's localisation in the cerebral cortex* (L. Garey, Trans., 3rd ed.). Singapore: World Scientific Publishing Co.
- Bruce, C., Desimone, R., & Gross, C. G. (1981). Visual properties of neurons in a polysensory area in superior temporal sulcus of the macaque. *Journal of Neurophysiology*, 46(2), 369–384.
- Burr, D. C., & Morrone, M. C. (1996). Temporal impulse response functions for luminance and colour during saccades. *Vision Research*, 36(14), 2069–2078.
- Chalupa, L. M. (1977). A review of cat and monkey studies implicating the pulvinar in visual function. *Behavioral Biology*, 20(2), 149–167.
- Cohen, Y. E., & Andersen, R. A. (2002). A common reference frame for movement plans in the posterior parietal cortex. *Nature Reviews Neuroscience*, 3(7), 553–562.
- Conway, B. R., Chatterjee, S., Field, G. D., Horwitz, G. D., Johnson, E. N., Koida, K. et al. (2010). Advances in color science: From retina to behavior. *Journal of Neuroscience*, 30(45), 14955–14963.
- Conway, B. R., Moeller, S., & Tsao, D. Y. (2007). Specialized color modules in macaque extrastriate cortex. *Neuron*, 56(3), 560–573.
- Corbetta, M. (1998). Frontoparietal cortical networks for directing attention and the eye to visual locations: Identical, independent, or overlapping neural systems? *Proceedings of the National Academy of Sciences USA*, 95(3), 831–838.
- Corbetta, M., Akbudak, E., Conturo, T. E., Snyder, A. Z., Ollinger, J. M., Drury, H. A. et al. (1998). A common network of functional areas for attention and eye movements. *Neuron*, 21(4), 761–773.
- Crick, F., Koch, C., Kreiman, G., & Fried, I. (2004). Consciousness and neurosurgery. *Neurosurgery*, 55(2), 273–281; discussion 281–272.
- Dacey, D. M. (2000). Parallel pathways for spectral coding in primate retina. *Annual Review of Neuroscience*, 23, 743–775.
- Dacey, D. M. (2004). Origins of perception: Retinal ganglion cell diversity and the creation of parallel visual pathways. In M. S. Gazzaniga (Ed.), *The Cognitive Neurosciences* (pp. 281–301). Cambridge: MIT Press.
- Dacey, D. M., Liao, H. W., Peterson, B. B., Robinson, F. R., Smith, V. C., Pokorny, J. et al. (2005). Melanopsin-expressing ganglion cells in primate retina signal colour and irradiance and project to the LGN. *Nature*, 433(7027), 749–754.
- Dacey, D. M., & Petersen, M. R. (1992). Dendritic field size and morphology of midget and parasol ganglion cells of the human retina. *Proceedings of the National Academy of Sciences USA*, 89(20), 9666–9670.
- Dahl, C. D., Logothetis, N. K., & Kayser, C. (2009). Spatial organization of multisensory responses in temporal association cortex. *Journal of Neuroscience*, 29(38), 11924–11932.
- Daniel, P. M., & Whitteridge, D. (1961). The representation of the visual field on the cerebral cortex in monkeys. *Journal of Physiology*, 159(2), 203–221.

- Dartnall, H. J., Bowmaker, J. K., & Mollon, J. D. (1983). Human visual pigments: Microspectrophotometric results from the eyes of seven persons. *Proceedings of the Royal Society London B: Biological Sciences*, 220(1218), 115–130.
- DeAngelis, G. C., Cumming, B. G., & Newsome, W. T. (1998). Cortical area MT and the perception of stereoscopic depth. *Nature*, 394(6694), 677–680.
- Desimone, R., Albright, T. D., Gross, C. G., & Bruce, C. (1984). Stimulus-selective properties of inferior temporal neurons in the macaque. *Journal of Neuroscience*, 4(8), 2051–2062.
- Desimone, R., Fleming, J., & Gross, C. G. (1980). Prestriate afferents to inferior temporal cortex: An HRP study. *Brain Research*, 184(1), 41–55.
- Diamond, M. R., Ross, J., & Morrone, M. C. (2000). Extraretinal control of saccadic suppression. *Journal of Neuroscience*, 20(9), 3449–3455.
- Distler, C., Boussaoud, D., Desimone, R., & Ungerleider, L. G. (1993). Cortical connections of inferior temporal area TEO in macaque monkeys. *Journal of Comparative Neurology*, 334(1), 125–150.
- Dodd, J. V., Krug, K., Cumming, B. G., & Parker, A. J. (2001). Perceptually bistable three-dimensional figures evoke high choice probabilities in cortical area MT. *Journal of Neuroscience*, 21(13), 4809–4821.
- Fattori, P., Pitzalis, S., & Galletti, C. (2009). The cortical visual area V6 in macaque and human brains. *Journal of Physiology, Paris*, 103(1–2), 88–97.
- Felleman, D. J., & Van Essen, D. C. (1991). Distributed hierarchical processing in the primate cerebral cortex. *Cerebral Cortex*, 1(1), 1–47.
- Field, G. D., & Chichilnisky, E. J. (2007). Information processing in the primate retina: Circuitry and coding. *Annual Review of Neuroscience*, 30, 1–30.
- Field, G. D., Gauthier, J. L., Sher, A., Greschner, M., Machado, T. A., Jepson, L. H. et al. (2010). Functional connectivity in the retina at the resolution of photoreceptors. *Nature*, 467(7316), 673–677.
- Flechsig, P. (1901). Developmental (myelogenetic) localisation of the cerebral cortex in the human subject. *Lancet*, 158(4077), 1027–1030.
- Friston, K. (2005). A theory of cortical responses. *Philosophical Transactions of the Royal Society of London B: Biological Sciences*, 360(1456), 815–836.
- Fujita, I., Tanaka, K., Ito, M., & Cheng, K. (1992). Columns for visual features of objects in monkey inferotemporal cortex. *Nature*, 360(6402), 343–346.
- Fukuda, K., Saito, N., Yamamoto, M., & Tanaka, C. (1994). Immunocytochemical localization of the alpha-, beta I-, beta II- and gamma-subspecies of protein kinase C in the monkey visual pathway. *Brain Research*, 658(1–2), 155–162.
- Gallant, J. L., Braun, J., & Van Essen, D. C. (1993). Selectivity for polar, hyperbolic, and Cartesian gratings in macaque visual cortex. *Science*, 259(5091), 100–103.
- Galletti, C., Fattori, P., Gamberini, M., & Kutz, D. F. (1999). The cortical visual area V6: Brain location and visual topography. *European Journal of Neuroscience*, 11(11), 3922–3936.
- Gilaie-Dotan, S., Perry, A., Bonneh, Y., Malach, R., & Bentin, S. (2009). Seeing with profoundly deactivated mid-level visual areas: Non-hierarchical functioning in the human visual cortex. *Cerebral Cortex*, 19(7), 1687–1703.
- Goense, J. B., & Logothetis, N. K. (2008). Neurophysiology of the BOLD fMRI signal in awake monkeys. *Current Biology*, 18(9), 631–640.
- Goldman-Rakic, P. S. (1988). Topography of cognition: Parallel distributed networks in primate association cortex. *Annual Review of Neuroscience*, 11, 137–156.

- Goodale, M. A., & Milner, A. D. (1992). Separate visual pathways for perception and action. *Trends in Neurosciences*, 15(1), 20–25.
- Greschner, M., Shlens, J., Bakolitsa, C., Field, G. D., Gauthier, J. L., Jepson, L. H. et al. (2011). Correlated firing among major ganglion cell types in primate retina. *Journal of Physiology*, 589(1), 75–86.
- Gross, C. G., Rocha-Miranda, C. E., & Bender, D. B. (1972). Visual properties of neurons in inferotemporal cortex of the Macaque. *Journal of Neurophysiology*, 35(1), 96–111.
- Gu, Y., Angelaki, D. E., & Deangelis, G. C. (2008). Neural correlates of multisensory cue integration in macaque MSTd. *Nature Neuroscience*, 11(10), 1201–1210.
- Gu, Y., DeAngelis, G. C., & Angelaki, D. E. (2007). A functional link between area MSTd and heading perception based on vestibular signals. *Nature Neuroscience*, 10(8), 1038–1047.
- Guitton, D., Buchtel, H. A., & Douglas, R. M. (1985). Frontal lobe lesions in man cause difficulties in suppressing reflexive glances and in generating goal-directed saccades. *Experimental Brain Research*, 58(3), 455–472.
- Hartline, H. K. (1938). The response of single optic nerve fibers of the vertebrate eye to illumination of the retina. *American Journal of Physiology*, 121(2), 400–415.
- Hayhoe, M., & Ballard, D. (2005). Eye movements in natural behavior. *Trends in Cognitive Sciences*, 9(4), 188–194.
- Hegde, J., & Van Essen, D. C. (2007). A comparative study of shape representation in macaque visual areas v2 and v4. *Cerebral Cortex*, 17(5), 1100–1116.
- Hein, G., & Knight, R. T. (2008). Superior temporal sulcus—it's my area: Or is it? *Journal of Cognitive Neuroscience*, 20(12), 2125–2136.
- Helmholtz, H. (1910). *Handbuch der physiologischen Optik* (3rd ed.; A. Gullstrand, J. von Kries, & W. Nagel, Eds.). Hamburg: Verlag von Leopold Voss. J. P. C. Southall, 1925 (Trans.), *Helmholtz's treatise on physiological optics*, Vol. 3. New York: Optical Society of America.
- Henderson, J. M. (2003). Human gaze control during real-world scene perception. *Trends in Cognitive Science*, 7(11), 498–504.
- Hendrickson, A. E., Wilson, J. R., & Ogren, M. P. (1978). The neuroanatomical organization of pathways between the dorsal lateral geniculate nucleus and visual cortex in Old World and New World primates. *Journal of Comparative Neurology*, 182(1), 123–136.
- Hendry, S. H., & Reid, R. C. (2000). The koniocellular pathway in primate vision. *Annual Review of Neuroscience*, 23, 127–153.
- Hendry, S. H., & Yoshioka, T. (1994). A neurochemically distinct third channel in the macaque dorsal lateral geniculate nucleus. *Science*, 264(5158), 575–577.
- Herrington, T. M., Masse, N. Y., Hachmeh, K. J., Smith, J. E., Assad, J. A., & Cook, E. P. (2009). The effect of microsaccades on the correlation between neural activity and behavior in middle temporal, ventral intraparietal, and lateral intraparietal areas. *Journal of Neuroscience*, 29(18), 5793–5805.
- Hikosaka, K., Iwai, E., Saito, H., & Tanaka, K. (1988). Polysensory properties of neurons in the anterior bank of the caudal superior temporal sulcus of the macaque monkey. *Journal of Neurophysiology*, 60(5), 1615–1637.
- Hilgetag, C. C., O'Neill, M. A., & Young, M. P. (1996). Indeterminate organization of the visual system. *Science*, 271(5250), 776–777.
- Hilgetag, C. C., O'Neill, M. A., & Young, M. P. (2000). Hierarchical organization of macaque and cat cortical sensory systems explored with a novel network processor. *Philosophical Transactions of the Royal Society of London B: Biological Sciences*, 355(1393), 71–89.

- Hof, P. R., Ungerleider, L. G., Webster, M. J., Gattass, R., Adams, M. M., Sailstad, C. A. et al. (1996). Neurofilament protein is differentially distributed in subpopulations of corticocortical projection neurons in the macaque monkey visual pathways. *Journal of Comparative Neurology*, 376(1), 112–127.
- Horton, J. C. (1984). Cytochrome oxidase patches: A new cytoarchitectonic feature of monkey visual cortex. *Philosophical Transactions of the Royal Society of London B: Biological Sciences*, 304(1119), 199–253.
- Horton, J. C., & Hedley-Whyte, E. T. (1984). Mapping of cytochrome oxidase patches and ocular dominance columns in human visual cortex. *Philosophical Transactions of the Royal Society of London B: Biological Sciences*, 304(1119), 255–272.
- Horton, J. C., & Hubel, D. H. (1981). Regular patchy distribution of cytochrome oxidase staining in primary visual cortex of macaque monkey. *Nature*, 292(5825), 762–764.
- Hsieh, P. J., & Tse, P. U. (2009). Microsaccade rate varies with subjective visibility during motion-induced blindness. *PLoS One*, 4(4), e5163. doi: 10.1371/journal.pone.0005163
- Hubel, D. H., & Wiesel, T. N. (1962). Receptive fields, binocular interaction and functional architecture in the cat's visual cortex. *Journal of Physiology*, 160(1), 106–154.
- Ibbotson, M. R., Price, N. S., Crowder, N. A., Ono, S., & Mustari, M. J. (2007). Enhanced motion sensitivity follows saccadic suppression in the superior temporal sulcus of the macaque cortex. *Cerebral Cortex*, 17(5), 1129–1138.
- Ito, M., Tamura, H., Fujita, I., & Tanaka, K. (1995). Size and position invariance of neuronal responses in monkey inferotemporal cortex. *Journal of Neurophysiology*, 73(1), 218–226.
- Jellema, T., & Perrett, D. I. (2003). Cells in monkey STS responsive to articulated body motions and consequent static posture: A case of implied motion? *Neuropsychologia*, 41(13), 1728–1737.
- Juan, C. H., Shorter-Jacobi, S. M., & Schall, J. D. (2004). Dissociation of spatial attention and saccade preparation. *Proceedings of the National Academy of Sciences USA*, 101(43), 15541–15544.
- Kaas, J. H., & Lyon, D. C. (2007). Pulvinar contributions to the dorsal and ventral streams of visual processing in primates. *Brain Research Reviews*, 55(2), 285–296.
- Kalisvaart, J. P., Rampersad, S. M., & Goossens, J. (2011). Binocular onset rivalry at the time of saccades and stimulus jumps. *PLoS One*, 6(6), e20017. doi: 10.1371/journal.pone.0020017
- Koch, C., & Ullman, S. (1985). Shifts in selective visual attention: Towards the underlying neural circuitry. *Human Neurobiology*, 4(4), 219–227.
- Kourtzi, Z., & Connor, C. E. (2011). Neural representations for object perception: Structure, category, and adaptive coding. *Annual Review of Neuroscience*, 34, 45–67.
- Krauzlis, R. J. (2005). The control of voluntary eye movements: New perspectives. *Neuroscientist*, 11(2), 124–137.
- Krug, K., Cumming, B. G., & Parker, A. J. (2004). Comparing perceptual signals of single V5/MT neurons in two binocular depth tasks. *Journal of Neurophysiology*, 92(3), 1586–1596.
- Kuffler, S. W. (1953). Discharge patterns and functional organization of mammalian retina. *Journal of Neurophysiology*, 16(1), 37–68.
- Lachica, E. A., Beck, P. D., & Casagrande, V. A. (1992). Parallel pathways in macaque monkey striate cortex: Anatomically defined columns in layer III. *Proceedings of the National Academy of Sciences USA*, 89(8), 3566–3570.
- Lee, J., & Maunsell, J. H. (2009). A normalization model of attentional modulation of single unit responses. *PLoS One*, 4(2), e4651. doi: 10.1371/journal.pone.0004651

- LeVay, S., Connolly, M., Houde, J., & Van Essen, D. C. (1985). The complete pattern of ocular dominance stripes in the striate cortex and visual field of the macaque monkey. *Journal of Neuroscience*, 5(2), 486–501.
- Lewis, J. W., & Van Essen, D. C. (2000a). Mapping of architectonic subdivisions in the macaque monkey, with emphasis on parieto-occipital cortex. *Journal of Comparative Neurology*, 428(1), 79–111.
- Lewis, J. W., & Van Essen, D. C. (2000b). Corticocortical connections of visual, sensorimotor, and multimodal processing areas in the parietal lobe of the macaque monkey. *Journal of Comparative Neurology*, 428(1), 112–137.
- Liu, J., & Newsome, W. T. (2005). Correlation between speed perception and neural activity in the middle temporal visual area. *Journal of Neuroscience*, 25(3), 711–722.
- Livingstone, M. S. (1996). Ocular dominance columns in New World monkeys. *Journal of Neuroscience*, 16(6), 2086–2096.
- Livingstone, M. S., & Hubel, D. (1988). Segregation of form, color, movement, and depth: Anatomy, physiology, and perception. *Science*, 240(4853), 740–749.
- Livingstone, M. S., & Hubel, D. H. (1983). Specificity of cortico-cortical connections in monkey visual system. *Nature*, 304(5926), 531–534.
- Livingstone, M. S., & Hubel, D. H. (1984). Anatomy and physiology of a color system in the primate visual cortex. *Journal of Neuroscience*, 4(1), 309–356.
- Livingstone, M. S., & Hubel, D. H. (1987). Connections between layer 4B of area 17 and the thick cytochrome oxidase stripes of area 18 in the squirrel monkey. *Journal of Neuroscience*, 7(11), 3371–3377.
- Lu, H. D., & Roe, A. W. (2008). Functional organization of color domains in V1 and V2 of macaque monkey revealed by optical imaging. *Cerebral Cortex*, 18(3), 516–533.
- Lui, L. L., Bourne, J. A., & Rosa, M. G. (2006). Functional response properties of neurons in the dorsomedial visual area of New World monkeys (*Callithrix jacchus*). *Cerebral Cortex*, 16(2), 162–177.
- Ma, W. J., Beck, J. M., Latham, P. E., & Pouget, A. (2006). Bayesian inference with probabilistic population codes. *Nature Neuroscience*, 9(11), 1432–1438.
- Ma, W. J., Beck, J. M., & Pouget, A. (2008). Spiking networks for Bayesian inference and choice. *Current Opinion in Neurobiology*, 18(2), 217–222.
- Malach, R., Amir, Y., Harel, M., & Grinvald, A. (1993). Relationship between intrinsic connections and functional architecture revealed by optical imaging and in vivo targeted biocytin injections in primate striate cortex. *Proceedings of the National Academy of Sciences USA*, 90(22), 10469–10473.
- Malpeli, J. G., Schiller, P. H., & Colby, C. L. (1981). Response properties of single cells in monkey striate cortex during reversible inactivation of individual lateral geniculate laminae. *Journal of Neurophysiology*, 46(5), 1102–1119.
- Martinez-Conde, S., Macknik, S. L., & Hubel, D. H. (2004). The role of fixational eye movements in visual perception. *Nature Reviews Neuroscience*, 5(3), 229–240.
- Martinez-Conde, S., Macknik, S. L., Troncoso, X. G., & Dyar, T. A. (2006). Microsaccades counteract visual fading during fixation. *Neuron*, 49(2), 297–305.
- Masland, R. H. (2001). The fundamental plan of the retina. *Nature Neuroscience*, 4(9), 877–886.
- Maunsell, J. H., & van Essen, D. C. (1983a). The connections of the middle temporal visual area (MT) and their relationship to a cortical hierarchy in the macaque monkey. *Journal of Neuroscience*, 3(12), 2563–2586.

- Maunsell, J. H., & Van Essen, D. C. (1983b). Functional properties of neurons in middle temporal visual area of the macaque monkey. I. Selectivity for stimulus direction, speed, and orientation. *Journal of Neurophysiology*, 49(5), 1127–1147.
- Maunsell, J. H., & Van Essen, D. C. (1983c). Functional properties of neurons in middle temporal visual area of the macaque monkey. II. Binocular interactions and sensitivity to binocular disparity. *Journal of Neurophysiology*, 49(5), 1148–1167.
- McAdams, C. J., & Maunsell, J. H. (1999). Effects of attention on orientation-tuning functions of single neurons in macaque cortical area V4. *Journal of Neuroscience*, 19(1), 431–441.
- Miller, E. K., & Cohen, J. D. (2001). An integrative theory of prefrontal cortex function. *Annual Review of Neuroscience*, 24, 167–202.
- Milner, A. D., & Goodale, M. A. (2008). Two visual systems re-viewed. *Neuropsychologia*, 46(3), 774–785.
- Moore, T., Armstrong, K. M., & Fallah, M. (2003). Visuomotor origins of covert spatial attention. *Neuron*, 40(4), 671–683.
- Morrone, M. C., Ross, J., & Burr, D. (2005). Saccadic eye movements cause compression of time as well as space. *Nature Neuroscience*, 8(7), 950–954.
- Munoz, D. P. (2002). Commentary: Saccadic eye movements: Overview of neural circuitry. *Progress in Brain Research*, 140, 89–96.
- Murphey, D. K., Maunsell, J. H., Beauchamp, M. S., & Yoshor, D. (2009). Perceiving electrical stimulation of identified human visual areas. *Proceedings of the National Academy of Sciences USA*, 106(13), 5389–5393.
- Nassi, J. J., & Callaway, E. M. (2009). Parallel processing strategies of the primate visual system. *Nature Reviews Neuroscience*, 10(5), 360–372.
- Nealey, T. A., & Maunsell, J. H. (1994). Magnocellular and parvocellular contributions to the responses of neurons in macaque striate cortex. *Journal of Neuroscience*, 14(4), 2069–2079.
- Nelissen, K., Vanduffel, W., & Orban, G. A. (2006). Charting the lower superior temporal region, a new motion-sensitive region in monkey superior temporal sulcus. *Journal of Neuroscience*, 26(22), 5929–5947.
- Newsome, W. T., & Pare, E. B. (1988). A selective impairment of motion perception following lesions of the middle temporal visual area (MT). *Journal of Neuroscience*, 8(6), 2201–2211.
- Nowak, L. G., & Bullier, J. (1997). The timing of information transfer in the visual system. In K. S. Rockland, J. H. Kaas & A. Peters (Eds.), *Cerebral cortex: Extrastriate cortex in primates* (pp. 205–241, Vol. 12). New York: Plenum Press.
- Nowak, L. G., Munk, M. H., Girard, P., & Bullier, J. (1995). Visual latencies in areas V1 and V2 of the macaque monkey. *Visual Neuroscience*, 12(2), 371–384.
- Ohki, K., Chung, S., Ch'ng, Y. H., Kara, P., & Reid, R. C. (2005). Functional imaging with cellular resolution reveals precise micro-architecture in visual cortex. *Nature*, 433(7026), 597–603.
- Orban, G. A. (2008). Higher order visual processing in macaque extrastriate cortex. *Physiological Reviews*, 88(1), 59–89.
- Orban, G. A., Kennedy, H., & Bullier, J. (1986). Velocity sensitivity and direction selectivity of neurons in areas V1 and V2 of the monkey: Influence of eccentricity. *Journal of Neurophysiology*, 56(2), 462–480.
- Orban, G. A., Van Essen, D., & Vanduffel, W. (2004). Comparative mapping of higher visual areas in monkeys and humans. *Trends in Cognitive Neuroscience*, 8(7), 315–324.
- Osterberg, G. (1935). Topography of the layer of rods and cones in the human retina. *Acta Ophthalmologica*, 13(S6), 1–103.

- Pasupathy, A., & Connor, C. E. (1999). Responses to contour features in macaque area V4. *Journal of Neurophysiology*, 82(5), 2490–2502.
- Pasupathy, A., & Connor, C. E. (2001). Shape representation in area V4: Position-specific tuning for boundary conformation. *Journal of Neurophysiology*, 86(5), 2505–2519.
- Pasupathy, A., & Connor, C. E. (2002). Population coding of shape in area V4. *Nature Neuroscience*, 5(12), 1332–1338.
- Perrett, D. I., Hietanen, J. K., Oram, M. W., & Benson, P. J. (1992). Organization and functions of cells responsive to faces in the temporal cortex. *Philosophical Transactions of the Royal Society of London B: Biological Sciences*, 335(1273), 23–30.
- Perry, V. H., Oehler, R., & Cowey, A. (1984). Retinal ganglion cells that project to the dorsal lateral geniculate nucleus in the macaque monkey. *Neuroscience*, 12(4), 1101–1123.
- Petrides, M., & Pandya, D. N. (1999). Dorsolateral prefrontal cortex: Comparative cytoarchitectonic analysis in the human and the macaque brain and corticocortical connection patterns. *European Journal of Neuroscience*, 11(3), 1011–1036.
- Pierrot-Deseilligny, C., Milea, D., & Muri, R. M. (2004). Eye movement control by the cerebral cortex. *Current Opinion in Neurology*, 17(1), 17–25.
- Pitzalis, S., Galletti, C., Huang, R. S., Patria, F., Committeri, G., Galati, G. et al. (2006). Wide-field retinotopy defines human cortical visual area v6. *Journal of Neuroscience*, 26(30), 7962–7973.
- Pitzalis, S., Sereno, M. I., Committeri, G., Fattori, P., Galati, G., Patria, F. et al. (2010). Human V6: The medial motion area. *Cerebral Cortex*, 20(2), 411–424.
- Posner, M. I. (1980). Orienting of attention. *Quarterly Journal of Experimental Psychology*, 32(1), 3–25.
- Purushothaman, G., Khaytin, I., & Casagrande, V. A. (2009). Quantification of optical images of cortical responses for inferring functional maps. *Journal of Neurophysiology*, 101(5), 2708–2724.
- Ramón y Cajal, S. (1893). *La rétine des vertébrés*. In La Cellule (S. A. Thorpe & M. Glickstein, 1972, Trans.), *The structure of the retina* (pp. 119–257). Springfield, Illinois: Thomas.
- Reynolds, J. H., & Heeger, D. J. (2009). The normalization model of attention. *Neuron*, 61(2), 168–185.
- Riggs, L. A., Ratliff, F., Cornsweet, J. C., & Cornsweet, T. N. (1953). The disappearance of steadily fixated visual test objects. *Journal of the Optical Society of America*, 43(6), 495–501.
- Rizzolatti, G., & Matelli, M. (2003). Two different streams form the dorsal visual system: Anatomy and functions. *Experimental Brain Research*, 153(2), 146–157.
- Rizzolatti, G., Riggio, L., Dascola, I., & Umiltà, C. (1987). Reorienting attention across the horizontal and vertical meridians: Evidence in favor of a premotor theory of attention. *Neuropsychologia*, 25(1A), 31–40.
- Rockland, K. S., & Pandya, D. N. (1979). Laminar origins and terminations of cortical connections of the occipital lobe in the rhesus monkey. *Brain Research*, 179(1), 3–20.
- Roe, A. W., Fritsches, K., & Pettigrew, J. D. (2005). Optical imaging of functional organization of V1 and V2 in marmoset visual cortex. *The Anatomical Record Part A*, 287(2), 1213–1225.
- Rosa, M. G., & Tweedale, R. (2001). The dorsomedial visual areas in New World and Old World monkeys: Homology and function. *European Journal of Neuroscience*, 13(3), 421–427.
- Ross, J., & Ma-Wyatt, A. (2004). Saccades actively maintain perceptual continuity. *Nature Neuroscience*, 7(1), 65–69.
- Salzman, C. D., Britten, K. H., & Newsome, W. T. (1990). Cortical microstimulation influences perceptual judgements of motion direction. *Nature*, 346(6280), 174–177.

- Schmolesky, M. T., Wang, Y., Hanes, D. P., Thompson, K. G., Leutgeb, S., Schall, J. D., & Leventhal, A. G. (1998). Signal timing across the macaque visual system. *Journal of Neurophysiology*, 79(6), 3272–3278.
- Seltzer, B., & Pandya, D. N. (1978). Afferent cortical connections and architectonics of the superior temporal sulcus and surrounding cortex in the rhesus monkey. *Brain Research*, 149(1), 1–24.
- Seltzer, B., & Pandya, D. N. (1986). Posterior parietal projections to the intraparietal sulcus of the rhesus monkey. *Experimental Brain Research*, 62(3), 459–469.
- Seltzer, B., & Pandya, D. N. (1989). Frontal lobe connections of the superior temporal sulcus in the rhesus monkey. *Journal of Comparative Neurology*, 281(1), 97–113.
- Seltzer, B., & Pandya, D. N. (1994). Parietal, temporal, and occipital projections to cortex of the superior temporal sulcus in the rhesus monkey: A retrograde tracer study. *Journal of Comparative Neurology*, 343(3), 445–463.
- Shepherd, M., Findlay, J. M., & Hockey, R. J. (1986). The relationship between eye movements and spatial attention. *Quarterly Journal of Experimental Psychology A: Human Experimental Psychology*, 38(3), 475–491.
- Sherman, S. M., & Guillery, R. W. (2006). *Exploring the thalamus and its role in cortical function* (2nd ed.). Cambridge, MA: MIT Press.
- Shipp, S., & Zeki, S. (1995). Segregation and convergence of specialised pathways in macaque monkey visual cortex. *Journal of Anatomy*, 187(3), 547–562.
- Shmuel, A., & Grinvald, A. (1996). Functional organization for direction of motion and its relationship to orientation maps in cat area 18. *Journal of Neuroscience*, 16(21), 6945–6964.
- Shoham, D., Hubener, M., Schulze, S., Grinvald, A., & Bonhoeffer, T. (1997). Spatio-temporal frequency domains and their relation to cytochrome oxidase staining in cat visual cortex. *Nature*, 385(6616), 529–533.
- Siegel, R. M., & Read, H. L. (1997). Analysis of optic flow in the monkey parietal area 7a. *Cerebral Cortex*, 7(4), 327–346.
- Sillito, A. M., Cudeiro, J., & Jones, H. E. (2006). Always returning: Feedback and sensory processing in visual cortex and thalamus. *Trends in Neurosciences*, 29(6), 307–316.
- Sincich, L. C., Adams, D. L., & Horton, J. C. (2003). Complete flatmounting of the macaque cerebral cortex. *Visual Neuroscience*, 20(6), 663–686.
- Sincich, L. C., & Horton, J. C. (2002). Divided by cytochrome oxidase: A map of the projections from V1 to V2 in macaques. *Science*, 295(5560), 1734–1737.
- Sincich, L. C., & Horton, J. C. (2005). The circuitry of V1 and V2: Integration of color, form, and motion. *Annual Review of Neuroscience*, 28, 303–326.
- Sommer, M. A., & Wurtz, R. H. (2002). A pathway in primate brain for internal monitoring of movements. *Science*, 296(5572), 1480–1482.
- Sparks, D. L. (2002). The brainstem control of saccadic eye movements. *Nature Reviews Neuroscience*, 3(12), 952–964.
- Stoerig, P., & Cowey, A. (1997). Blindsight in man and monkey. *Brain*, 120(3), 535–559.
- Tanaka, K. (1996). Inferotemporal cortex and object vision. *Annual Review of Neuroscience*, 19, 109–139.
- Tanaka, K. (2003). Columns for complex visual object features in the inferotemporal cortex: Clustering of cells with similar but slightly different stimulus selectivities. *Cerebral Cortex*, 13(1), 90–99.
- Tanaka, K., Saito, H., Fukada, Y., & Moriya, M. (1991). Coding visual images of objects in the inferotemporal cortex of the macaque monkey. *Journal of Neurophysiology*, 66(1), 170–189.

- Tanji, J., & Hoshi, E. (2008). Role of the lateral prefrontal cortex in executive behavioral control. *Physiological Reviews*, 88(1), 37–57.
- Thier, P., & Ilg, U. J. (2005). The neural basis of smooth-pursuit eye movements. *Current Opinion in Neurobiology*, 15(6), 645–652.
- Thompson, K. G., Biscoe, K. L., & Sato, T. R. (2005). Neuronal basis of covert spatial attention in the frontal eye field. *Journal of Neuroscience*, 25(41), 9479–9487.
- Tootell, R. B., Dale, A. M., Sereno, M. I., & Malach, R. (1996). New images from human visual cortex. *Trends in Neurosciences*, 19(11), 481–489.
- Tootell, R. B., Tsao, D., & Vanduffel, W. (2003). Neuroimaging weighs in: Humans meet macaques in “primate” visual cortex. *Journal of Neuroscience*, 23(10), 3981–3989.
- Troncoso, X. G., Macknik, S. L., Otero-Millan, J., & Martinez-Conde, S. (2008). Microsaccades drive illusory motion in the Enigma illusion. *Proceedings of the National Academy of Sciences USA*, 105(41), 16033–16038.
- Tsao, D. Y., Freiwald, W. A., Knutsen, T. A., Mandeville, J. B., & Tootell, R. B. (2003). Faces and objects in macaque cerebral cortex. *Nature Neuroscience*, 6(9), 989–995.
- Tsao, D. Y., Freiwald, W. A., Tootell, R. B., & Livingstone, M. S. (2006). A cortical region consisting entirely of face-selective cells. *Science*, 311(5761), 670–674.
- Tsao, D. Y., Moeller, S., & Freiwald, W. A. (2008). Comparing face patch systems in macaques and humans. *Proceedings of the National Academy of Sciences USA*, 105(49), 19514–19519.
- Tsunoda, K., Yamane, Y., Nishizaki, M., & Tanifuji, M. (2001). Complex objects are represented in macaque inferotemporal cortex by the combination of feature columns. *Nature Neuroscience*, 4(8), 832–838.
- Uka, T., & DeAngelis, G. C. (2006). Linking neural representation to function in stereoscopic depth perception: Roles of the middle temporal area in coarse versus fine disparity discrimination. *Journal of Neuroscience*, 26(25), 6791–6802.
- Ungerleider, L. G., & Desimone, R. (1986). Cortical connections of visual area MT in the macaque. *Journal of Comparative Neurology*, 248(2), 190–222.
- Ungerleider, L. G., Galkin, T. W., Desimone, R., & Gattass, R. (2008). Cortical connections of area V4 in the macaque. *Cerebral Cortex*, 18(3), 477–499.
- Ungerleider, L. G., & Mishkin, M. (1982). Two cortical visual systems. In D. J. Ingle, R. J. W. Mansfield & M. S. Goodale (Eds.), *The analysis of visual behaviour* (pp. 549–586). Cambridge, MA: MIT Press.
- van Dam, L. C., & van Ee, R. (2006). The role of saccades in exerting voluntary control in perceptual and binocular rivalry. *Vision Research*, 46(6–7), 787–799.
- Van Essen, D. C., Maunsell, J. H., & Bixby, J. L. (1981). The middle temporal visual area in the macaque: Myeloarchitecture, connections, functional properties and topographic organization. *Journal of Comparative Neurology*, 199(3), 293–326.
- Van Horn, S. C., Erisir, A., & Sherman, S. M. (2000). Relative distribution of synapses in the A-laminae of the lateral geniculate nucleus of the cat. *Journal of Comparative Neurology*, 416(4), 509–520.
- Walker, A. E. (1940). A cytoarchitectural study of the prefrontal area of the macaque monkey. *Journal of Comparative Neurology*, 75(1), 59–86.
- Weliky, M., Bosking, W. H., & Fitzpatrick, D. (1996). A systematic map of direction preference in primary visual cortex. *Nature*, 379(6567), 725–728.
- Wiesel, T. N., & Hubel, D. H. (1974). Ordered arrangement of orientation columns in monkeys lacking visual experience. *Journal of Comparative Neurology*, 158(3), 307–318.

- Wittenberg, M., Bremmer, F., & Wachtler, T. (2008). Perceptual evidence for saccadic updating of color stimuli. *Journal of Vision*, 8(14), 9. doi: 10.1167/8.14.9
- Xiao, Y., & Felleman, D. J. (2004). Projections from primary visual cortex to cytochrome oxidase thin stripes and interstripes of macaque visual area 2. *Proceedings of the National Academy of Sciences USA*, 101(18), 7147–7151.
- Yabuta, N. H., & Callaway, E. M. (1998). Functional streams and local connections of layer 4C neurons in primary visual cortex of the macaque monkey. *Journal of Neuroscience*, 18(22), 9489–9499.
- Yabuta, N. H., Sawatari, A., & Callaway, E. M. (2001). Two functional channels from primary visual cortex to dorsal visual cortical areas. *Science*, 292(5515), 297–300.
- Yamane, Y., Carlson, E. T., Bowman, K. C., Wang, Z., & Connor, C. E. (2008). A neural code for three-dimensional object shape in macaque inferotemporal cortex. *Nature Neuroscience*, 11(11), 1352–1360.
- Yarbus, A. (1967). *Eye movements and vision*. New York: Plenum Press.
- Young, M. P. (1992). Objective analysis of the topological organization of the primate cortical visual system. *Nature*, 358(6382), 152–155.
- Zaidi, F. H., Hull, J. T., Peirson, S. N., Wulff, K., Aeschbach, D., Gooley, J. J. et al. (2007). Short-wavelength light sensitivity of circadian, pupillary, and visual awareness in humans lacking an outer retina. *Current Biology*, 17(24), 2122–2128.
- Zeki, S. (1996). Are areas TEO and PIT of monkey visual cortex wholly distinct from the fourth visual complex (V4 complex)? *Proceedings of the Royal Society of London B: Biological Sciences*, 263(1376), 1539–1544.

Early views on binocular rivalry

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Contributions from 19th Century scholars to binocular rivalry research are well recognized, however, observations concerning the phenomenon commenced centuries earlier and suggest a rich seam of research that is much less well known. This chapter discusses these early investigations, along with conflicting views and observations thereafter. We also discuss the early application of notions of attention and consciousness to rivalry. Such notions have more recently been the subject of concerted investigation into distinguishing brain activity mediating the rivaling states from that underlying visual stimulation. Observations in the literature that preceded this key principle are discussed. We also trace the rivalry studies that followed and note their relevance to current thinking on the phenomenon.

Introduction

The sensations of the senses are tokens for our consciousness, it being left to our intelligence to learn to comprehend their meaning.
(Helmholtz, 1925, p. 533)

Our experience of the world, as mediated by the senses, is stable and unitary. That is, we are conscious of a single and stable external world. This occurs despite the fact that our bodies and body parts move relative to the world and our sense organs are paired. It is this latter aspect of unitary visual experience, mediated by spatially displaced eyes, that we will examine. Indeed, appreciating the existence of binocular rivalry has its origins in departures from singleness of vision. For example, Aristotle discussed binocular single vision, but it tended to be in the context of its breakdown (diplopia) either by distorting one eye or in strabismus. More than two thousand years later, the inventor of the stereoscope, Charles

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Wheatstone, wrote: “No question relating to vision has been so much debated as the cause of the single appearance of objects seen by both eyes” (Wheatstone, 1838, p. 387). He also examined binocular rivalry using the stereoscope. A paradox in the history of research on binocularity is that rivalry was examined experimentally before the involvement of retinal disparity in depth perception was demonstrated (by Wheatstone). Nor was the stereoscope the first binocular instrument, but the earlier ones were enlisted to examine the experience of rivalry rather than depth.

Binocular vision in antiquity

In binocularity we find one of the supremely psychological phenomena of vision, hence the constant interest that has been given to it since antiquity. There are many aspects to binocularity including the pathways from the two eyes to the brain, the combination of colors and contours, binocular rivalry, eye movements as well as binocular single and double vision. Binocular single vision has been discussed at least since the time of Aristotle.

Aristotle did discuss binocular single vision, but it tended to be in the context of its breakdown (double vision). He described one of the most common ways of inducing double vision – by gently pushing one eye with the finger. Singleness of vision with two eyes has been examined experimentally since Ptolemy (Smith, 1996), who defined lines of visual correspondence for the two eyes. The concept is probably embodied in the mythological cyclops who forged thunderbolts for Zeus, and in the Homeric *Odyssey*, where cyclops was a one-eyed giant. The location of the single eye was central in the forehead, and the locus of binocular visual direction is now referred to as the cyclopean eye. Ptolemy effectively defined the plane of binocular singleness as passing through the fixation point and perpendicular to the common axis. This was repeated by Galen (May, 1968), Ibn al-Haytham (also known as Alhazen, 1572), and by Aguilonius (1613), who named and defined it as the horopter. On the basis of his observations, Aguilonius proposed that singleness of vision is a consequence of fusion between the corresponding images in each eye.

Theoretical issues have directed, and been derived from, observations on binocular rivalry, eye dominance, and strabismus, and comparisons between tasks performed with one or two eyes similarly conflate observation and theory. As with many other aspects of visual perception, binocularity has been analyzed in terms of phenomenology and optics.

Over two thousand years ago, Euclid examined binocular vision with the consistency that he had adopted for other aspects of spatial vision – it could be reduced to optical projections. In fact, his discussion of the projections from two

eyes was rather cursory, being restricted to three different sizes of sphere with respect to the interocular distance. During the 2nd Century A.D. the situation was transformed by Ptolemy in optics, and by Galen in ophthalmology. The difference between Euclid and Ptolemy is marked, and the latter can be considered as paving the way for modern approaches to binocular vision (see Howard & Rogers, 2012; Howard & Wade, 1996; Wade & Ono, 2012). Ptolemy carried out controlled observations of the perceived locations of vertical cylinders; from these he specified the conditions for singleness of vision, the distinction between crossed and uncrossed disparities, and the direction in which objects are seen with two eyes. Remarkably little was added to Ptolemy's analysis until the 17th Century; it was extended somewhat by Ibn al-Haytham who profited considerably from a thorough knowledge of Ptolemy's work. Ptolemy probably influenced his near contemporary, Galen, who pursued similar lines of enquiry. Galen took Ptolemy's demonstrations into the real world: rather than viewing cylinders arranged on a board, Galen looked at cylinders, or columns, laid out before him.

The essence of investigating binocular vision was distilled from the methods adopted for stimulating the two eyes. An ancient technique involved fixating on one object located further from the eyes than another. This method was introduced by Ptolemy, and elaborated by Ibn al-Haytham, before its widespread adoption in the 17th and 18th Centuries. Another technique involved placing a septum between the eyes, so that peripheral objects could be seen by one eye but not the other, a method described by Galen.

Ptolemy appreciated that monocular and binocular visual directions were not necessarily the same. In order to confirm this empirically, he constructed a board on which he could place vertical rods at different distances in the midline. There followed a description of one of the most commonly used examples of crossed and uncrossed visual directions: with fixation on the far rod, the nearer one appeared double, and to the left with the right eye and to the right with the left eye; the reverse occurred with fixation on the nearer rod. Essentially the same demonstration is now more frequently made with two fingers, rather than rods, held at different distances from the eyes. Ptolemy stated that singleness of vision with two eyes occurred when the two visual directions corresponded, thus introducing the concept of correspondence into binocular vision. He modified his board to take three rods, in the manner that is shown in the accompanying diagram (Figure 1), and found that objects appeared single to two eyes when they were in the same plane as the fixation point. These facts were interpreted in terms of the visual axes and the common axis. Ibn al-Haytham made a similar board on which he placed wax cylinders, but of different colors.

The notion of rivalry between the two eyes was given empirical support by Giambattista della Porta (1593) in his book *De Refractione*. When considering

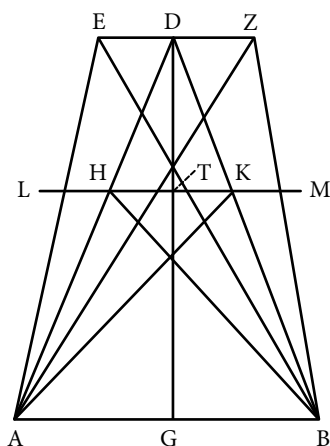


Figure 1. Ptolemy's board for studying binocular vision; the eyes were located at A and B. He wrote: "If we join lines *ae*, *az*, *zb*, *eb*, *ta*, *tb*, *bh*, *ak*, any of *e*, *d*, and *z* will appear in one location, since *ad* and *bd* are the visual axes, and the visual lines which converge on *e* and *z* are corresponding visual lines because *ae* corresponds to *be* and *az* corresponds to *bz*. But *h* and *k*, will appear in one location *t*, since *ah* and *bk* are visual axes. Because *bh* and *ak* are non-corresponding visual lines *h* and *k* will appear at points *l* and *m*: Because visual lines *at* and *bt* are non-corresponding, point *t* will appear in two locations *h*, *k*." (Lejeune, 1956, pp. 104–105)

singleness of vision with two eyes, he adopted the theory that we only use one at once, and this could be simply demonstrated:

Nature has given us two eyes, one on the right and the other on the left, so that if we are to see something on the right we use the right eye, and on the left the left eye. It follows that we always see with one eye, even if we think both are open and that we see with both. We may prove it by these arguments: To separate the two eyes, let us place a book before the right eye and read it; then someone shows another book to the left eye, it is impossible to read it or even see the pages, unless for a short moment of time the power of seeing is taken from the right eye and borrowed by the left. (Porta, 1593, pp. 142–143)

Porta's view became known as suppression theory, and suppression is now known not to be restricted to an eye but can operate within parts of the eyes. The contrary view, that we fuse or combine the images from each eye, was proposed soon after by Aguilonius. Since the early 17th Century, the study of binocular vision has often been seen as a contrast, even a conflict, between suppression and fusion theories. Although Porta applied suppression theory to spatial vision, experimental studies from the 18th Century were generally concerned with color rather than contour rivalry.

Binocular color rivalry: From color mixture to perceptual grouping

The combination of different colors presented to corresponding regions of each retina became an issue of theoretical importance following Isaac Newton's (1704) experiments on color mixing: are colors combined by either eye as they are when selected from the spectrum? It was Jean Théophile Desaguliers (1716), an advocate of Newtonian optics, who was amongst the first to draw attention to the phenomenon of color rivalry. He applied a method of binocular combination that became widely employed in other studies of binocular vision, namely, placing an aperture in such a position that two adjacent objects were in the optical axes of each eye (Figure 2). In particular, he showed that dichoptically presented colored lights, or patches of color, rival rather than combine as in Newton's experiments on color mixing.

Desaguliers' method was applied by John Taylor (1738), who added the refinement of placing colored glasses in front of candle flames; he found that colors combined rather than engaged in rivalry. Etienne-François Du Tour (1760) provided a clear description of binocular color rivalry. He achieved dichoptic combination by another means: he placed a board between his eyes and attached blue and yellow fabric in equivalent positions on each side, or the fabric was placed in front of the fixation point (Figure 3). When he converged his eyes to look at them they did not mix but alternated in color. That is, his visual awareness fluctuated between the colors presented to the two eyes.

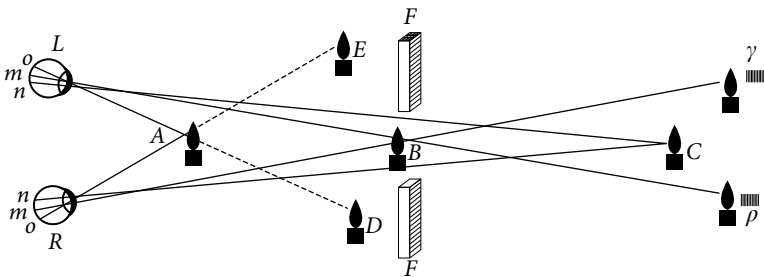


Figure 2. Desaguliers's (1716) diagram illustrating how different stimuli could be presented to corresponding parts of each eye: "But if instead of the Candles, ρ be a piece of red Silk, and γ a piece of green Silk, the same Position of the Eyes will make the Image at B, appearing like a red and green Spot together without a Mixture of Colours. If ρ be a red hot Iron, and γ a Candle of Sulphur, the Phænomenon will be more distinct." (Desaguliers, 1716, p. 451)

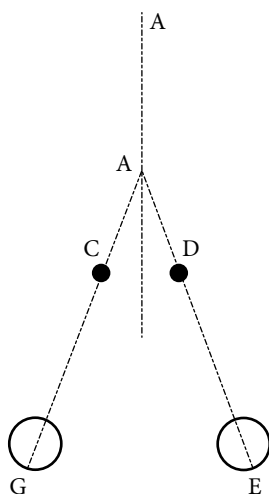


Figure 3. Du Tour's (1760) method of combining colored patches in order to examine rivalry. He wrote: "I glued a round patch of blue taffeta of about an inch in diameter onto one side of a sheet of cardboard, and on the opposite side, another patch of yellow taffeta of the same size, so that the two were exactly back to back. I placed the cardboard against my nose in a vertical plane and perpendicular to my face. Through my right eye I saw the blue patch and not the yellow, and vice versa for my left eye. Thus each one of the two patches formed separate images; blue in my right eye, yellow in my left eye. However, I was aware of only one patch. If that awareness was the result of the simultaneous combination of two images, should not the patch have seemed to be green? Now I was unable to discern the least tint of green. That single patch I saw sometimes appeared blue, sometimes yellow, apparently according to the rays of light from one or the other patches striking my eyes with more energy. Also, sometimes the patch appeared partly blue and yellow.... If one looks with both eyes at a point A, four or six inches away, and places on the optical axes EA, GA, short of the point A and their intersection, two small pieces of taffeta, one blue at D, the other yellow at C, one sees only a single spot of blue or yellow or a combination of colours, and never green." (pp. 514–515)

Du Tour argued that with slight differences in curvature between the eyes, rather than achieving complete fusion, one of the presented colors (or objects) projected more clearly to one eye at a given time than the other color to the second eye. During simultaneous presentation, the two different impressions on the retinas would meet in the brain where the optic nerves came together. He proposed that the more distinct impression then affected the mind and became visible, whereas the other less clearly defined impression would not have such an effect or did not draw the mind's attention. He also argued, in keeping with the suppression theory,

that during simultaneous presentation of two different colors, the eyes acted in alternation to see one and then the other image. Such alternate and intermittent action of the two eyes was to avoid fatigue in both simultaneously, through inhibiting one eye while the other eye viewed the presented object.

Du Tour also applied the method of observing the colors through an aperture, as adopted by Desaguliers, and obtained the same outcome. A similar technique was applied by Giovanni Battista Venturi (1802), who compared the combination of sounds to two ears with that of colors presented to different eyes (see Wade & Ono, 2005). He placed blue and yellow papers next to one another on a table and over-converged his eyes to combine them: "I have repeated this experiment often and with care, and I have never experienced a third colour from the two overlapping colours" (translated from Venturi, 1802, p. 389). This was taken to be evidence that the nerves from the two eyes do not combine in the brain.

Yet another technique was to view different colored objects through two long tubes, one in each optic axis. This method was used by Thomas Reid (1764), and he saw the colors combined, although his description was not without its ambiguity: the colors were not only said to be combined, but also one "spread over the other, without hiding it" (p. 326). That is, a single color was not seen, which was also the conclusion of William Charles Wells (1792), Charles Bell (1803) and Ernst Heinrich Weber (1834). Wells amplified this by noting that one or other color was dominant during this 'transparent' phase. Haldat (1806) reported that differently colored liquids placed in prisms before each eye appeared as an intermediate color.

The complexity of the binocular percepts is evident from Johannes Müller's (1838) account: sometimes one or the other color will predominate, whereas at other times "nebulous spots" of one color are visible on the other. Fechner (1861) examined rivalry with colored glasses and with the stereoscope and noted the importance of attention in the alternations that occurred. He also pointed to the similarities of the processes involved in binocular and binaural combination (see Wade & Deutsch, 2008; Wade & Ono, 2005).

One of the problems associated with most of the techniques described above is that the observer needed to uncouple accommodation from convergence. Wheatstone dispensed with these difficulties by viewing different colors with the stereoscope. The outcome was binocular rivalry, but this was either of the whole monocular stimulus or local parts of the two colored discs:

If a blue disc be presented to the right eye and a yellow disc to the corresponding part of the left eye, instead of a green disc which would appear if these two colours had mingled before their arrival at a single eye, the mind will perceive the two colours distinctly one or the other alternately predominating either partially or wholly over the disc.

(Wheatstone, 1838, pp. 386–387)

Thus, Wheatstone was describing the fluctuations in the visibility of the different colors while no changes took place in the colors themselves. The changes in visual awareness corresponded to his inferential theory of vision in which binocularity was considered to be cognitive rather than physiological. Hermann Helmholtz followed Wheatstone theoretically (as is evident from the quotation at the head of this chapter) and he also embraced color rivalry as evidence in its favor. His antagonist, Ewald Hering (1861), argued for a physiological interpretation of rivalry and much of the dispute surrounded the visibility of yellow from dichoptic combinations of red and green. Hering did establish a number of stimulus parameters that influenced rivalry: small color patches yielded more clear-cut rivalry and brief stimulus presentation favored combination rather than competition.

In the early 1860s, binocular rivalry with color images was also investigated by Joseph Towne, a medical sculptor at Guy's Hospital with an interest in binocular vision. In particular, he first sought to understand the relationship between corresponding retinal areas during rivalry using complementary stimulus pairs. Color pairings were introduced to the complementary stimuli. With vertically split discs, the outer semicircle viewed by each eye was the same color while the inner semicircles were another color. When red and black were used (Figure 4a), the colors combined and alternations were not observed. With blue and yellow however (Figure 4b), he observed interocular grouping during binocular rivalry, or stimulus rivalry:

In the next experiment, the two temporal halves of the retinae are submitted to yellow, while the two nasal halves are submitted to blue; these colours being disharmonic, it follows that disharmonic colours fall on corresponding parts of the two retinae, the result being that the colours antagonise, first one, then the other being seen, with now or then an iridescent appearance over the whole field, occasioned by the gleaming of one colour over the surface of the other colour. The disturbance occasioned by this means is sometimes very striking; the four halves of the retinae appear to be thrown into separate action, so that their respective images are brought together, but not united; and for a second they appear as if struggling, so to speak, for their respective places. Under these circumstances, the changes which occur are remarkable; at one moment there will be a complete disc of yellow, the blue being altogether lost; at the next the yellow will entirely disappear over exactly one half of the disc, so that the resultant image is one half yellow, the other half blue, then the reverse, and so on, with constant alternations.

(Towne, 1863, p. 121)

With the observations gained from such stimulus presentation, Towne acknowledged the essential utility provided by the stereoscope in their demonstration. In further experimentation, one eye viewed an image of a star composed of yellow

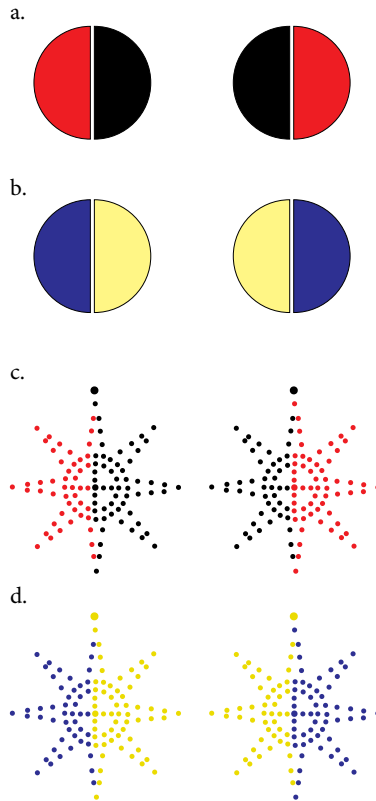


Figure 4. Color stimuli used by Towne to study corresponding retinal areas during binocular rivalry. (a) The two discs are “so arranged that the different colours fall upon *corresponding* parts of the two retinae; *red and black harmonize, and the two co-mingle*” while in (b), “[t]hese colours *do not harmonize*; the result is *antagonism* of the two impressions, and that the colours *do not mingle*” (figures reprinted from Towne, 1863, Plate II). (c) “These are figures of stars in which identical points of the retinae are simultaneously submitted to harmonic colours. The blending of the two colours may be observed by comparing the spots that form the *star* with the larger spot, which, when viewed in the stereoscope, appears over the resultant image” (figure reprinted from Towne, 1864; Plate, Fig. 1). When these stimuli were viewed dichoptically, a single stable star of a black-red color mixture was observed. In contrast, perceptual alternations occurred with their blue and yellow counterpart (d), which were not depicted in Towne’s (1864) paper and have been illustrated here based on (c).

dots in one vertically symmetrical half and blue dots in the remaining half, while the other eye viewed the complementary image (Figure 4d). What ensued was concurrent binocular combination and rivalry between local zones (i.e., piecemeal rivalry), rather than regular alternations between global coherent percepts as might be expected from his previous observations:

Over the greater portion of the resultant image, the spots will appear double, the blue and yellow dots lying side by side, while in other parts of the figure there will be constant alternation; *but in no part will the discordant colours blend, or the two images be permanently superposed*; in short, the result may be thus broadly stated – that we have in this instance a double star, or rather a star composed of double rows of spots, excepting where the images occasionally alternate.

(Towne, 1864, pp. 129–130)

Binocular contour rivalry: Conflicting views and philosophical traditions

Binocular single vision occurs when similar images are projected to corresponding parts of each eye. As David Brewster (1844) noted, it can be difficult to distinguish between seeing two similar things and seeing their combination. No such doubts arise about binocular rivalry, which is one of the reasons why suppression theory has been so ardently supported. When dissimilar images are presented to corresponding areas of each eye they do not combine, but compete. Binocular contour rivalry is more clear-cut; the debate has been about whether alternation between the views of each eye occurs rather than whether rivalry exists. In the 2nd Century, Ptolemy arranged stimuli on a board in a manner that would have produced binocular rivalry, but his description of the outcome was ambiguous (see Howard & Wade, 1996; Wade, 1983, 1998).

As noted above, Porta (1593) placed pages of different books before each eye, and stated that the right eye was dominant. Porta was not in a position to relate his observations to functioning within the visual system because he did not have an adequate understanding of the optics of the eye. This was provided a decade later by Johannes Kepler (1604), who described how images are brought to a focus on the eye. The 17th Century heralded the scientific renaissance. The scientific methods that had proved so successful in the physical and chemical sciences were seen as relevant to life processes. The anatomy of the senses and the brain were gradually elucidated, and these anatomical structures were related to function. In vision, Christoph Scheiner (1619) integrated Kepler's dioptrics with an accurate description of the gross anatomy of the mammalian eye. Thereafter, phenomena like binocular single vision could be related to the optics and anatomy of the eye. In addition, the lessons of science were absorbed into philosophy. René Descartes

(1637, 1664) did distinguish between the mechanical body and the immaterial mind, but his application of scientific rigor to understanding the senses set psychology on a course from which it has seldom wavered. His analysis of binocular vision posited its singleness in a singular organ in the brain, the pineal body. Corresponding points on each retina projected to the same locations on the pineal body, thus defining single vision (see Figure 5, left). The spur to studying binocular vision by his opponents was to attack this theory. For example, Sébastien Le Clerc (1679) argued that retinal disparity would not yield single vision:

Monsieur Descartes having considered that according to his principles external objects should make an impression on both eyes, and that the soul nevertheless had only one perception believed that the images of the same object found in the two eyes are reunited in the brain; but if this great genius had reflected a little more on the demonstrations which he gave in his Treatise on Man, he would have recognised that the images in the two eyes although produced by the same object, are different, and because of these differences their reunion is impossible.

(Le Clerc, 1679, pp. 44–46)

Le Clerc provided clear diagrams of retinal disparities but he did not see the link between disparities and depth; rather he used disparities to disparage Descartes' theory. Le Clerc (1712) went on to examine binocular rivalry, adopting the method of over-convergence to present different figures to each eye, and remarked that alternation took place. Du Tour (1761) held a prism in front of one eye, and produced the clearest early description of contour rivalry: either the stimulus presented to one or the other eye would be visible, or some mixture of the two views would present itself.

If one applies a prism held vertically before one of the eyes, so only refracted rays of light are passed to that eye, and with the other eye open, it is certain that different objects will be projected on corresponding portions of the two retinas.... sometimes I would see only objects projected in the bare eye, sometimes only those in the eye covered by the prism, and sometimes the objects projected in one would seem to me to intermingle with the objects projected in the other.

(Du Tour, 1761, p. 500)

Descartes relied on Andreas Vesalius (1543) for his visual anatomy, whereas Newton performed his own dissections, although they were not published. He alluded to these in Query XV of his *Opticks* where he asked whether the fibers from corresponding regions of each eye were united before they reached the brain, adding a telling reflection on species differences in the visual pathways to the brain. In fact, he had carried out experiments on optic nerves around 1682 but he did not publish details of them; his notes were later printed by Joseph Harris (1775) and Brewster (1855). Newton conducted experiments on optic nerves; he

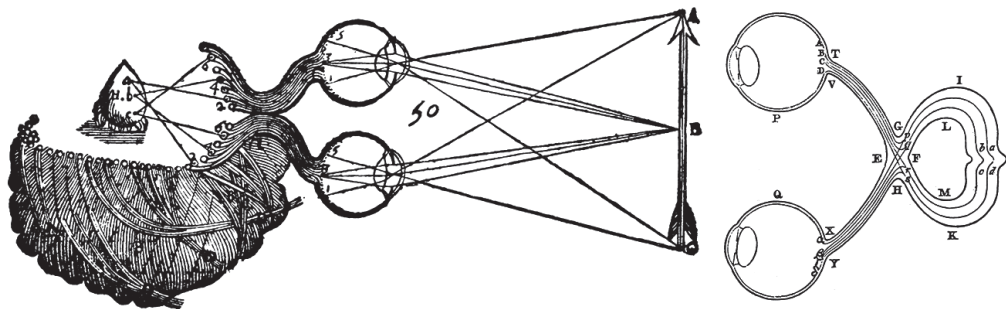


Figure 5. Left, Descartes' (1664) diagram of the visual pathways, with union of corresponding fibers in the pineal body: "the spirits that tend to enter each of the tubules 2, 4, 6, and the like do not come indifferently from all points on the surface of the gland *H* but each from a particular point; those that come from point *a* of this surface, for example, tend to enter tube 2, those from points *b* and *c* tend to enter tubes 4 and 6, and so on. As a result, at the same instant that the orifices of these tubes enlarge, the spirits begin to leave the facing surfaces of the gland more freely and rapidly than they otherwise would. And [suppose] that just as [*a*] the different ways in which tubes 2, 4, and 6 are opened trace on the internal surface of the brain a figure corresponding to that of object *ABC*, so [*b*] [the different ways] in which the spirits leave the points *a*, *b*, and *c* trace that figure on the surface of this gland" (Hall, 1972, p. 85). Right, Newton's pathways (from a diagram in Brewster, 1855) displaying partial decussation. He wrote: "though one thing may appear in two places by distorting the eyes, yet two things cannot appear in one place. If the picture of one thing fall upon *A*, and another upon *a* [its corresponding point in the other eye], they may both proceed to *p* [in the optic chiasm], but no farther; they cannot both be carried on the same pipes *pa* into the brain; that which is strongest or most helped by phantasy will there prevail, and blot out the other" (Harris, 1775, p. 110).

made the first representation of partial decussation at the optic chiasm (shown in Figure 5, right), and proposed a theory of binocular single vision based upon it. Thus, Newton's anatomy specified that rivalry would result from stimulating corresponding points with different stimuli.

Thus, there were experimental philosophers, like Newton, who wished to remain in contact with the phenomena they examined. For them observation and experiment provided the bedrock of science. Newton did not desire to entertain hypotheses – principles that could not be supported by experiment. Rationalist philosophers, like Descartes, were not so constrained, although he did add to the mechanistic approach in a multitude of ways. The anatomy of the senses received benefits from both shades of philosopher, and this was clearly displayed in binocular vision. Both Descartes and Newton brought their brilliance to bear on binocular combination. However, they took the nerves in different directions. Descartes combined them in the pineal body, sacrificing anatomy to philosophy. Newton observed and experimented on the pathways from eyes to the brain, or sensorium, where the signals coalesced. Neither could be confident in their conclusions because so little was known about nerves and their central connections.

While there is no doubt about Descartes' central role in early views on binocular vision and consciousness, it was not until two centuries later that the notion of consciousness was applied specifically to binocular rivalry. In the late 17th Century the term 'consciousness' had become well established in English philosophy writings, while its German counterpart 'Bewusstsein' entered the European lexicon a few decades thereafter (see Palaia, 2012). Further attacks on Descartes' rationalist philosophy issued from Newton's friend, John Locke (1690), who was a leading proponent of British empiricism (or sensism). Locke maintained that knowledge and understanding was acquired only through sensory experience. Therefore, rejecting a distinction between sensory perception and consciousness, it was considered that

...perception and consciousness are one and the same thing, though they have two distinct names. As far as one looks at this operation as an impression in the mind, one can keep the term perception; as far as one is aware of it, one can call it consciousness. (Jaucourt, 1753; translated in Palaia, 2012, p. 303)

The empiricist tradition was subsequently followed by Wheatstone, Helmholtz and others in examining binocular vision and binocular rivalry. Explicit reference to consciousness however, in writings about rivalry, was not made until the mid-1800s and not considered more widely until the end of that century (see below).

In the 19th Century, psychology emerged as the interface between philosophy and the natural sciences. It addressed the eternal questions of philosophy by deed rather than by word: it embraced the scientific method to frame the questions

empirically. The methods adopted initially were adapted from other sciences, most notably from physics and physiology. From the mid-19th Century new methods were developed for studying perception and performance that distinguished psychology from both philosophy and physiology. Nonetheless, the 17th and 18th Centuries did make inroads into the study of the senses, and it is from these that the edifice of 19th Century psychology was erected. Vision provides the lens through which this history can be observed, and it was instruments invented to study vision that transformed psychology into an experimental discipline.

The stereoscope, perhaps more than any other instrument, ushered in the era of experimentation to vision. It is a simple optical device that presents slightly different figures to each eye; if these figures have appropriate horizontal disparities then depth is seen. It could also be adapted to study binocular color or contour rivalry. All the problems with previous devices were removed when radically different shapes are viewed with the aid of a stereoscope (Figure 6). Wheatstone (1838) surrounded two letters by equivalent circles (to ensure binocular alignment) and noted the rivalry that took place. Not only did he describe the alternation, but he also examined a stimulus variable (illumination) that could favor one stimulus over the other:

If *a* and *b* are each presented at the same time to a different eye, the common border will remain constant, while the letter within it will change alternately from that which would be perceived by the right eye alone to that which would be perceived by the left eye alone. At the moment of change the letter which has just been seen breaks into fragments, while fragments of the letter which is about to appear mingle with them, and are immediately after replaced by the entire letter. It does not appear to be in the power of the will to determine the appearance of either of the letters, but the duration of the appearance seems to depend on causes which are under our control: thus if the two pictures be equally illuminated, the alternations appear in general of equal duration; but if one picture be more illuminated than the other, that which is less so will be perceived during a shorter time.

(Wheatstone, 1838, p. 386)

After Wheatstone's article was translated into German (Wheatstone, 1842), its impact was dramatic. On the one hand, it argued against the prevailing view of single vision advanced by Gerhard Vieth (1818) and Müller (1826), and on the other it presented an empiricist interpretation of binocular vision. It opened up new ways of examining and analyzing combination and competition between the eyes. William James (1890) said that Wheatstone's first paper "contains the germ of all the methods applied since to the study of optical perception" (p. 226). Fourteen years later, Wheatstone (1852) published his second article in which he described and illustrated an adjustable mirror stereoscope, a prism stereoscope,

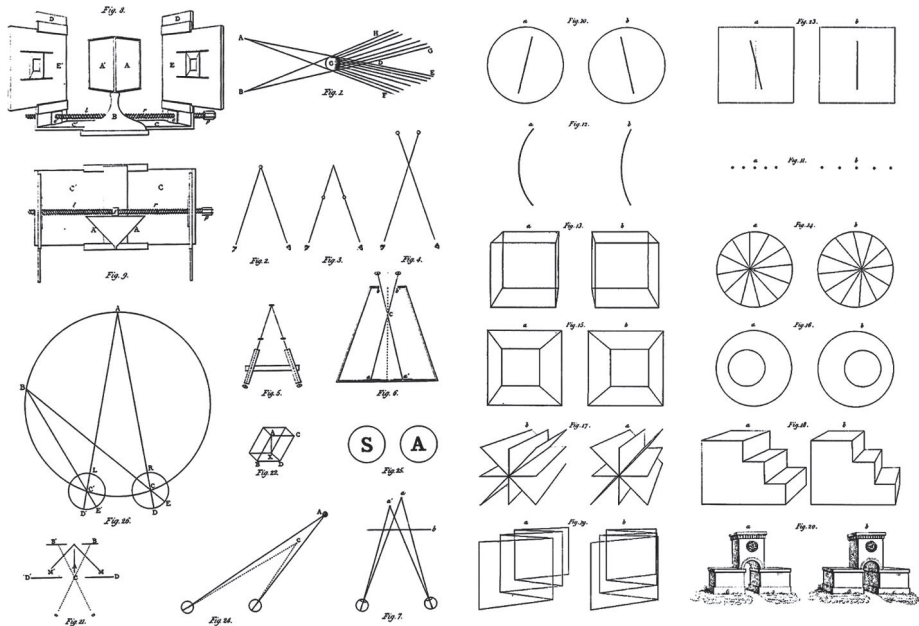


Figure 6. Two plates from Wheatstone (1838) showing the mirror stereoscope and the stimuli he observed with it. Rivalry was examined with Fig. 25 consisting of different letters (S and A) which were presented in equivalent circles, ensuring binocular alignment.

and a pseudoscope for reversing disparities. It was in this article that he drew an explicit distinction between mental and physical philosophy; that is, between psychology and physics, and he placed binocular vision in the province of psychology.

One of those to take up the challenge posed by Wheatstone's work was Peter Ludvig Panum (1858). Not only did he introduce the concept of fusional areas that now bear his name, but he ushered in the stimuli that have been employed more than others for the study of binocular rivalry – orthogonal gratings (Figure 7). He remarked that gratings produced the strongest rivalry and that it was difficult to represent the ensuing changes: occasionally complete gratings were briefly visible but the dynamically varying, mosaic-like composites were seen most of the time. Panum took these to be indices of the physiological processes at play in binocular vision:

Following the lawful rules that have been stated, the mosaic-like filling of the general visual field, combined with partial fusion of the impressions taking place, arises from neither psychological causes, attention, imagination or the like, nor from any dread of double images, nor from a total alternative paralysis of the two retinas, but from very characteristic means of perception or sensory energies emanating from the simultaneous action of the excitation of corresponding retinal points on the central organ of vision (in the brain).

(Panum, 1858, pp. 93–94)

Panum's fusional areas were seen as a way of salvaging Müller's concept of identical retinal points from Wheatstone's attack on it. One of the first German sensory physiologists to defend Müller's concept was Brücke (1841): he argued that stereoscopic vision occurred as a consequence of directing the visual axes successively to different parts of an object. This was so despite Wheatstone's (1838) description of stereoscopic vision with afterimages, which was confirmed by Dove (1841). Nonetheless, eye movements continued to play an interpretive role in binocular rivalry as did attention. Fechner (1861) considered that rivalry phenomena provided a clear example of attentional shifts, while Wundt (1862) placed more emphasis on eye movements. Wundt stated that the actual basis for rivalry resided in changes in the convergence angle of the eyes. He examined rivalry between vertical and horizontal gratings and supported the eye movement hypothesis by demonstrating that when the vertical grating is physically moved horizontally it becomes dominant, and vice versa. Without physical movement either one or the other grating is visible or a mosaic made up from them can be seen. Wundt introduced a subtle variation on the stimuli used for rivalry: he presented very wide vertical and horizontal stripes but the wide stripes had finer lines of the same orientation within them. When one set of the wide stripes was dominant both the wide and fine lines in the orthogonal orientation disappeared.

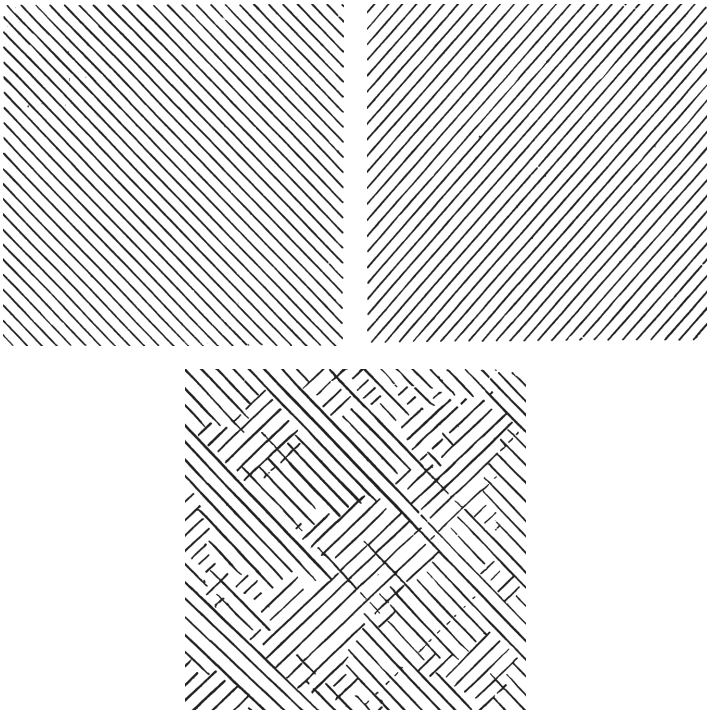


Figure 7. Panum's (1858) diagram of orthogonal gratings presented to contralateral eyes with an impression of their fragmented perception; in addition to intervals during which either grating alone is visible.

Towne (1862a) at the time had also examined binocular contour rivalry. He surmised that the function of the eyes was to receive and transmit images, while that of the mind was to perceive and interpret them. Other stimuli included a vertically split image of a camel or two vertically split discs. With the camel half-images, its front half was presented to the right nasal hemiretina and the rear half to the left nasal hemiretina, yet a whole coherent image of the animal was perceived. The same perceptual outcome occurred when the camel's front and rear halves were presented respectively to left and right temporal hemiretina. Towne concluded that

...in both examples, the circumstances under which the symmetry of the animal is restored, and note how far these circumstances agree, with what for *convenience*, may be spoken of as the *retinal law* of visual direction.... which rules that the image shall be referred in a direction opposite to the part of the retina affected.

(Towne, 1863, p. 117–118)

This initial interpretation would be pursued in subsequent studies on visual direction. Following his four papers on rivalry (Towne, 1862a, 1862b, 1863, 1864), he devoted four other papers to the study of visual direction. This body of work however had remained largely neglected until it was recently brought to light (Wade, Ono, & Mapp, 2006). Thus despite emanating from a defining period in rivalry research, Towne's report of perceptual grouping and stimulus rivalry alternations had otherwise not been recognized. A similar fate had befallen his important role in demonstrating the laws of visual direction (see Ono & Wade, 2012; Wade et al., 2006), which were later credited to Hering despite the fact that Towne acknowledged Wells' earlier work. With the invention of the stereoscope, the perception of depth had become the prevailing experimental and theoretical topic of interest. This instrument of change contributed to Towne's work on visual direction being neglected, though it was the same instrument that also enabled his novel observations on binocular rivalry.

Helmholtz (1867, 1925) was opposed to Panum's analysis of binocular rivalry, as he was to Hering's, because they were physiological rather than psychological. Nonetheless, he did use some of Panum's figures in his *Handbuch*, like two broad black lines, one vertical and the other horizontal, or two thin, orthogonal lines in each eye. Helmholtz also modified the stimuli so that he viewed a grid with one eye and a broad cross with the other, or provided binocular fixation aids in the centers of orthogonal gratings (Figure 8). Helmholtz took great pride in his ability to maintain stable fixation while controlling the location of his attention, and interpreted the pattern of visibility in terms of attentional control:

These experiments show that man possesses the faculty of perceiving images in each eye separately, without being disturbed by those in the other eye, provided it is possible for him, by some of the methods indicated above, to concentrate his whole attention on the objects in this one field. This is an important fact, because it signifies, that *the content of each separate field comes to consciousness without being fused with that of the other field by means of organic mechanisms*; and that, therefore, *the fusion of the two fields in one common image, when it does occur, is a psychic act.* (Helmholtz, 1925, p. 490)

It is this statement and its implications that were a source of dispute between Helmholtz and Hering (1864), who like Panum (1858), adopted a physiological interpretation of rivalry. Helmholtz's confidence in his ability to maintain stable fixation might have been misplaced. As he himself acknowledged, eye movements, even very small ones, in one direction relative to orthogonal gratings will have differential consequences for the stimulation of the retinas.

Wheatstone can be seen as the link between British empiricist philosophy and Helmholtz. Both were philosophically empiricists and were trained in physics, so that they could adopt the methods of physics to study binocular rivalry and

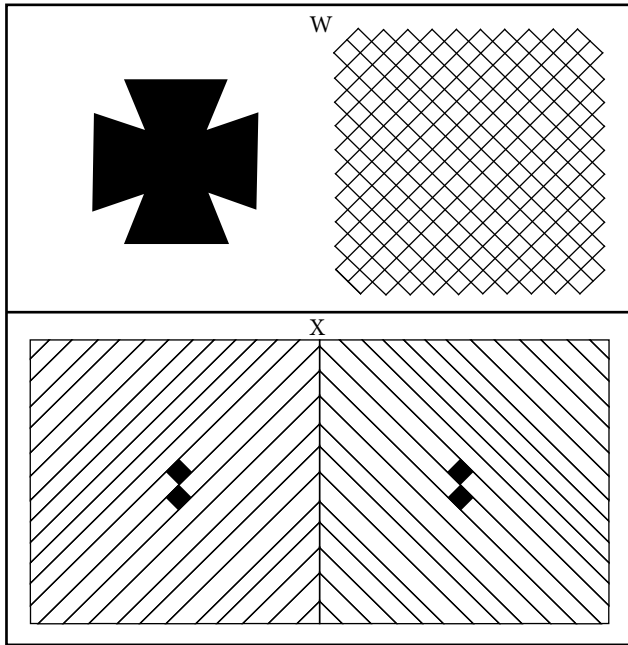


Figure 8. Figures used by Helmholtz (1867, 1925) to study binocular rivalry. With regard to the upper pair of rivalry figures (W) he claimed that “I simply have to count the squares in a row or to compare them to each other and notice whether they are all of one size or whether the lines are perpendicular, etc. As long as I devote my attention to this part of the figure, it stays in sight. On the contrary, the moment I let my attention be distracted to a corner of the cross or to one of its sides, the lines vanish more or less completely, and I see the cross steadily” (Helmholtz, 1925, pp. 496–497). With regard to the lower pair (X) he said that we “generally get the impression of an irregular blending of the two patterns, with one system of lines predominating at some places in the field, and the other system of lines at other places” (p. 497).

interpret it in terms of learning. The contributions made by Helmholtz to visual science are legion, but his most lasting impact was his theory of perception: he followed the empiricist philosophers in arguing that perception is like unconscious problem-solving – making unconscious inferences about the nature of the external world based upon the inadequate information furnished by the senses. Helmholtz appreciated that the process of perception takes place in the brain, following transmission of the neural signals from the sensory receptors – the brain only had indirect access to the external world, via the senses, and it could only process messages in the language of nerve impulses. This realization made any

equation of the retinal image with perception unnecessary. By adopting a starkly empiricist interpretation of perception, and by contrasting it so sharply with nativism, he reopened a debate that has reverberated throughout perception research ever since. The debate was personified in the conflict between Helmholtz and Hering, and the main battle-grounds were color vision and stereoscopic depth perception (see Turner, 1994).

The bitter rivalry, both theoretical and personal, between Helmholtz and Hering was matched by an earlier one between Wheatstone and Brewster concerning the nature of binocular combination (Wade, 1983). However, it could be argued that the stereoscope has performed a singular disservice to our understanding of binocular rivalry. As Helmholtz noted, rivalry is a natural consequence of our binocular interactions with the world; it is a resolution of conditions that apply to most of what we see when using two eyes. It occurs when the differences between the images in the two eyes are too large to be combined, and stereoscopic depth cannot be extracted from disparity. When we bifixate on part of an object most of what is projected to the peripheral retinas is too disparate to yield depth; because the peripheral stimuli arise from different depths their retinal images also tend to be out of focus. We are not generally aware of this binocular rivalry as both visual resolution and attention are typically associated with the fixated object rather than peripheral ones. If attention shifts to a peripheral object then the eyes also move to bifixate it. Using stereoscopes, binocular rivalry is rarely examined under these conditions of natural stimulation. It is typically studied with different patterns presented to corresponding foveal regions of the two eyes – as if we are bifixating two different objects. Thus, the conditions under which binocular rivalry is investigated experimentally seldom occur in normal binocular vision. Implications for consciousness studies arise from these considerations if binocular rivalry is taken as some index of its operation. In the following section, we trace the development of conceptual precursors that are now a focus of modern rivalry studies into visual consciousness.

Alternations in attention and consciousness

From the end of the 19th Century, neural theories of consciousness based on rivalry experiments were first put forward by Burtis Burr Breese (1899). Along with examining the effects of motor inhibition on memory, he used binocular rivalry as a paradigm to examine the inhibition of sensations and argued that consciousness had a sensorimotor basis. More importantly, he made the first quantitative measures of binocular rivalry. He examined: (i) the effect of stimulus strength changes (e.g., motion, size, luminance) on perceptual predominance

and alternation rate; (ii) individual variation in alternation rate (see also below); (iii) the effect of unilateral motor activity on predominance; (iv) rivalry between after-images and their slower alternation rate compared to real stimuli; and (iv) the phenomenon of monocular rivalry. He also investigated the influence of willpower on binocular rivalry. Subjects could voluntarily hold attention on one image with the (inadvertent) use of eye movements, but without eye movements such voluntary control was limited (see also Blake, 2005).

Breese argued that binocular rivalry could not be explained by purely mental conditions because complete control over the alternations could not be demonstrated. Correspondingly, physical conditions such as retinal adaptation could not solely explain the effect of different brightness levels on rivalry rate, which may have also been due to greater attention directed towards the brighter image. Instead, he concluded that the phenomenon “would be at once ‘psychical’ and ‘physiological’ in that it is dependent upon central processes, and is affected by the nature of motor adaptations” (1899, p. 48). Breese subsequently elaborated on the distinction between consciousness and attention during rivalry, along with postulating their associated activity in the brain:

...in the case of the alternating red and green squares in the stereoscope, if, when I give my attention to the red square, the green square displaces it in sensory consciousness, I may still be thinking about the red square, attending to its quality, size, et cetera, so that the change in consciousness is not a change of attention. What really happens in this case is that part of the time I am attending to the sensory perception of the red square, and part of the time to its memory image. On the other hand, the green square may not occupy clear or attention-consciousness at all... So we infer that the brain activities corresponding to attention-consciousness involve larger areas than those corresponding to mere sensation or perception. We conclude, therefore, that attention may change with the changes of sense-stimuli or may act independently of them. Shifting of the attention involves more factors than those involved in the fluctuation of minimal sensations or in the rivalry of objects presented to the sense-organs. (Breese, 1917, pp. 74–75)

Ten years after his original study, Breese (1909) repeated the rivalry experiments on himself and noted that his alternation rate was almost identical. This within-individual retest reliability of binocular rivalry rate was also reported by others (McDougall, 1906), as was his earlier finding of individual variation in alternation rate (Bose, 1902, 1907). Such variation across different individuals had been found a decade prior by a Scottish eye surgeon, Thomas Reid (1889), who is better known for developing the portable ophthalmometer (Gutmark & Guyton, 2010). The quantitative rivalry experiments conducted by Breese and his interpretation of their findings reflected the broader development of psychology into a scientific discipline. They were also a reflection of increasing knowledge about the brain

and interest in the neural basis of attention and consciousness. Both notions of attention and consciousness had been central to early views of the mind, thus not surprisingly the advent of experimental psychology also marked the beginnings of a science of consciousness.

The close relationship between attention and consciousness stemmed from very early notions of levels or degrees of consciousness, that is, the conscious mind and subconscious mind, and their interaction in acquiring new ideas and knowledge. On this basis, Gottfried Leibniz, one of the leading rationalist philosophers of the 17th Century, conceived the notion of 'apperception', which was later developed by Immanuel Kant and Johann Herbart. Apperception was conceptualized as the means by which conscious sense impressions were understood in terms of subconscious prior experience (Pillsbury, 1908; Titchener, 1908).

The notions of apperception and levels of consciousness were taken up by Wundt (1874). He proposed however that while consciousness had levels, these were characterized instead as levels of attention. Attention was therefore considered to have a single focus wherein an object was held in consciousness at any given moment (now commonly understood as selective attention or an attentional spotlight). Meanwhile for objects or events outside this focus, an individual was less aware or not conscious of them. This early notion of attention as an adaptive function and action of the mind became a common explanatory concept in 19th Century continental Europe. For example, binocular rivalry was thought to involve an act of attention (Fechner, 1861; Funke, 1857), before the publication of Helmholtz's third volume of his *Handbuch* and the combined presentation of all three volumes in Gustav Karsten's *Allgemeine Encyklopädie der Physik* in 1867. Others had also considered attention as being involuntary, with binocular rivalry involving alternations in attention rather than alternations in retinal fatigue (Meyer, 1856), or had interpreted the alternations as being due to involuntary avoidance of double images (Brücke, 1841). More broadly, the conceptualization of attention on the Continent was in opposition to the parallel advancement of British associationism, which was reductionist in its approach and considered mind as a passive state.

To understand mental processes and the active mind, Wundt had utilized trained introspection in highly controlled laboratory conditions. This approach was taken on by his student, Edward Bradford Titchener, who instead characterized consciousness by levels of clearness rather than attention. Having originally studied in England, Titchener was also influenced by the ideas of David Hume, another leading advocate of British associationism. After moving to America in the 1890s, Titchener founded structural psychology, which sought to elucidate basic elements of the mind, including the brain basis of mental events. Meanwhile, strong opposition was gathering from functional psychology, which emphasized

individual differences and studying the adaptive function of consciousness with both introspective and objective experimental methods. Its main proponent was William James (1890), whose student James Rowland Angell further championed this school of thought. Angell, using ambiguous figures as an example, also proposed a basic mechanism regarding their perception:

It is clear that a consideration of illusion affords new and striking confirmation of the part played in perception by previous experience. The cortical reaction suggested by the stimulus does not happen to correspond to the object actually present. But this cortical reaction is evidently determined by the impress of old perceptual experiences whose traces have been preserved. The same point is admirably illustrated by such drawings as the accompanying, figures 52 and 53. We can see the [Schröder's] stairs, either as they appear from above, or from below. In one case the surface *a* seems nearer to us; in the other case *b* seems nearer. We can see in the other [Wheatstone] figure a big picture frame, the frustum of a pyramid, or the entrance to a square tunnel. Yet one and the same object is presented to the retina in each case. The eye can hardly be accused of responsibility for the shifting results. But lines like these have actually been connected in our former perceptions with the several objects named, and in consequence the cortical reaction appropriate to either of them *may* be called out. It would seem abundantly certain, therefore, that while a portion of what we perceive is always supplied from without, another portion, and often the dominant portion, is supplied from within ourselves.

(Angell, 1904, pp. 134–135, bracketed information added)

Angell thus suggested that both neural activity associated with either rivaling image and constructive processes were required to achieve perceptual dominance. This proposal was consistent with the empiricist view of perception, yet he was also highly critical of structural psychology's reductionist approach to consciousness:

The more extreme and ingenuous conceptions of structural psychology seem to have grown out of an unchastened indulgence in what we may call the 'states of consciousness' doctrine. I take it that this is in reality the contemporary version of Locke's 'idea.' If you adopt as your material for psycho-[l]ogical analysis the isolated 'moment of consciousness,' it is very easy to become so absorbed in determining its constitution as to be rendered somewhat oblivious to its artificial character.

(Angell, 1907, p. 64)

While many early 20th Century psychologists discussed consciousness and its investigation in their writings, very few did so specifically in relation to rivalry. Angell was an exception, as was William McDougall. McDougall had a special interest in biology during his undergraduate years, a period when he also researched muscular contraction in Cambridge and at the St Thomas' Hospital physiological laboratory in London headed by Charles Sherrington. As a graduate

student he then worked with W.H. R. Rivers, who had been invited to give lectures at Cambridge on the physiology of the sense organs. It was after this period that McDougall developed a keen interest in experimental work on vision, in particular through his opposition to Hering's opponent processing theory (see McDougall, 1911, 1930). In studies using Schröder's staircase and binocular color rivalry, he found similarities in their (successive) interval durations, and in the effect of voluntary control and monocular atropine administration on percept dominance (1901a, 1901b, 1903a, 1906). He also experimented with a bistable rotating wind-mill illusion, and presented a multi-path hierarchical representation of the nervous system (i.e., spinal and subcortical centers, sensory cortical areas, association areas; McDougall, 1902). From this background, McDougall hypothesized that such phenomena represented

...a principal condition of the alternating appearance in consciousness of two objects, while the impression made on the sense-organ remains unchanged, is fatigue of the cortical tract concerned in the perception of either object, a fatigue which is induced during the period of perception, and which rapidly passes away during the period of rest in which the other object is present to consciousness. ... [T]he paths which suffer fatigue and become alternately active and passive or, in other words, alternately transmit the stream of nervous energy coming in from the sense-organ and cease to transmit it while it is diverted to the alternative path, these paths are, in the case of the binocular rivalry of colours, paths of the sensory area of the cortex, paths of the second level in the scheme...; while in the case of ambiguous figures...the nervous energy coming in from the sense-organ is continuously transmitted by the paths of the sensory level while it penetrates alternately to one or other of two higher-level paths.

(McDougall, 1906, pp. 346–347)

From this passage, it is clear that McDougall provided an early multi-level neurophysiological account of perceptual rivalry (i.e., binocular rivalry, ambiguous figures and bistable motion illusions). This account is also the key forerunner to the principle of neural dissociation that is now common in modern mechanistic studies of rivalry (i.e., distinguishing neural activity mediating the alternate percepts from that corresponding to the constant sensory input).

McDougall's work was the earliest specifically to compare binocular rivalry with other rivalry types, that is, comparing alternating visual phenomena induced by dichoptic and dioptic presentation, respectively. Over fifty years prior to this, similarities had been noted between binocular rivalry and olfactory perceptual alternations with dichorhnic stimulation – presenting a different odor to each nostril (Valentin, 1848). From the end of the 19th Century experimenters further examined such olfactory rivalry (e.g., Henning, 1916; Zwaardemaker, 1895), and also explored the effect of auditory stimulation on binocular color mixture and rivalry predominance (Urbantschitsch, 1903).

Returning to McDougall, his account above regarding visual rivalry was also notable by articulating elements of Gestalt satiation theory which would be formulated decades later. In addition, it has been argued that his conceptualization of both neural fatigue and reciprocal inhibition between neurons (McDougall, 1901b, 1903b) provided a clearer explanation for Sherrington's (1906) finding of rhythmic alternations between antagonistic muscle groups (see Reiss, 1962). McDougall also applied his approach to binocular rivalry, thereby enunciating key aspects of modern reciprocal inhibition models of the phenomenon. Moreover, he first reported observations of another phenomenon closely related to binocular rivalry, now known as flash suppression:

...if, when a red field is presented to one eye and a blue field to the corresponding area of the other eye, one eye be closed or covered for a brief period – one second will suffice – the colour presented to that eye always predominates over and inhibits the colour presented to the other eye as soon as the eye is uncovered, *i.e.*, the rested tract predominates over the relatively fatigued tract, even if the period of rest be not more than one second. (McDougall, 1901b, p. 598)

Despite the precedence of such observations, there were also detractors of McDougall's inhibition model, along with the utility of rivalry itself: "The whole field of bilateral rivalry is too little known to permit its exploitation as proof of anything except our ignorance" (Dodge, 1926, p. 113). In further experiments he also examined the effects of pharmacological agents on a bistable windmill illusion (McDougall & Smith, 1920), which were followed by other drug studies on ambiguous figures (Ewen, 1931; George, 1936) and binocular rivalry (Bárány & Halldén, 1947; George, 1936).

With the rise of American behaviorism and functionalism early in the 20th Century, there also came increasing criticism of the study of consciousness and attention given their highly subjective nature. Scepticism was similarly directed at the interpretation of empirical work in the light of such notions. This view, coupled with the emergence of rigorous animal behavior studies (e.g., Pavlovian conditioning), lead to the establishment of behaviorism as the prevailing objective scientific approach in psychology – rejecting introspective methods. The dominance of behaviorism was partly reflected in over two decades of waning interest in binocular rivalry, especially outside of Germany. It was considered a subjective phenomenon that could not be examined objectively with the methods available at the time (Lack, 1978). Correspondingly, studies directly comparing binocular rivalry with other rivalry types were rare (e.g., George, 1936; Washburn & Gillette, 1933). In the late 1920s, Margaret Washburn, a former student of Titchener, then conducted a series of studies on ambiguous figures, binocular rivalry and stereoscopic vision until her death in 1939. Based upon that work, she argued for the importance of motor responses in the voluntary control of rivalry and in explanations of consciousness.

Early in the 1940s different types of visual rivalry were used by Louis Thurstone, a former student of Angell, in an exploratory multiple-factor analytic study. The number of rivalry alternations among a battery of other perceptual, motor and cognitive measures were recorded, with the aim of using the perceptual tests as a measure of personality. This aim was based on his hypothesis that “the dynamics of perception, and of other restricted functions, are not isolated and that these several functions are so related that some characteristics of the person as a whole might be inferred from the dynamics of one of these functions” (Thurstone, 1944, p. 3). In addition, it was thought that individual differences in the perceptual measures might reflect a central rather than peripheral parameter associated with an individual’s personality. In a small twin study, the number of binocular rivalry alternations was also used among several other measures to explore a genetic (hereditary) basis for differences between identical and fraternal twin pairs (Thurstone, Thurstone, & Strandskov, 1953, 1955; see also chapter by Ngo, Barsdell, Law, & Miller, this volume).

Several years earlier, McDougall (1926) had proposed an association between personality types and ambiguous-figure rivalry. He suggested that extraversion (identified in hysteria and manic-depressives) was associated with a slow rivalry rate, while introversion (identified in neurasthenia and schizophrenia) was associated with a fast rivalry rate. This hypothesis was tested by investigators such as Margaret Washburn, Joy Guilford (also a former student of Titchener), Raymond Cattell and Hans Eysenck (e.g., Cattell, 1933; Cattell & Tiner, 1949; Eysenck, Granger, & Brengelmann, 1957; Eysenck, Holland, & Trouton, 1957; Guilford & Braly, 1931; Washburn, Keeler, & Parshall, 1929). Among other measures, alternation rate was examined as an indicator of personality subtypes and psychiatric disorders (see also chapter by Ngo et al., this volume). The work in particular by Guilford, Cattell and Eysenck, like that of Thurstone, was within the context of psychometrics rather than characterizing rivalry phenomena and their underlying mechanisms.

From the late 1940s onwards, renewed interest in examining attention saw a gradual resurgence in studies of binocular rivalry (Lack, 1978). This work came from three perspectives: (i) using the phenomenon to discern individual differences and intrinsic factors (e.g., personality, learning, motivation, intelligence, semantic value, heredity, pharmacological effects, subliminal perception), (ii) the effect of stimulus manipulations (i.e., extrinsic factors), and (iii) the relationship between binocular rivalry and stereoscopic vision (see also chapter by Klink, van Wezel, & van Ee, this volume). At the end of the 1960s, enquiry from an intrinsic factors perspective began to wane. This decline likely reflected the influence of rigorous neurophysiological studies into mechanisms of retinal disparity processing (Barlow, Blakemore, & Pettigrew, 1967; Hubel & Wiesel, 1962). At the time

there was also a shift towards quantitative psychophysical methods to examine binocular rivalry. Other lines of enquiry that developed during this period were the psychophysics of structure-from-motion perception and bistable motion phenomena (Braunstein, 1976; Wallach & O'Connell, 1953), and a cognitive processing approach to studies of ambiguous figures and form perception (e.g., Fisher, 1968; Vickers, 1972). With binocular rivalry, novel experiments conducted by Robert Fox, Paul Whittle and Willem Levelt, for example, revealed further key features of the phenomenon (see Blake, 2005; chapter by Brascamp & Baker, this volume). This body of work, along with human electrophysiological studies of rivalry conducted by others, marked a revival in the field that has continued to flourish ever since.

Summary and conclusions

In historical terms, binocular rivalry has been considered in the context of single-ness of vision. For Greek and medieval philosophers it was a problem associated with misalignment of the eyes. In the 16th Century, Porta proposed that it was a solution to binocular single vision as he supposed that only one eye operated at one time – mostly the right eye. From the time of Descartes and Newton single-ness of vision was posited in speculative anatomical combinations. French scholars used binocular rivalry to attack Descartes' theory and in the process introduced new methods to examine it. Color rivalry was examined by these methods before contour rivalry was investigated.

In the 19th Century the experimental study of binocular rivalry was transformed by Wheatstone's invention of the stereoscope and contour rivalry was examined in more detail because of its close relationship to stereoscopic depth perception. Factors affecting rivalry, like attention and eye movements, became the focus of theoretical interpretations, and the implications of the phenomenon for consciousness emerged. At the turn of the century, Breese measured the durations of dominance for the stimuli presented to each eye during rivalry, heralding the quantitative era. However, the rise of behaviorism suppressed interest in a phenomenon for which there were no external correlates, despite the investigation into personality and clinical correlates of binocular rivalry and ambiguous figures. The resurgence of studies in the 1960s linked rivalry on the one hand, to the growing knowledge about the neurophysiology of binocular combination, and on the other to similar fluctuating visual phenomena like ambiguous figures and bistable motion illusions. These phenomena and variants like flash suppression are now powerful tools in contemporary research on mechanisms of visual consciousness.

References

- Aguilonius, F. (1613). *Opticorum Libri Sex. Philosophis juxta ac Mathematicis utiles*. Antwerp: Moreti.
- Alhazen (1572). *Opticae Thesaurus*. F. Risner (Ed.). Basel: Gallia.
- Angell, J.R. (1904). *Psychology: An introductory study of the structure and function of human consciousness*. New York: Henry Holt & Co.
- Angell, J.R. (1907). The province of functional psychology. *Psychological Review*, 14(2), 61–91.
- Bárány, E. H., & Halldén, U. (1947). The influence of some central nervous depressants on the reciprocal inhibition between the two retinae as manifested in retinal rivalry. *Acta Physiologica Scandinavica*, 13(4), 296–316.
- Barlow, H. B., Blakemore, C., & Pettigrew, J. D. (1967). The neural mechanism of binocular depth discrimination. *Journal of Physiology*, 193(2), 327–342.
- Bell, C. (1803). *The anatomy of the human body*, Vol. 3. London: Longman, Rees, Cadell and Davies.
- Blake, R. (2005). Landmarks in the history of binocular rivalry. In D. Alais & R. Blake (Eds.), *Binocular rivalry* (pp. 1–27). Cambridge, MA: MIT Press.
- Bose, J. C. (1902). *Response in the living and non-living*. London: Longmans, Green, and Co.
- Bose, J. C. (1907). *Comparative electro-physiology: A physico-physiological study*. London: Longmans, Green, and Co.
- Braunstein, M. L. (1976). *Depth perception through motion*. New York: Academic Press.
- Breese, B. B. (1899). On inhibition. *Psychological Monographs*, 3(1), 1–65.
- Breese, B. B. (1909). Binocular rivalry. *Psychological Review*, 16(6), 410–415.
- Breese, B. B. (1917). *Psychology*. New York: C. Scribner's Sons.
- Brewster, D. (1844). On the law of visible position in single and binocular vision, and on the representation of solid figures by the union of dissimilar plane pictures on the retina. *Transactions of the Royal Society of Edinburgh*, 15, 349–368.
- Brewster, D. (1855). *Memoirs of the life, writings, and discoveries of Sir Isaac Newton*. Edinburgh: Constable.
- Brücke, E. (1841). Ueber die stereoskopischen Erscheinungen und Wheatstone's Angriff auf die Lehre von den identischen Stellen der Netzhäute. *Archiv für Anatomie, Physiologie und wissenschaftliche Medizin*, 5, 459–476.
- Cattell, R. B. (1933). Temperament tests. II. Tests. *British Journal of Psychology*, 24(1), 20–49.
- Cattell, R. B., & Tiner, L. G. (1949). The varieties of structural rigidity. *Journal of Personality*, 17(3), 321–341.
- Desaguliers, J. T. (1716). A plain and easy experiment to confirm Sir Isaac Newton's doctrine of the different refrangibility of the rays of light. *Philosophical Transactions of the Royal Society*, 34, 448–452.
- Descartes, R. (1637/1902). *La Dioptrique*. In C. Adam and P. Tannery (Eds.), *Oeuvres de Descartes*, Vol. 6 (pp. 81–228). Paris: Cerf.
- Descartes, R. (1664/1909). *Traité de l'Homme*. In C. Adam and P. Tannery (Eds.), *Oeuvres de Descartes*, Vol. 11 (pp. 119–215). Paris: Cerf.
- Dodge, R. (1926). Theories of inhibition. Part I. *Psychological Review*, 33(2), 106–122.
- Dove, H. (1841). Über die Combination der Eindrücke beider Ohren unde beider Augen zu einem Eindruck. *Bericht über die zur Bekanntmachung geeigneten Verhandlungen der Königlich Preussische Akademie der Wissenschaften zu Berlin*, 41, 251–252.

- Du Tour, E.-F. (1760). Discussion d'une question d'optique. *Mémoires de Mathématique et de Physique, présentés à l'Académie Royale des Sciences, par divers Savans, & lus dans ses Assemblées*, 3, 514–530.
- Du Tour, E.-F. (1761). Addition au Mémoire intitulé. Discussion d'une question d'Optique. *Mémoires de Mathématique et de Physique, présentés à l'Académie Royale des Sciences, par divers Savans, & lus dans ses Assemblées*, 4, 499–511.
- Ewen, J. H. (1931). The psychological estimation of the effects of certain drugs upon the syntonetic and schizophrenic psychoses: With a brief enquiry into a physiological basis of temperament. *Journal of Mental Science*, 77(319), 742–766.
- Eysenck, H. J., Granger, G. W., & Brengelmann, J. C. (Eds.) (1957). *Perceptual processes and mental illness*. New York: Basic Books.
- Eysenck, H. J., Holland, H., & Trouton, D. S. (1957). Drugs and personality. IV. The effects of stimulant and depressant drugs on the rate of fluctuation of a reversible perspective. *Journal of Mental Science*, 103(432), 656–660.
- Fechner, G. T. (1861). Über einige Verhältnisse des binocularen Sehens. *Abhandlungen der mathematisch-physischen Classe der Königlich Sächsischen Gesellschaft der Wissenschaften*, 7, 337–563.
- Fisher, G. H. (1968). Ambiguity of form: Old and new. *Perception & Psychophysics*, 4(3), 189–192.
- Funke, O. (1857). *Lehrbuch der Physiologie für akademische Vorlesungen und zum Selbststudium*, Vol. 2. Leipzig: Voss.
- George, R. W. (1936). The significance of the fluctuations experienced in observing ambiguous figures and in binocular rivalry. *Journal of General Psychology*, 15(1), 39–61.
- Guilford, J. P., & Braly, K. W. (1931). An experimental test of McDougall's theory of extroversion-introversion. *Journal of Abnormal and Social Psychology*, 25(4), 382–389.
- Gutmark, R., & Guyton, D. L. (2010). Origins of the keratometer and its evolving role in ophthalmology. *Survey of Ophthalmology*, 55(5), 481–497.
- Haldat, C. (1806). Expérience sur la double vision. *Journal de Physique, de Chimie, et d'Histoire Naturelle*, 63, 387–401.
- Hall, T. S. (1972). *Treatise of man. René Descartes*. Cambridge, MA: Harvard University Press.
- Harris, J. (1775). *A treatise of optics: Containing elements of the science; in two books*. London: White.
- Helmholtz, H. (1867). *Handbuch der physiologischen Optik*. In G. Karsten (Ed.), *Allgemeine Encyklopädie der Physik*, Vol. 9. Leipzig: Voss.
- Helmholtz, H. (1925). *Helmholtz's treatise on physiological optics*, Vol. 3. J. P. C. Southall (Trans.). New York: Optical Society of America.
- Henning, H. (1916). Der Geruch. II. *Zeitschrift für Psychologie*, 74, 305–434.
- Hering, E. (1861). *Beiträge zur Physiologie. I. Vom Ortsinne der Netzhaut*. Leipzig: W. Engelmann.
- Hering, E. (1864). *Beiträge zur Physiologie. V. Vom binocularen Tiefsehen. Kritik einer Abhandlung von Helmholtz über den Horopter*. Leipzig: W. Engelmann.
- Howard, I. P., & Rogers, B. J. (2012). *Perceiving in depth: Vol. 2, Stereoscopic vision*. New York: Oxford University Press.
- Howard, I. P., & Wade, N. J. (1996). Ptolemy's contributions to the geometry of binocular vision. *Perception*, 25(10), 1189–1202.
- Hubel, D. H., & Wiesel, T. N. (1962). Receptive fields, binocular interaction and functional architecture in the cat's visual cortex. *Journal of Physiology*, 160(1), 106–154.
- James, W. (1890). *Principles of psychology* (Vol 2). London: Macmillan.

- Jaucourt, L. de (1753). Conscience. In D. A. Diderot & J. Le Rond d'Alembert (Eds.), *Encyclopédie, ou Dictionnaire raisonné des sciences, des arts et des métiers, par une société de gens de lettres*, Vol 3. (p. 902). Paris: Briasson, David, Le Breton, Durand.
- Kepler, J. (1604). *Ad Vitellionem Paralipomena*. Frankfurt: Marinium and Aubrii.
- Lack, L. C. (1978). *Selective attention and the control of binocular rivalry*. Mouton Publishers: The Hague, The Netherlands.
- Le Clerc, S. (1679). *Discours Touchant de Point de Veue, dans lequel il es prouvé que les chose qu'on voit distinctement, ne sont veues que d'un oeil*. Paris: Jolly.
- Le Clerc, S. (1712). *Système de la Vision*. Paris: Delaulne.
- Lejeune, A. (1956). *L'Optique de Claude Ptolémée dans la version Latine d'après l'Arabe de l'Émir Eugène de Sicile*. Louvain: Université de Louvain.
- Locke, J. (1690). *An essay concerning human understanding* (Book II). London: T. Basset.
- May, M. T. (1968). *Galen. On the useful of the parts of the body*. Ithaca, NY: Cornell University Press.
- Meyer, H. (1856). Ueber den Einfluss der Aufmerksamkeit auf die Bildung des Gesichtsfeldes überhaupt und des gemeinschaftlichen Gesichtsfeldes beider Augen im Besonderen. *Archiv für Ophthalmologie*, 2(2), 77–92.
- McDougall, W. (1901a). IV. – Some new observations in support of Thomas Young's theory of light- and colour-vision (II.). *Mind*, 10(38), 210–245.
- McDougall, W. (1901b). On the seat of the psycho-physical processes. *Brain*, 24(4), 579–630.
- McDougall, W. (1902). II. – The physiological factors of the attention-process (I.). *Mind*, 11(43), 316–351.
- McDougall, W. (1903a). III. – The physiological factors of the attention-process (III.). *Mind*, 12(48), 473–488.
- McDougall, W. (1903b). The nature of the inhibitory processes within the nervous system. *Brain*, 26(2), 153–191.
- McDougall, W. (1906). III. – Physiological factors of the attention-process (IV.). *Mind*, 15(59), 329–359.
- McDougall, W. (1911). On the relations between corresponding points of the two retinae. *Brain*, 33(4), 371–388.
- McDougall, W. (1926). *Outline of abnormal psychology*. New York: Charles Scribner's Sons.
- McDougall, W. (1930). William McDougall. In C. Murchison (Ed.), *A history of psychology in autobiography*. Vol. I (pp. 191–223). Worcester, MA: Clark University Press.
- McDougall, W., & Smith, M. (1920). The effects of alcohol and some other drugs during normal and fatigued conditions. *Medical Research Council Special Reports Series*, No. 56. London: His Majesty's Stationery Office.
- Müller, J. (1826). *Zur vergleichenden Physiologie des Gesichtssinnes des Menschen und der Thiere, nebst einen Versuch über die Bewegung der Augen und über den menschlichen Blick*. Leipzig: Cnobloch.
- Müller, J. (1838). *Handbuch der Physiologie des Menschen*, Vol. 2. Coblenz: Hölscher.
- Newton, I. (1704). *Opticks: or, a treatise of the reflections, refractions, inflections and colours of light*. London: Smith and Walford.
- Ono, H., & Wade, N. J. (2012). Two historical strands in studying visual direction. *Japanese Psychological Research*, 54(1), 71–88.
- Palaia, R. (2012). Theories of consciousness in early-modern philosophy. In F. Paglieri (Ed.), *Consciousness in interaction: The role of the natural and social context in shaping*

- consciousness (pp. 301–310). *Advances in Consciousness Research* (Vol. 86). Amsterdam: John Benjamins Publishers.
- Panum, P. L. (1858). *Physiologische Untersuchungen über das Sehen mit zwei Augen*. Kiel: Schwerssche Buchhandlung. C. Hübscher, 1940 (Trans.), *Physiological investigations concerning vision with two eyes*. Hanover, NH: Dartmouth Eye Institute.
- Pillsbury, W. B. (1908). *Attention*. New York: The Macmillan Company.
- Porta, J. B. (1593). *De Refractione. Optices Parte. Libri Novem*. Naples: Carlinum and Pacem.
- Reid, T. (1764). *An inquiry into the human mind, on the principles of common sense*. Edinburgh: Millar, Kincaid & Bell.
- Reid, T. (1889). Intermittent sensations. *Nature*, 40(1031), 318.
- Reiss, R. F. (1962). A theory and simulation of rhythmic behavior due to reciprocal inhibition in small nerve nets. *Proceedings of the 1962 A.F.I.P.S. Spring Joint Computer Conference* (Vol. 21, pp. 171–194). Palo Alto, California: National Press.
- Scheiner, C. (1619). *Oculus, hoc est fundamentum opticum*. Innsbruck: Agricola.
- Sherrington, C. S. (1906). *Integrative action of the nervous system*. New Haven: Yale University Press.
- Smith, A. M. (1996). *Ptolemy's theory of visual perception: An English translation of the Optics with introduction and commentary*. Philadelphia: The American Philosophical Society.
- Taylor, J. (1738). *Le Mechanisme ou le Nouveau Traité de l'Anatomie du globe de l'oeil, avec l'usage de ses différentes parties, & de celles qui lui sont contigues*. Paris: David.
- Titchener, E. B. (1908). *Lectures on the elementary psychology of feeling and emotion*. New York: The Macmillan Company.
- Towne, J. (1862a). Remarks on the stereoscopic theory of vision; with observations on the experiments of Professor Wheatstone – Section I. *Guy's Hospital Reports*, 8, 70–80.
- Towne, J. (1862b). The stereoscope, and stereoscopic results – Section II. *Guy's Hospital Reports*, 8, 81–98.
- Towne, J. (1863). The stereoscope, and stereoscopic results – Section III. *Guy's Hospital Reports*, 9, 103–126.
- Towne, J. (1864). The stereoscope, and stereoscopic results – Section V. *Guy's Hospital Reports*, 10, 125–141.
- Thurstone, L. L. (1944). *A factorial study of perception*. Chicago, IL: University of Chicago Press.
- Thurstone, T. G., Thurstone, L. L., & Strandskov, H. H. (1953). *A psychological study of twins. 1. Distributions of absolute twin differences for identical and fraternal twins* (Report No. 4). Chapel Hill, NC: The Psychometric Laboratory, University of North Carolina.
- Thurstone T. G., Thurstone L. L., Strandskov H. H. (1955). *A psychological study of twins. 2. Scores of one hundred and twenty-five pairs of twins on fifty-nine tests* (Report No. 12). Chapel Hill, NC: The Psychometric Laboratory, University of North Carolina.
- Turner, R. S. (1994). *In the eye's mind. Vision and the Helmholtz-Hering controversy*. Princeton, NJ: Princeton University Press.
- Urbantschitsch, V. (1903). Ueber die Beeinflussung subjectiver Gesichtsempfindungen. *Archiv für die gesamte Physiologie des Menschen und der Tiere*, 94(7–8), 347–448.
- Valentin, G. (1848). *Lehrbuch der Physiologie des Menschen. Für Ärzte und Studierende* (2nd ed., Vol. 2, Part 2). Braunschweig: Friedrich Vieweg und Sohn.
- Venturi, J. B. (1802). Betrachtungen über die Erkenntniss der Entfernung, die wir durch das Werkzeug des Gehörs erhalten. *Archiv für die Physiologie*, 5(3), 383–392.
- Vesalius, A. (1543). *De Humani corporis fabrica Libri septem*. Basel.
- Vickers, D. (1972). A cyclic decision model of perceptual alternation. *Perception*, 1(1), 31–48.

- Vieth, G. U. A. (1818). Ueber die Richtung der Augen. *Annalen der Physik*, 58(3), 233–253.
- Wade, N. J. (1983). *Brewster and Wheatstone on vision*. London: Academic Press.
- Wade, N. J. (1998). *A natural history of vision*. Cambridge, MA: MIT Press.
- Wade, N. J., & Deutsch, D. (2008). Binaural hearing – before and after the stethophone. *Acoustics Today*, 4(3), 16–27.
- Wade, N. J., & Ono, H. (2005). From dichoptic to dichotic: Historical contrasts between binocular vision and binaural hearing. *Perception*, 34(6), 645–668.
- Wade, N. J., & Ono, H. (2012). Early studies of binocular and stereoscopic vision. *Japanese Psychological Research*, 54(1), 54–70.
- Wade, N. J., Ono, H., & Mapp, A. P. (2006). The lost direction in binocular vision: The neglected signs posted by Wells, Towne, and LeConte. *Journal of the History of Behavioral Sciences*, 42(1), 61–86.
- Wallach, H., & O'Connell, D. N. (1953). The kinetic depth effect. *Journal of Experimental Psychology*, 45(4), 205–217.
- Washburn, M. F., & Gillette, A. (1933). Motor factors in voluntary control of cube perspective fluctuations and retinal rivalry fluctuations. *American Journal of Psychology*, 45(2), 315–319.
- Washburn, M. F., Keeler, K., New, K. B., & Parshall, F. M. (1929). Experiments on the relation of reaction-time, cube fluctuations, and mirror drawing to temperamental differences. *American Journal of Psychology*, 41(1), 112–117.
- Weber, E. H. (1834). *De Pulsu, Resorptione, Auditu et Tactu*. Leipzig: Koehler.
- Wells, W. C. (1792). *An essay upon single vision with two eyes: Together with experiments and observations on several other subjects in optics*. London: Cadell.
- Wheatstone, C. (1838). Contributions to the physiology of vision. – Part the first. On some remarkable, and hitherto unobserved, phenomena of binocular vision. *Philosophical Transactions of the Royal Society*, 128, 371–394.
- Wheatstone, C. (1842). Beiträge zur Physiologie des Gesichtssinnes. Erster Teil. *Annalen der Physik und Chemie*, 131(S1), 1–48.
- Wheatstone, C. (1852). Contributions to the physiology of vision. – Part the second. On some remarkable, and hitherto unobserved, phenomena of binocular vision. *Philosophical Transactions of the Royal Society*, 142, 1–17.
- Wundt, W. (1862). *Beiträge zur Theorie der Sinneswahrnehmung*. Leipzig: C. F. Winter'sche Verlagshandlung.
- Wundt, W. (1874). *Grundzüge der physiologischen Psychologie*. Leipzig: W. Engelmann.
- Zwaardemaker, H. (1895). *Die Physiologie des Geruchs*. Leipzig: W. Engelmann.

Psychophysics of binocular rivalry

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For a given visual stimulus, much can be inferred about its neural representation by measuring an observer's responses on simple behavioral tasks. This is the essence of psychophysics, the method of examining sensory processing by studying the relation between stimulation and perception or behavior. Binocular rivalry is the phenomenon of alternating perception that occurs when the two eyes receive conflicting images. Psychophysical techniques have been used extensively in combination with rivalry, both to investigate the phenomenon itself, and using rivalry as a tool for addressing other questions. Recent techniques have permitted major advances in both areas, as we discuss here. We will also summarize the value and limitations of rivalry for consciousness research.

What is psychophysics?

The classic notion of psychophysics is closely tied to the beginnings of psychology as a scientific discipline. Introduced by Gustav Fechner in 1860 (Fechner, 1860), psychophysics in the classical sense refers to the scientific study of sensation through systematic mapping of physical variables, such as luminance, onto associated sensations, such as experienced brightness (Gescheider, 1997). An example of a psychophysical result in this sense is the Weber-Fechner law (Weber, 1834). To stick with the example of luminance, this empirical law states that the minimum change in luminance that an observer can reliably detect is a constant fraction of the starting luminance. In other words, the intensity of a bright object needs to change by a larger amount before we notice the difference than the intensity of a dim object, in a quantifiable way.

A related, but broader definition of psychophysics that may be more familiar today, is the experimental study of brain function through controlled sensory stimulation and behavioral report. In psychophysics in this broader sense there is not always an obvious mapping between a physical variable and a sensation. For instance, a psychophysical result in this sense is the finding that, when observers report their perception during binocular rivalry, the frequency histogram of

percept durations has a single peak and a rightward skew (Levelt, 1967), which provides clues regarding the neural mechanisms behind rivalry (Shapiro, Moreno-Bote, Rubin, & Rinzel, 2009; Wilson, 2007).

The use of behavioral report as its measure distinguishes psychophysics from other empirical approaches in neuroscience, such as neurophysiology and functional imaging, which measure (concomitants of) brain processes at their source in the head rather than as reflected in behavioral output. Still, there has always been a tight linkage between psychophysics and more direct measures of brain function (including imaging, electrophysiology and lesion studies), with some labs combining multiple approaches (notably the Physiological Laboratory at the University of Cambridge, which became hugely influential in the 1960s and 1970s by using a combination of psychophysical and single-cell techniques to uncover the multi-channel representation of visual information in cortex). The inferences drawn from psychophysical findings are frequently supported by more direct techniques. A recent, rivalry-specific example is the demonstration that traveling waves of suppression experienced perceptually (Wilson, Blake, & Lee, 2001) propagate at the same speed as changes of cortical activity measured using functional magnetic resonance imaging (fMRI; see Lee, Blake, & Heeger, 2005).

Psychophysics of binocular rivalry

Two classes of binocular rivalry psychophysics

When considered within the context of consciousness research, it makes sense to subdivide the psychophysics of binocular rivalry into two classes. The first is formed by studies that characterize the properties of binocular rivalry in order to understand the phenomenon itself. For example, the fact that during binocular rivalry observers may simultaneously perceive patches of one eye's image in some regions of space and patches of the other image elsewhere (Blake, O'Shea, & Mueller, 1992; Wheatstone, 1838; Yang, Rose, & Blake, 1992), suggests that rivalry draws on so-called retinotopic brain areas, where different neurons represent different regions of space. Whilst experiments in this category can certainly be of relevance for understanding consciousness, here we discuss them separately from experiments in a second class that are designed more explicitly with this objective in mind. Experiments of this second kind are not primarily aimed at understanding the rivalry phenomenon but, instead, use binocular rivalry as a means of preventing visual input from accessing consciousness in order to investigate the differences between conscious and unconscious visual processing (Crick & Koch, 1998).

Class I. Phenomenology of binocular rivalry

Binocular rivalry alternations were reported by several early researchers, but were typically treated as a curiosity (one esoteric paper by Creed, 1935, used postage stamps as stimuli). The drive to parameterize the rivalry process began in earnest with the work of Levelt (1966, 1967), who applied quantitative techniques to the phenomenon, and made several key observations (detailed below). Since then, numerous studies have investigated how various stimulus manipulations influence rivalrous percepts. One aim of such work is to produce a description (perhaps in the form of a computational model) of the rivalry process that is sufficient to predict conscious perception to an arbitrary novel set of rivaling stimuli, at least at a statistical level. Despite some notable successes, this goal is yet to be fully realized, in part due to the wide variety of factors that influence rivalry, as discussed in the following section.

Alternation cycle. The most salient property of rivalry, central to most descriptions of the phenomenon, is the ongoing cycle of alternating perception that ensues whenever one views a rivalry stimulus. Many existing psychophysical studies of rivalry are aimed at characterizing this alternation cycle. One main objective is to understand what determines the duration of the intervals that separate consecutive perceptual alternations from one eye's view to the other.

Observer variables of influence on percept durations. During binocular rivalry, the typical rate at which perception alternates between the two eyes' views is once every few seconds. The interval duration between two consecutive alternations varies unpredictably from one interval to the next (Fox & Herrmann, 1967; Levelt, 1967), but the average interval duration across several alternations is quite reproducible for a given observer. This average percept duration does differ considerably between observers, and this variation correlates with observers' responses to other visual stimuli that involve some competition element (Baker & Graf, 2009b; Carter & Pettigrew, 2003; Shannon, Patrick, Jiang, Bernat, & He, 2011; Sheppard & Pettigrew, 2006), as well as being partly predicted by clinical disorders (Pettigrew & Miller, 1998), personality traits (Nagamine et al., 2007) and observers' genetic makeup (Miller et al., 2010; Shannon et al., 2011; see also chapter by Bressler, Denison, & Silver, this volume). Within individuals, the duration moreover changes with age (Jalavisto, 1964; Ukai, Ando, & Kuze, 2003), history of prior exposure to binocular rivalry (Lehky, 1995; Suzuki & Grabowecky, 2007; van Ee, 2005) and intake of various psychoactive substances (Bárány & Halldén, 1947; Carter, Hasler, Pettigrew, Wallis, Liu, & Vollenweider, 2007; Donnelly & Miller, 1995; Frecska, White, & Luna, 2004; George, 1936; see also chapter by Bressler et al., this volume).

One longstanding question in rivalry research is whether observers can alter the binocular rivalry alternation cycle through mental effort. This question has received renewed interest in recent years, and is discussed in detail in the chapter by Bressler et al. in this volume.

Stimulus variables of influence on percept durations. Changes to the visual stimuli used to instigate binocular rivalry often affect the interval duration between consecutive perceptual alternations. Particularly well documented is the dependence of the perceptual alternation cycle on the physical properties of the rivaling images themselves, which are said to determine the ‘stimulus strength’ of the images (Levelt, 1966). These properties include the rival targets’ motion content (Blake, Yu, Lokey, & Norman, 1998; Bossink, Stalmeier, & de Weert, 1993; Breese, 1909; Haynes & Rees, 2005; Wade, de Weert, & Swanston, 1984), spatial frequency content (i.e., spatial grain, related to the degree of blurring; Arnold, Grove, & Wallis, 2007; Baker & Graf, 2009a; Fahle, 1982; Levelt, 1966), color difference (Bossink et al., 1993; Wade, 1975) and location in the visual field (Breese, 1909; Chen & He, 2003; Fahle, 1987; Levelt, 1966). The most important factor may be image contrast, a variable that quantifies the luminance difference between an image’s brightest and darkest parts. The influence of contrast on dominance durations has been quantified in some detail (Bossink et al., 1993; Brascamp, van Ee, Noest, Jacobs, & van den Berg, 2006; Fox & Rasche, 1969; Kang, 2009; Levelt, 1966; Mueller & Blake, 1989), providing an effective experimental handle on the alternation cycle, as well as a starting point for many computational models of binocular rivalry (see chapter by Wilson, this volume). The effects of contrast (and, by extension, ‘stimulus strength’ in general) on percept durations can be summarized by two rules. First, simultaneously lowering the contrasts of both rivaling images reduces the rate at which perception alternates, with individual dominance episodes taking longer when the images are fainter (Levelt, 1966). Second, lowering the contrast of only one of the images reduces the relative proportion of time it is perceived. It was long believed that this latter reduction stems primarily from lengthened dominance periods of the image whose contrast is being kept constant, rather than from shortened dominance periods of the image whose contrast is being reduced (Levelt’s influential ‘second proposition’; Levelt, 1966), but this is now known to depend on stimulus particulars (Brascamp et al., 2006; Kang, 2009).

Percept durations are also affected by placing the rivaling images within a surrounding context, as discussed in detail in the chapter by Bressler et al. in this volume. It is plausible that several effects of surrounding patterns on rivalry are related to real world situations in which an element may be seen by one eye but occluded from view to the other eye: it appears the visual system infers from the

visual context which eye is being occluded and adjusts the weight of the eyes' images accordingly (Ooi & He, 2006; Shimojo & Nakayama, 1990). Surround effects may also in part be responsible for the tendency for dominance to become entrained between adjacent regions within a rivaling stimulus when these regions match in some feature, such as pattern orientation or color (Alais & Blake, 1999; Alais, Lorenceau, Arrighi, & Cass, 2006; Silver & Logothetis, 2004). This tendency for matching regions to dominate simultaneously is partially maintained, even if the matching regions do not belong to the same image but, instead, are distributed across the eyes, a phenomenon called 'interocular grouping' (Díaz-Caneja, 1928; Kovács, Papathomas, Yang, & Fehér, 1996; Ngo, Miller, Liu, & Pettigrew, 2000; Suzuki & Grabowecky, 2002; though see Lee & Blake, 2004).

There is considerable evidence that the meaningful content of images engaged in rivalry affects dominance durations (Engel, 1956; Kohn, 1960). For instance, images that depict a coherent, recognizable object enjoy more perceptual dominance than images that do not have these configural properties but that are otherwise similar (Yu & Blake, 1992). Much work, especially in recent years, has investigated whether the emotional content of images also plays a role, the overall conclusions being that pictures of faces tend to dominate over less socially relevant stimuli, including those same face pictures shown upside-down (Bannerman, Milders, de Gelder, & Sahraie, 2008; Engel, 1956), and that this predominance is further enhanced when the faces show a strong emotion (Alpers & Gerdes, 2007; Coren & Russel, 1992; Yoon, Hong, Joormann, & Kang, 2009). This same conclusion extends to non-face stimuli with strong emotional content (Alpers, Ruhleder, Walz, Mühlberger, & Pali, 2005; Sheth & Pham, 2008). There has been discussion about the extent to which this type of finding reflects observers' response biases and/or the physical, rather than emotional, properties of the images used (Alpers & Pauli, 2006; Sheth & Pham, 2008), as well as about the extent to which some images used are suitable for inducing robust binocular rivalry (Gray, Adams, & Garner, 2009). Considering the whole literature on this topic, however, a dependence of binocular rivalry dominance on the meaningful and emotional content of the images used is plausible.

Stochastic properties of the alternation cycle. The perceptual alternation cycle contains a random element, in that the duration of individual dominance periods varies unpredictably from one period to the next. There has been some interest in characterizing this stochastic component, mainly because it may inform about the mechanisms underlying binocular rivalry (Brascamp, van Ee, Pestman, & van den Berg, 2005; Fox & Herrmann, 1967; Lehky, 1995; Levelt, 1967; Murata, Matsui, Miyauchi, Kakita, & Yanagida, 2003; Moreno-Bote, Rinzel, & Rubin, 2007; Shpiro et al., 2009).

One consistent result is that, even though individual percept durations are unpredictable, plotting a frequency histogram of all percept durations that occurred during a given session reveals a similar distribution every time (Figure 1). This distribution peaks near the average percept duration for that session, and has a relatively long tail towards the right. In other words, durations close to the average are most common, yet percepts of much longer duration invariably also occur. This result is so consistent that a replication of this distribution shape is often considered a validity check for data obtained using binocular rivalry or related paradigms (Logothetis, Leopold, & Sheinberg, 1996; O'Shea, Parker, La Rooy, & Alais, 2009), for instance when the experimental subject is a monkey and one cannot ask it directly whether it is experiencing rivalry (Leopold & Logothetis, 1996). There is some tradition of comparing distributions of percept durations to theoretically derived 'gamma distributions' (Kovács et al., 1996; Leopold & Logothetis, 1996; Levelt, 1967; Logothetis et al., 1996; Murata et al., 2003; O'Shea et al., 2009), but this practical convention should not be taken to indicate that gamma distributions have inherent significance in this context: other theoretical distributions are also suitable (Brascamp et al., 2005; Lehky, 1995; Moreno-Bote et al., 2007; Shpiro et al., 2009; Zhou et al., 2004).

A second property that is sometimes mentioned in the literature as a hallmark of rivalry's stochastic behavior is sequential independence of successive dominance durations or, in other words, the characteristic that a given dominance duration is entirely non-predictive of the next (Fox & Herrmann, 1967; Lehky, 1995; Leopold & Logothetis, 1996; O'Shea et al., 2009; Walker, 1975). More recent evidence, however, indicates that some degree of predictability exists (Gao et al., 2006; Pastukhov & Braun, 2011; van Ee, 2009).

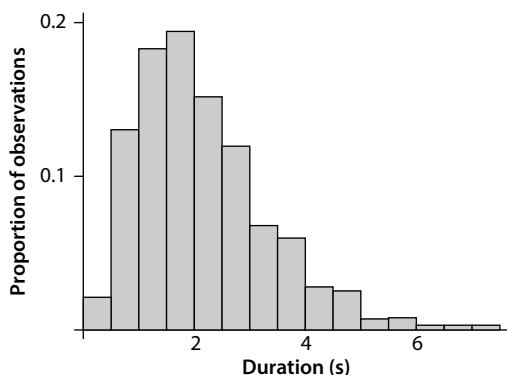


Figure 1. A typical distribution of dominance durations observed during a binocular rivalry session.

Mixed perception. With most of rivalry's appeal and utility stemming from the fact that it can render an otherwise obvious image invisible even when the observer looks straight at it, it is easily overlooked that part of the time while viewing a binocular rivalry stimulus neither image is entirely invisible and instead observers perceive a mixture of both images simultaneously (Blake et al., 1992; Hollins, 1980; O'Shea, Sims, & Govan, 1997; Wade, 1975; Wheatstone, 1838).

These mixtures come in various kinds (Yang et al., 1992), the most common ones often being referred to as 'piecemeal dominance' and 'superimposition'. During piecemeal dominance a single eye's view dominates in any given region of the visual field, but eye dominance differs from one region to the next, often resulting in a mosaic-like appearance (Blake et al., 1992). Piecemeal dominance is especially common for larger displays (>1 degree) but also occurs for small ones (Blake et al., 1992; O'Shea et al., 1997; Yang et al., 1992). In particular, perceptual transitions from one eye's view to the other often start in a local region of the visual field and then spread across the stimulus area until the transition is complete. New methods have recently been developed to control and investigate these 'traveling waves' of dominance and suppression. Wilson et al. (2001) used a pair of annular stimuli, textured with rivaling contours, to steer the propagation of dominance waves around a circular path. Transiently increasing the stimulus contrast in a local region of the suppressed image initiated a transition at a known location and time, which reliably traveled around the annulus. Recent studies have extended this technique to further explore the spread of interocular suppression across space (Kang, Heeger, & Blake, 2009; Knapen, van Ee, & Blake, 2007; Nichols & Wilson, 2009).

During the second kind of mixed perception, 'superimposition', both images are perceived transparently, superimposed at the same location (Liu, Tyler, & Schor, 1992; Wolfe, 1983; Yang et al., 1992). This happens most consistently for very briefly presented stimuli (Wolfe, 1983), but can also occur during continuous viewing (Brascamp et al., 2006; Liu et al., 1992; Klink, Brascamp, Blake, & van Wezel, 2010). It appears that both the increase in mixed perception that occurs with decreasing stimulus contrast (Hollins, 1980) and the increase observed after prolonged exposure to a rivalry stimulus (Hollins & Hudnell, 1980) primarily reflect increases in this second kind of mixture, superimposition (Brascamp et al., 2006; Klink et al., 2010; Liu et al., 1992).

Much less common but equally interesting are cases where one of the images is rendered fully invisible but the image that remains seen takes on properties of the unseen image. For instance, when each eye is shown a different picture and, in addition, these pictures are printed in different colors, observers sometimes perceive the picture presented to one eye, but in the color seen by the other eye (Creed, 1935; Hastorf & Myro, 1959; Holmes, Hancock, & Andrews, 2006;

Hong & Blake, 2009; Lange-Malecki, Creutzfeldt, & Hinse, 1985). Related findings show that while one of the images remains entirely suppressed, its properties can still influence the perceived motion (Andrews & Blakemore, 1999, 2002; Carney, Shadlen, & Switkes, 1987), orientation (Pearson & Clifford, 2005b) and flicker (Carlson & He, 2000) of the remaining image.

Onset dominance. Although the alternating perceptual cycle might be the most conspicuous aspect of binocular rivalry, other properties of rivalry convey valuable information as well. In particular, instead of asking how long a particular image dominates during rivalry, one can ask which image is perceived first after a stimulus appeared (e.g., Carter & Cavanagh, 2007; Hastorf & Myro, 1959; Mitchell, Stoner, & Reynolds, 2004; Stanley, Carter, & Forte, 2011; Wolfe, 1984). The binary choice involved in reporting such 'onset dominance' has been argued to rely less on an individual observer's criterion settings than reporting dominance durations (Gray et al., 2009; Walker, 1978), a notion that makes sense given the occurrence of mixed perception accompanying perceptual alternations (see above). Another practical benefit of focusing on onset dominance is that, whereas it is hard to predict which percept will dominate at any given moment throughout viewing, one can quite effectively control which percept will be perceived first using experimental manipulations, which is useful in many situations (see also the section headed 'Methods for controlling binocular rivalry').

In general, the dependencies of onset dominance are similar to those of dominance durations during prolonged viewing. For instance, both variables are influenced in a qualitatively similar way by stimulus contrast (Chong & Blake, 2006; Kamphuisen, van Wezel, & van Ee, 2007; Mamassian & Goutcher, 2005), and by attention to one of the images (Chong & Blake, 2006; Hancock & Andrews, 2007; Klink, van Ee, Nijs, Brouwer, Noest, & van Wezel, 2008b; Mitchell et al., 2004). Having said that, onset dominance tends to depend more strongly on these factors than do dominance durations (Carter & Cavanagh, 2007; Chong & Blake, 2006; Mamassian & Goutcher, 2005). For instance, a twofold contrast difference between the two images can cause the high-contrast image to gain dominance on about 85% of all stimulus onsets (Kamphuisen et al., 2007), amounting to an onset dominance ratio of about 1:6, whereas a similar contrast difference consistently yields a ratio of dominance durations of 1:2 or less at a range of stimulus settings (Bossink et al., 1993; Brascamp et al., 2006; Mueller & Blake, 1989). In addition, there is evidence that some factors that influence onset dominance may not impact dominance during prolonged viewing at all (Carter & Cavanagh, 2007; Stanley et al., 2011).

An aspect of onset dominance that has received renewed attention in recent years is its pronounced dependence on prior visual stimulation. That is, previewing

either the rivalry stimulus itself or one of its constituent monocular images strongly influences which percept will dominate first upon renewed presentation (Pearson & Brascamp, 2008). Previewing only one of the constituent images in most cases causes the alternative image to gain initial perceptual dominance upon subsequent rivalrous viewing (Pearson & Clifford, 2005a; Wade & de Weert, 1986; Wolfe, 1984), a phenomenon called 'flash suppression'. In contrast, previewing the full rivalry stimulus itself usually causes the same percept that dominated during the preview to gain dominance again upon renewed presentation (Chen & He, 2004; Leopold, Wilke, Maier, & Logothetis, 2002; Pearson & Clifford, 2004). It deserves mention that the above descriptions are generalizations: there are conditions (such as at low contrast) where the exact opposite effects are observed, so that previewing a rivalry stimulus causes dominance of the previously suppressed percept upon renewed presentation (Brascamp, Pearson, Blake, & van den Berg, 2009a; Kanai, Knapen, van Ee, & Verstraten, 2007; Klink et al., 2008b; Noest, van Ee, Nijs, & van Wezel, 2007), and so that previewing just one constituent image causes dominance of exactly that image upon rivalrous presentation (Brascamp, Knapen, Kanai, van Ee, & van den Berg, 2007; Pearson, Clifford, & Tong, 2008).

Sensitivity during suppression. Whereas the approaches described above all rely on introspective reports of perceptual dominance as their only measure, other psychophysical methods investigate binocular rivalry in a more objective fashion. One such method is to assess observers' performance on detecting events that occur either in the dominant image or in the suppressed image. For instance, Fox and Check (1968) set an element of one of the two rivaling images in motion, and asked observers to report any perceived motion as quickly as possible. The authors relied on observers' responses of perceptual dominance prior to applying the motion stimulus to make its presentation coincide with either dominance or suppression. Response times were much longer for motion in the suppressed image compared to the dominant image, providing objective verification for a loss of sensitivity associated with perceptual suppression.

When an image is suppressed in binocular rivalry, is the associated sensitivity loss restricted to the features of that suppressed image itself, or is any target that one may superimpose on the suppressed image harder to detect? This question bears on the issue of what exactly is suppressed during binocular rivalry. Several experiments show that even targets that have little in common with the rivaling images themselves become more difficult to detect when they are superimposed on the suppressed image compared to the dominant image (Blake & Camisa 1978; Blake & Fox, 1974b; Fox & Check, 1968; Nguyen, Freeman, & Wenderoth, 2001; O'Shea & Crassini, 1981b; Smith, Levi, Harwerth, & White, 1982). As an example, such a target might have an orientation that differs greatly from the orientations

present in the rivaling images, yet its detection will still be affected by suppression. These findings indicate that rivalry suppression has a fairly non-selective effect on any input from the retinal region of the suppressed image. Nevertheless, suppression does show a certain degree of selectivity (Ooi & Loop, 1994; O'Shea & Crassini, 1981b; Smith et al., 1982; Stuit, Cass, Paffen, & Alais, 2009; Walker & Powell, 1979), with one recent report indicating that detection of targets similar to the suppressed image suffers more strongly from suppression than detection of highly dissimilar targets (Stuit et al., 2009).

Apart from depending somewhat on the nature of the item to be detected, the degree of detection impairment during suppression is thought to depend on both the spatial location within the rivaling images, being stronger near the center than near the edge (Fukuda, 1981), and on the moment within a suppression period: detection in a suppressed retinal region is impaired more strongly if the image just became suppressed, than if it is about to regain dominance (Alais, Cass, O'Shea, & Blake, 2010). This latter finding contrasts with well-known earlier reports which state that detection is equally impaired at any moment within a suppression period (Fox & Check, 1972; Norman, Norman, & Bilotta, 2000). This discrepancy is likely due to methodological details, as discussed by Alais et al. (2010).

When it comes to detection performance during perceptual suppression, one mystery remains only partly resolved. When expressed in terms of image contrast, for a 'probe' item presented upon a rivalry stimulus during suppression to be detected it has to be about twice as intense as that same item presented during dominance (Blake & Camisa, 1978; Nguyen et al., 2001). In comparison, the complete invisibility that characterizes the phenomenal impression of a suppressed image corresponds to a contrast reduction of much more than a factor two. Moreover, even though the detectability of a probe item introduced during suppression depends on many properties of both that item itself (see above) and of the suppressing image (Norman et al., 2000), it is not usually thought that such factors affect the phenomenal impression of the suppressed image: if the image is properly suppressed no phenomenal awareness exists of any element at any moment during suppression. It thus appears that reduced visual sensitivity, although associated with perceptual suppression, cannot fully explain the subjective disappearance of an image during binocular rivalry.

There are two possible explanations for how observers are able to respond to a probe presented upon a suppressed stimulus. The first is that the introduction of a probe stimulus breaks the suppression, and causes a reversal of dominance. Because sudden changes are known to draw attention even during perceptual suppression, and to sometimes reverse perceptual dominance (Blake, Westendorf, & Fox, 1990; Ooi & He, 1999; O'Shea & Crassini, 1981b), most studies try to avoid this by using a smooth temporal envelope for the probe (e.g., Alais et al., 2010).

However, no study has yet investigated this issue rigorously, so the possibility that probes might interrupt rivalry dominance enough for them to be phenomenally experienced has not been ruled out.

A second possibility is of greater interest to consciousness research. It is that performance on a detection task during suppression might be above chance level without any phenomenal awareness of the probe item. Such a finding is reminiscent of neurological reports of patients with 'blindsight', who are able to detect stimuli of which they are consciously unaware (Weiskrantz, 1986). Similar phenomena have been described in healthy observers in other psychophysical paradigms (e.g., Dienes, 2008; Kolb & Braun, 1995; Sandberg, Timmermans, Overgaard, & Cleeremans, 2010), many of which involve dichoptic presentation (i.e., presenting different stimuli to the two eyes). These results could indicate that detection performance depends on activity early in the processing hierarchy, whereas subjective perception also requires more advanced processing that may be more compromised during perceptual suppression. Such a notion is supported by the finding (Nguyen, Freeman, & Alais, 2003) that sensitivity becomes increasingly impaired for stimuli that are more complex (in either form or motion) and that arguably rely on neural events higher up in the cortical processing hierarchy (see also Li, Freeman, & Alais, 2005). One way to assess the phenomenal awareness of probes during binocular rivalry is to ask observers to respond when they are consciously aware of a probe or to report the perceived contrast of suppressed or dominant stimuli. These methods would extend existing studies, which use forced choice methods that require a response at fixed times, regardless of phenomenal state.

Although the bulk of research on visual sensitivity during rivalry suppression has simply measured the degree to which detection is impaired in the suppressed eye, some studies have attempted to go beyond this and to investigate in more detail the respects in which detection is affected. This work has shown that the reduced ability to detect an item during perceptual suppression may be due, in part, to a reduced strength of the neural representation of that item (Ling, Hubert-Wallander, & Blake, 2010; Watanabe, Paik, & Blake, 2004) and, in part, to reduced fidelity of that representation (Ling & Blake, 2009).

Competition between eyes or between images? Any exploration of binocular rivalry literature from the past decade or so will inevitably turn up references to the following question. Does binocular rivalry really entail competition between signals specifically associated with the two eyes (as suggested, e.g., by the fact that any probe item presented to the suppressed eye is hard to detect, even if it is dissimilar to the images engaged in rivalry; see above) or, alternatively, does it entail competition between two signals representing incompatible images at a level that

is independent of the eye of origin (as suggested, e.g., by the ‘interocular grouping’ phenomenon discussed above)? We mention this debate because of its recent prominence but we will not review the evidence here. This is, in part, because the field has now reached a consensus that monocular signals and eye-independent signals both play a role in rivalry and, in part, because excellent reviews of this issue exist elsewhere (Blake & Logothetis, 2002; Keliris, Logothetis & Tolia, 2010; Tong, Meng, & Blake, 2006).

Class II. Binocular rivalry as a tool for probing unconscious processing

Recent years have seen an increase in psychophysical studies that do not investigate the rivalry phenomenon itself but that, instead, use binocular rivalry to render an image invisible with the objective of investigating what neural processing of the unseen image remains. Although placing these studies in a separate category is somewhat arbitrary, it is justified in the present context, given that these studies are the ones most explicitly aimed at furthering our understanding of consciousness. In very general terms, their common motivation is to understand the difference between conscious and unconscious neural events by measuring behavioral and neural activity associated with the image that is temporarily suppressed during rivalry, and comparing it to that associated with the same image when it is visible.

Methods for controlling binocular rivalry. As described above, rivalry alternations are generally stochastic. However, several techniques (see Figure 2) have been developed to influence the dominance state of binocular rivalry and thereby gain control over which image will be invisible at any time. These techniques play a large role in the literature that uses binocular rivalry to study visual consciousness, because there the objective is often exactly that: to suppress a predetermined image from consciousness at a controlled time.

One method, previously mentioned in the section titled ‘Onset dominance’, is the flash suppression paradigm (Wolfe, 1984). Here a stimulus is presented to only one eye for around 1 to 2 seconds. This stimulus is then removed, and rivaling stimuli are displayed at the same location. The image to become suppressed from awareness first is quite reliably the one shown to the eye that previously received the monocular stimulus, especially if this monocular stimulus resembles the image that same eye subsequently receives during rivalry.

Flash suppression can be used to render a specific image invisible at the onset of the binocular rivalry stimulus, but for longer presentations perceptual alternations occur, and perception becomes unpredictable again. An influential technique developed more recently, called continuous flash suppression (CFS; Tsuchiya & Koch, 2005), builds on the flash suppression paradigm by presenting a rapid

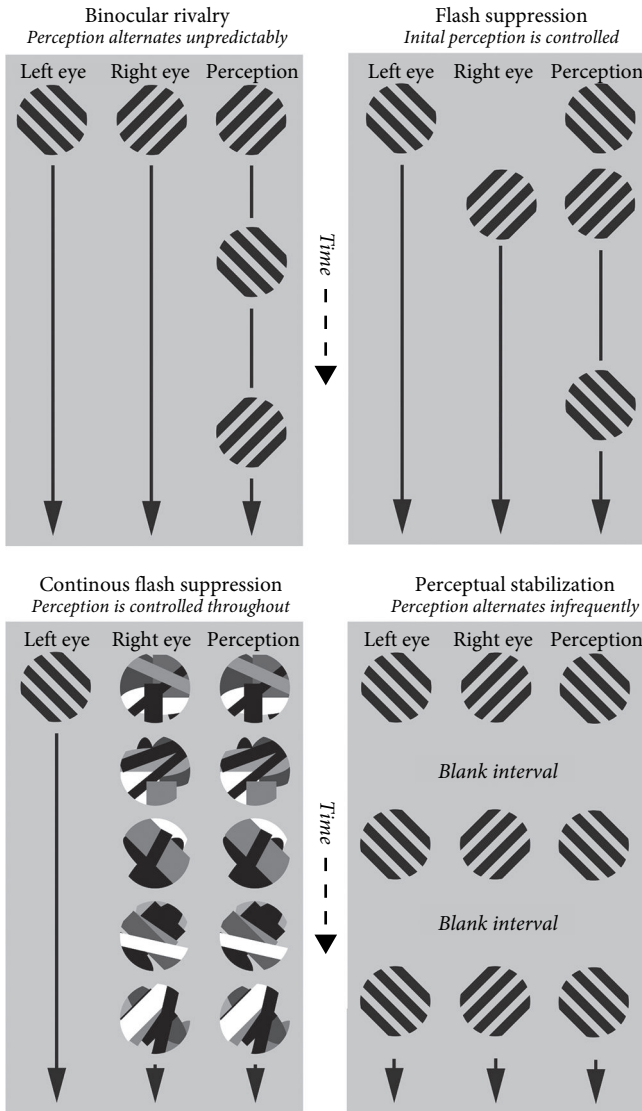


Figure 2. Techniques for controlling perception during binocular rivalry.

sequence of high contrast patterns to one eye, and a stationary target image to the other eye. The target image remains invisible for extended periods of time (in the order of tens of seconds or minutes), and appears to be suppressed more deeply than in traditional rivalry when using a probe task (Tsuchiya, Koch, Gilroy, & Blake, 2006). A variant of this technique involves switching the stimuli between

the eyes around once per second (binocular switch suppression; Arnold, Law, & Wallis, 2008), which can lead to even greater suppression. In the context of consciousness research such quasi-permanent binocular suppression techniques are of particular importance, because the sustained nature of suppression allows a much greater flexibility of the type of questions one can answer regarding the processing of the suppressed stimuli. For instance, studies that rely on adaptation as an index of unconscious processing (see below) nowadays often use CFS rather than traditional binocular rivalry, because CFS allows more prolonged exposure periods which result in more robust adaptation. See also the chapters by Sengpiel and Sterzer (this volume) for further examples of the flash suppression and CFS techniques.

The characteristic percept alternations during rivalry can be arrested by a surprisingly simple manipulation, in which the stimuli are periodically removed from view (Leopold et al., 2002; Pearson & Brascamp, 2008). This stabilizes the conscious percept for periods of several minutes or more, depending on the duration of the removal period (Brascamp et al., 2009a), thus providing another handle on perception during binocular rivalry. This method is termed perceptual stabilization and it builds on the tendency, mentioned in the section titled 'Onset dominance', for perception at rivalry onset to conform to perception during prior viewing of the same stimulus. The method is particularly robust because this effect of prior perception accumulates across repeated presentations during an intermittent presentation sequence (Brascamp, Knapen, Kanai, Noest, van Ee, & van den Berg, 2008; Brascamp et al., 2009a; Pastukhov & Braun, 2008).

Adaptation and priming. Many standard psychophysical approaches that rely on reported perception can clearly not be used for an item that is perceptually suppressed, but several indirect measures of processing during invisibility are available. Two related psychophysical phenomena that have been extensively used in this context are adaptation and priming. Adaptation, in a psychophysical context, refers to the fact that exposure to a particular sensory input can affect subsequent perception of similar input, both by impairing sensitivity and by biasing perceptual judgments away from the properties of the previewed item. For example, viewing a vertical line for some time will impair detection of subsequent vertical lines (Blakemore & Campbell, 1969), as well as causing slightly off-vertical orientations to be judged as tilted farther from vertical than they really are (Campbell & Maffei, 1971). Such perceptual effects of adaptation are usually called 'aftereffects'. Priming is a very similar phenomenon. By definition, it differs from adaptation in that performance is biased towards, rather than away from, the previewed item. By and large, priming tends to be more common in higher-level cognitive tasks, such as those involving language, whereas adaptation is often observed with simpler tasks involving, for instance, detection of a visual stimulus. The key characteristic

of adaptation and priming that renders these phenomena suitable for assessing unconscious processing, is that processing of a prior item, which may be invisible, is indexed in terms of behavioral responses to a subsequent, visible, item.

An overview of the literature on priming and adaptation in the context of binocular rivalry shows that not all processing of an invisible stimulus is abolished, yet that processing is clearly impoverished compared to that of a visible stimulus (Lin & He, 2009). This results in different kinds of aftereffects being reduced to varying extents by perceptual suppression of the adapting stimulus (summarized in Figure 3). In general, adaptation and priming effects that arguably rely on fairly early (and therefore simpler) sensory processes, such as those related to judgments of orientation or motion direction, tend to be quite well preserved when the adapting (priming) stimulus is rendered invisible during binocular rivalry (Blake, Ahlström, & Alais, 1999; Blake & Fox, 1974a; Blake & Overton, 1979; Blake, Tadin, Sobel, Raissian, & Chong, 2006; Lehmkuhle & Fox, 1975; Moradi, Koch, & Shimojo, 2005; O'Shea & Crassini, 1981a; van der Zwan & Wenderoth, 1994; van der Zwan, Wenderoth, & Alais, 1993; Wade & Wenderoth, 1978; White, Petry, Riggs, & Miller, 1978). For instance, the 'translational motion aftereffect', a tendency to perceive stationary patterns as flowing upward after prolonged exposure to a pattern that flows down, is only slightly reduced if the downward motion remained unperceived due to binocular rivalry (Blake et al., 2006; Lehmkuhle & Fox, 1975; O'Shea & Crassini, 1981a; van der Zwan et al., 1993). Having said that, the impression from earlier literature that effects of this kind are not at all reduced by binocular rivalry suppression is no longer supported by experimental evidence (Blake et al., 2006; Brascamp, van Boxtel, Knapen, & Blake, 2009b; Gilroy & Blake, 2005; Lehky & Blake, 1991; Tsuchiya & Koch, 2005; van Boxtel, Tsuchiya, & Koch, 2010; van der Zwan et al., 1993; van der Zwan & Wenderoth, 1994).

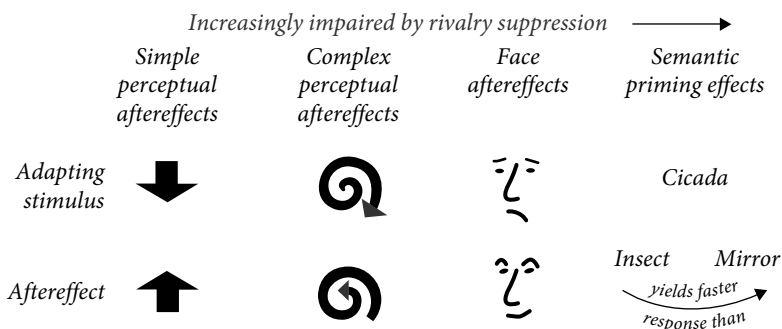


Figure 3. Perceptual suppression of an adapting stimulus impairs the formation of different types of aftereffects to different extents.

In contrast to the 'simple' adaptation and priming effects summarized above, which are generally only mildly affected by binocular rivalry suppression, many effects that arguably draw on more central, integrated, processing are strongly reduced and sometimes entirely abolished when the inducing stimulus is rendered invisible in binocular rivalry. This is true, for example, of various forms of motion adaptation for which (in contrast to the 'translational motion aftereffect') the responses of a single population of motion-responsive neurons are insufficient and that instead require responses to be pooled across various neural populations with different motion sensitivities (Lack, 1978; van der Zwan et al., 1993; Wiesenfelder & Blake, 1990). For instance, the illusory inward spiraling motion that is perceived after being exposed to an outward spiraling pattern, is much reduced when that outward moving pattern is perceptually suppressed.

Another kind of adaptation that is greatly impaired by binocular rivalry suppression is adaptation to facial features such as identity, gender and emotional expression (Adams, Gray, Garner, & Graf, 2010, 2011; Moradi et al., 2005; Shin, Stolte, & Chong, 2009; Yang, Hong, & Blake, 2010). In a typical face adaptation experiment, neutral faces are perceived as happy when displayed after exposure to a sad face. Such effects can be very strongly reduced and in some cases abolished when the adapting face is perceptually suppressed (Moradi et al., 2005; Shin et al., 2009; Yang et al., 2010; though see Adams et al., 2010, 2011). Similarly, semantic priming phenomena, which require analysis of printed text or images at the level of their meaning, are often eliminated under binocular rivalry suppression (Cave et al., 1998; Zimba & Blake, 1983).

One might summarize the findings in this section by the rule that 'higher level' neural analysis tends to be abolished or impaired during binocular rivalry suppression, whereas simple and more peripheral processing remains relatively unaffected (Figure 3). However, several recent findings provide evidence for an exception to this rule. A kind of semantic priming that requires images of tools to be differentially processed compared to other objects is partially preserved under suppression (Almeida, Mahon, Nakayama, & Caramazza, 2008). Similarly, perceptual suppression does not abolish numerical priming by Arabic numerals, which requires assessment of the quantity abstractly conveyed by these symbols (Bahrami, Vetter, Spolaore, Pagano, Butterworth, & Rees, 2010). These findings are thought to point to relatively spared processing up to advanced levels in the 'dorsal processing stream' whose main function is to guide motor responses (though it also mediates numerosity; see Eger, Sterzer, Russ, Gigaud, & Kleinschmidt, 2003; Piazza, Izard, Pinel, Bihan, & Dehaene, 2004), as compared to the 'ventral processing stream', more closely associated with perception (Goodale & Milner, 1992).

It is of interest to note that several adaptation effects that are reduced or abolished under binocular rivalry suppression are partially restored when observers are required to direct their attention to the location or features of the adapting stimulus they cannot perceive (Bahrami, Carmel, Walsh, Rees, & Lavie, 2008; Kanai, Tsuchiya, & Verstraten, 2006; Shin et al., 2009; Yang et al., 2010; van Boxtel et al., 2010), even though this attention manipulation does not restore visibility of the suppressed stimulus. This demonstrates that modulation of these effects by binocular rivalry suppression is not solely attributable to invisibility per se.

Breaking from suppression. A relatively new approach in the psychophysical study of unconscious processing during binocular rivalry is to simultaneously switch on a relatively weak ‘target’ stimulus to one eye and a much stronger suppressing stimulus to the other eye (e.g., a CFS suppressor, see the section above titled ‘Methods for controlling binocular rivalry’). In this design the suppressing stimulus is perceptually dominant from the onset, and the observer is entirely unaware of what the target stimulus even is until it breaks from this suppression. It then becomes interesting to ask what properties of the target stimulus can modulate the time it takes for this break in suppression to occur, the reasoning being that these properties can only have this effect if they are processed unconsciously.

Several studies that use this approach have provided evidence that facial features can to some extent be processed outside of consciousness (Jiang, Costello, & He, 2007; Stein, Senju, Peelen, & Sterzer, 2011; Tsuchiya, Moradi, Felsen, Yamazaki, & Adolphs, 2009; Yang, Zald, & Blake, 2007). For instance, images of emotional faces break from suppression earlier than do images of neutral faces (Yang et al., 2007), an effect that is modulated by certain disorders and personality traits (Sterzer, Hilgenfeldt, Freudenberg, Bermpohl, & Adli, 2011; see also Gray et al., 2009). Related experiments using semantic stimuli have shown that characters of a script that is known to the observer break from suppression faster than unknown characters (Jiang et al., 2007), as do words that have been semantically primed compared to ones that have not (Costello, Jiang, Baartman, McGlennen, & He, 2009) and words that carry emotional meaning (Yang & Yeh, 2011).

This series of findings thus suggests that some processing of both semantic content and facial expression remains during perceptual suppression, even though evidence from adaptation and priming, reviewed above, indicates that these types of processing are much impaired.

Other evidence. Several other psychophysical observations speak to the issue of unconscious processing during binocular rivalry. A small number of studies have investigated whether the allocation of attention within a scene can be driven by perceptually suppressed visual input. These studies indicate that attention

cues whose meaning has to be learned, such as a leftward pointing arrow, lose their potential to guide attention when invisible (Schall, Nawrot, Blake, & Yu, 1993), but that automatic attention allocation to, for instance, erotic images is preserved when these images remain unperceived (Jiang, Costello, Fang, Huang, & He, 2006).

Finally, there is evidence that items that are suppressed during binocular rivalry can exert an influence on the perception of visible items displayed at nearby locations. For instance, the impression of motion one experiences when, say, a flash of light is quickly followed by an identical light flash somewhat to its right, giving the perception that a light is moving rightward, is preserved even when the first flash remains perceptually suppressed (Wiesenfelder & Blake, 1991). Also, the apparent brightness of an item, which is influenced by the brightness of the item's visual surroundings, is still subject to this influence when these surroundings themselves are rendered invisible in binocular rivalry (Harris, Schwarzkopf, Song, Bahrami, & Rees, 2011).

Parallels with other ambiguous stimuli

Although the focus of this volume is on binocular rivalry, it is worth mentioning that rivalry shares characteristics with other bistable stimuli. Classic bistable figures include Rubin's face/vase illusion and the Necker cube, both of which can be perceived in more than one way, with alternations occurring during extended viewing. Other work has yielded compelling bistable displays using motion, including bistable structure-from-motion stimuli (Nawrot & Blake, 1991; Wallach & O'Connell, 1953), bistable plaid patterns (Hupé & Rubin, 2003), and motion-induced blindness (Bonneh, Cooperman, & Sagi, 2001). There are many psychophysical parallels between different bistable stimuli, suggesting similarities in their neural basis. The observation that dominance durations conform to a gamma-like distribution, for instance, is common to many stimuli (Borsellino, de Marco, Allazetta, Rinesi, & Bartolini, 1972; Brascamp et al., 2005; Nawrot & Blake, 1991), as is the observed dependence of dominance durations on the relative strengths of the competing interpretations (Klink, van Ee, & van Wezel, 2008a; Moreno-Bote, Shpiro, Rinzel, & Rubin, 2010). Many characteristics described above regarding rivalry's dependence on prior visual experience are also observed for other bistable stimuli (Leopold et al., 2002; Long, Toppino, & Mondin, 1992; Kanai & Verstraten, 2005). Finally, alternation rates for different bistable stimuli (including binocular rivalry) show strong correlations within subjects (Carter & Pettigrew, 2003; Shannon et al., 2011; Sheppard & Pettigrew, 2006), again suggesting a dependence on common processes. Compared to other bistable stimuli, one distinct

advantage of binocular rivalry for the experimental study of consciousness is that an arbitrary visual stimulus can be rendered invisible (Kim & Blake, 2005), allowing greater experimental flexibility than other stimuli, which usually rely on a very particular stimulus design to give rise to bistable perception.

Concluding remarks: What have we learnt about consciousness?

Given the focus of this book it is appropriate at this point to discuss the implications of the above findings for the scientific understanding of consciousness. Surprisingly, based on what we summarized in this chapter one might draw two very different conclusions. On the one hand one might point to the exquisite control rivalry permits over the contents of consciousness and therefore its power in the hands of a consciousness researcher; on the other hand one might point to important remaining questions when trying to interpret the resulting data in terms of consciousness.

Regarding the ability to effectively and flexibly control access of visual input to conscious experience, binocular rivalry is probably the most powerful experimental tool available to researchers today. Psychophysical investigations of binocular rivalry have a long history, and have in large part evolved independently of questions about visual consciousness. This work has led to detailed knowledge about the characteristics of the phenomenon. The utility of binocular rivalry for consciousness research is bolstered by this extensive psychophysical knowledge built up in past years, and continues to grow thanks to new developments in binocular rivalry psychophysics, such as the introduction of continuous flash suppression less than a decade ago. As a result of these efforts, binocular rivalry has taught us much about which processes continue under conditions of perceptual suppression, and which do not. This chapter, following existing literature, has focused on these aspects of binocular rivalry.

A different question about binocular rivalry has not been extensively addressed in existing literature, yet is arguably as important for those investigators interested in consciousness. This is the question of what it means, in terms of consciousness research, if a particular phenomenon correlates with visibility during binocular rivalry. Broadly speaking, research in 'Class II' described above aims to learn about consciousness by studying correlates of visibility during binocular rivalry. However, paraphrasing, to apply to psychophysics, a seminal paper on the neuroscience of consciousness (Crick & Koch, 1998): just because a particular phenomenon correlates with visibility during binocular rivalry, does not automatically imply that this phenomenon has anything in particular to do with consciousness. Specifically, a consideration that, we believe, requires more attention in our

field is that any correlation with visibility observed during binocular rivalry may be specific to the binocular rivalry paradigm itself, rather than of general relevance. To illustrate this point, consider closing one's eyes as a means of controlling conscious perception: we generally do not believe all psychophysical phenomena affected by this act, such as pupil size or the formation of retina-based afterimages, to be informative regarding the neural basis of consciousness. Just the same, we cannot assume that binocular rivalry, when it causes an image to phenomenally disappear, does single out only those neural events that one would be interested in from the perspective of consciousness research. If an ultimate goal of consciousness research is to investigate whether any neural events consistently correlate with conscious experience, then we should make an effort to exclude ones that do so only in a binocular rivalry setting.

Binocular rivalry unquestionably informs about consciousness by allowing one to identify neural events that are, apparently, insufficient for conscious perception. For instance, the observation that certain aftereffects arise in response to stimuli rendered invisible during binocular rivalry, shows that neural activity that gives rise to these aftereffects does not, by itself, support consciousness. However, what does it mean when a particular phenomenon *is* abolished or affected by binocular rivalry suppression? Does this phenomenon reflect neural events that do have some special relation with consciousness? Several psychophysical findings suggest this does not necessarily follow, implying that binocular rivalry suppression also acts on neural events that are not directly involved in conscious experience. The examples in the remainder of this paragraph draw on findings discussed in the section above titled 'Adaptation and priming'. Findings summarized in that section show that directing attention to the unseen image during binocular rivalry suppression can strengthen, and in some cases even restore from absence, the build-up of aftereffects. This suggests that some neural events affected by binocular rivalry suppression can be recovered by attention manipulations without restoring visibility. Those events would thus fall into a category of events that are modulated by perceptual suppression during binocular rivalry, yet that do not support conscious perception.

Along similar lines, forms of semantic priming that are abolished when binocular rivalry suppression renders the priming stimulus invisible, do seem to survive invisibility if it is attained through different means (such as masking or anesthesia: Fowler, Wolford, Slade, & Tassinary, 1981; Kihlstrom, Schacter, Cork, Hurt, & Behr, 1990; Marcel, 1983; Somekh & Wilding, 1973; although see Merikle & Reingold, 1992). This situation prompted Cave et al. (1998) to conclude that 'the neural events critical for [these forms of] priming transpire at a stage intermediate between those mediating [binocular rivalry] suppression and those supporting conscious visual awareness'. Finally, although binocular rivalry

suppression can corrupt the formation of simple perceptual aftereffects, research into another form of suppression, termed motion-induced blindness, has hitherto shown no influence on those same aftereffects (Hofstoetter, Koch, & Kiper, 2004; Montaser-Kouhsari, Moradi, Zandvakili, & Estely, 2004). Given that conscious perception of the suppressed image is equally lacking in both paradigms, this would suggest that binocular rivalry's effects on these aftereffects is not related to consciousness per se.

In the light of such findings, it may be overconfident to speak of observations related to binocular rivalry suppression as 'correlates of consciousness'. A more appropriate term might be 'correlates of binocular rivalry suppression', treating any relation to consciousness, for now, as tentative. Accordingly, we believe that an important future objective for the binocular rivalry field should be to understand which of our many observations are really consciousness-related and which are not. One could envision several angles to approach this issue. One useful and feasible approach suggested by the above examples is to compare across different paradigms besides binocular rivalry. If some phenomenon consistently correlates with consciousness regardless of paradigm, rather than only during binocular rivalry, studying this phenomenon might be particularly fruitful in furthering our understanding of the neural basis of consciousness.

References

- Adams, W. J., Gray, K. L. H., Garner, M., & Graf, E. W. (2010). High-level face adaptation without awareness. *Psychological Science*, 21(2), 205–210.
- Adams, W. J., Gray, K. L. H., Garner, M., & Graf, E. W. (2011). On the "special" status of emotional faces... Comment on Yang, Hong, and Blake (2010). *Journal of Vision*, 11(3), 10. doi: 10.1167/11.3.10
- Alais, D., & Blake, R. (1999). Grouping visual features during binocular rivalry. *Vision Research*, 39(26), 4341–4353.
- Alais, D., Cass, J., O'Shea, R., & Blake, R. (2010). Visual sensitivity underlying changes in visual consciousness. *Current Biology*, 20(15), 1362–1367.
- Alais, D., Lorenceau, J., Arrighi, R., & Cass, J. (2006). Contour interactions between pairs of Gabors engaged in binocular rivalry reveal a map of the association field. *Vision Research*, 46(8–9), 1473–1487.
- Almeida, J., Mahon, B., Nakayama, K., & Caramazza, A. (2008). Unconscious processing dissociates along categorical lines. *Proceedings of the National Academy of Sciences USA*, 105(39), 15214–15218.
- Alpers, G., & Gerdes, A. (2007). Here is looking at you: Emotional faces predominate in binocular rivalry. *Emotion*, 7(3), 495–506.
- Alpers, G., & Pauli, P. (2006). Emotional pictures predominate in binocular rivalry. *Cognition & Emotion*, 20(5), 596–607.

- Alpers, G., Ruhleder, M., Walz, N., Mühlberger, A., & Pauli, P. (2005). Binocular rivalry between emotional and neutral stimuli: A validation using fear conditioning and EEG. *International Journal of Psychophysiology*, 57(1), 25–32.
- Andrews, T. J., & Blakemore, C. (1999). Form and motion have independent access to consciousness. *Nature Neuroscience*, 2(5), 405–406.
- Andrews, T. J., & Blakemore, C. (2002). Integration of motion information during binocular rivalry. *Vision Research*, 42(3), 301–309.
- Arnold, D. H., Grove, P. M., & Wallis, T. S. A. (2007). Staying focused: A functional account of perceptual suppression during binocular rivalry. *Journal of Vision*, 7(7), 7. doi: 10.1167/7.7.7
- Arnold, D. H., Law, P., & Wallis, T. S. A. (2008). Binocular switch suppression: A new method for persistently rendering the visible ‘invisible’. *Vision Research*, 48(8), 994–1001.
- Bahrami, B., Carmel, D., Walsh, V., Rees, G., & Lavie, N. (2008). Unconscious orientation processing depends on perceptual load. *Journal of Vision*, 8(3), 12. doi: 10.1167/8.3.12
- Bahrami, B., Vetter, P., Spolaore, E., Pagano, S., Butterworth, B., & Rees, G. (2010). Unconscious numerical priming despite interocular suppression. *Psychological Science*, 21(2), 224–233.
- Baker, D. H., & Graf, E. W. (2009a). Natural images dominate in binocular rivalry. *Proceedings of the National Academy of Sciences USA*, 106(13), 5436–5441.
- Baker, D. H., & Graf, E. W. (2009b). On the relation between dichoptic masking and binocular rivalry. *Vision Research*, 49(4), 451–459.
- Bannerman, R. L., Milders, M., De Gelder, B., & Sahraie, A. (2008). Influence of emotional facial expressions on binocular rivalry. *Ophthalmic & Physiological Optics*, 28(4), 317–326.
- Bárány, E. H., & Halldén, U. (1947). The influence of some central nervous depressants on the reciprocal inhibition between the two retinæ as manifested in retinal rivalry. *Acta Psychologica Scandinavica*, 13(4), 296–316.
- Blake, R., Ahlström, U., & Alais, D. (1999). Perceptual priming by invisible motion. *Psychological Science*, 10(2), 145–150.
- Blake, R., & Camisa, J. (1978). Is binocular vision always monocular? *Science*, 200(4349), 1497–1499.
- Blake, R., & Fox, R. (1974a). Adaptation to invisible gratings and the site of binocular rivalry suppression. *Nature*, 249(456), 488–490.
- Blake, R., & Fox, R. (1974b). Binocular rivalry suppression: insensitive to spatial frequency and orientation change. *Vision Research*, 14(8), 687–692.
- Blake, R., & Overton, R. (1979). The site of binocular rivalry suppression. *Perception*, 8(2), 143–152.
- Blake, R., O’Shea, R., & Mueller, T. (1992). Spatial zones of binocular rivalry in central and peripheral vision. *Visual Neuroscience*, 8(5), 469–478.
- Blake, R., Tadin, D., Sobel, K. V., Raissian, T. A., & Chong, S. C. (2006). Strength of early visual adaptation depends on visual awareness. *Proceedings of the National Academy of Sciences USA*, 103(12), 4783–4788.
- Blake, R., Westendorf, D., & Fox, R. (1990). Temporal perturbations of binocular rivalry. *Perception & Psychophysics*, 48(6), 593–602.
- Blake, R., & Logothetis, N. K. (2002). Visual competition. *Nature Reviews Neuroscience*, 3(1), 13–21.
- Blake, R., Yu, K., Lokey, M., & Norman, H. (1998). Binocular rivalry and motion perception. *Journal of Cognitive Neuroscience*, 10(1), 46–60.

- Blakemore, C., & Campbell, F. W. (1969). On the existence of neurones in the human visual system selectively sensitive to the orientation and size of retinal images. *Journal of Physiology*, 203(1), 237.
- Bonneh, Y., Cooperman, A., & Sagi, D. (2001). Motion-induced blindness in normal observers. *Nature*, 411(6839), 798–801.
- Borsellino, A., de Marco, A., Allazetta, A., Rinesi, S., & Bartolini, B. (1972). Reversal time distribution in the perception of visual ambiguous stimuli. *Kybernetik*, 10(3), 139–144.
- Bossink, C. J., Stalmeier, P. F., & de Weert, C. M. (1993). A test of Levelt's second proposition for binocular rivalry. *Vision Research*, 33(10), 1413–1419.
- Brascamp, J. W., Knapen, T. H., Kanai, R., van Ee, R., & van den Berg, A. V. (2007). Flash suppression and flash facilitation in binocular rivalry. *Journal of Vision*, 7(12), 12. doi: 10.1167/7.12.12
- Brascamp, J. W., Pearson, J., Blake, R., & van den Berg, A. V. (2009a). Intermittent ambiguous stimuli: Implicit memory causes periodic perceptual alternations. *Journal of Vision*, 9(3), 3. doi: 10.1167/9.3.3
- Brascamp, J. W., Knapen, T. H., Kanai, R., Noest, A. J., van Ee, R., & van den Berg, A. V. (2008). Multi-timescale perceptual history resolves visual ambiguity. *PLoS ONE*, 3(1), e1497. doi: 10.1371/journal.pone.0001497
- Brascamp, J. W., van Boxtel, J. J., Knapen, T. H., & Blake, R. (2009b). A dissociation of attention and awareness in phase-sensitive but not phase-insensitive visual channels. *Journal of Cognitive Neuroscience*, 22(10), 2326–2344.
- Brascamp, J. W., van Ee, R., Noest, A. J., Jacobs, R. H., & van den Berg, A. V. (2006). The time course of binocular rivalry reveals a fundamental role of noise. *Journal of Vision*, 6(11), 8. doi: 10.1167/6.11.8
- Brascamp, J. W., van Ee, R., Pestman, W. R., & van den Berg, A. V. (2005). Distributions of alternation rates in various forms of bistable perception. *Journal of Vision*, 5(4), 1. doi: 10.1167/5.4.1
- Breese, B. (1909). Binocular rivalry. *Psychological Review*, 16(6), 410–415.
- Campbell, F. W., & Maffei, L. (1971). The tilt after-effect: A fresh look. *Vision Research*, 11(8), 833–840.
- Carlson, T. A., & He, S. (2000). Visible binocular beats from invisible monocular stimuli during binocular rivalry. *Current Biology*, 10(17), 1055–1058.
- Carney, T., Shadlen, M., & Switkes, E. (1987). Parallel processing of motion and colour information. *Nature*, 328(6131), 647–649.
- Carter, O., & Cavanagh, P. (2007). Onset rivalry: Brief presentation isolates an early independent phase of perceptual competition. *PLoS ONE*, 2, e343. doi: 10.1371/journal.pone.0000343
- Carter, O. L., Hasler, F., Pettigrew, J. D., Wallis, G. M., Liu, G. B., & Vollenweider, F. X. (2007). Psilocybin links binocular rivalry switch rate to attention and subjective arousal levels in humans. *Psychopharmacology*, 195(3), 415–424.
- Carter, O. L., & Pettigrew, J. D. (2003). A common oscillator for perceptual rivalries? *Perception*, 32(3), 295–305.
- Cave, C. B., Blake, R., & McNamara, T. P. (1998). Binocular rivalry disrupts visual priming. *Psychological Science*, 9(4), 299–302.
- Chen, X., & He, S. (2003). Temporal characteristics of binocular rivalry: Visual field asymmetries. *Vision Research*, 43(21), 2207–2212.

- Chen, X., & He, S. (2004). Local factors determine the stabilization of monocular ambiguous and binocular rivalry stimuli. *Current Biology*, 14(11), 1013–1017.
- Chong, S. C., & Blake, R. (2006). Exogenous attention and endogenous attention influence initial dominance in binocular rivalry. *Vision Research*, 46(11), 1794–1803.
- Coren, S., & Russell, J. A. (1992). The relative dominance of different facial expressions of emotion under conditions of perceptual ambiguity. *Cognition & Emotion*, 6(5), 339–356.
- Costello, P., Jiang, Y., Baartman, B., McGlennen, K., & He, S. (2009). Semantic and subword priming during binocular suppression. *Consciousness and Cognition*, 18(2), 375–382.
- Creed, R. S. (1935). Observations on binocular fusion and rivalry. *Journal of Physiology*, 84(4), 381–392.
- Crick, F., & Koch, C. (1998). Consciousness and neuroscience. *Cerebral Cortex*, 8(2), 97–107.
- Díaz-Caneja, E. (1928). Sur l'alternance binoculaire. *Annales D'Oculistique*, 165, 721–731.
- Dienes, Z. (2008). Subjective measures of unconscious knowledge. *Progress in Brain Research*, 168, 49–64.
- Donnelly, M., & Miller, R. J. (1995). Ingested ethanol and binocular rivalry. *Investigative Ophthalmology & Visual Science*, 36(8), 1548–1554.
- Eger, E., Sterzer, P., Russ, M. O., Giraud, A.-L., & Kleinschmidt, A. (2003). A supramodal number representation in human intraparietal cortex. *Neuron*, 37(4), 719–725.
- Engel, E. (1956). The role of content in binocular resolution. *American Journal of Psychology*, 69(1), 87–91.
- Fahle, M. (1982). Cooperation between different spatial frequencies in binocular rivalry. *Biological Cybernetics*, 44(1), 27–29.
- Fahle, M. (1987). Naso-temporal asymmetry of binocular inhibition. *Investigative Ophthalmology & Visual Science*, 28(6), 1016–1017.
- Fechner, G. T. (1860). *Elemente der psychophysik*. Leipzig: Breitkopf & Härtel.
- Fowler, C. A., Wolford, G., Slade R., & Tassinari, L. (1981). Lexical access with and without awareness. *Journal of Experimental Psychology: General*, 110(3), 341–362.
- Fox, R., & Check, R. (1968). Detection of motion during binocular rivalry suppression. *Journal of Experimental Psychology*, 78(3), 388–395.
- Fox, R., & Check, R. (1972). Independence between binocular rivalry suppression duration and magnitude of suppression. *Journal of Experimental Psychology*, 93(2), 283–289.
- Fox, R., & Herrmann, J. (1967). Stochastic properties of binocular rivalry alternations. *Perception & Psychophysics*, 2(9), 432–436.
- Fox, R., & Rasche, F. (1969). Binocular rivalry and reciprocal inhibition. *Perception & Psychophysics*, 5(4), 215–217.
- Frecska, E., White, K. D., & Luna, L. E. (2004). Effects of ayahuasca on binocular rivalry with dichoptic stimulus alternation. *Psychopharmacology*, 173(1–2), 79–87.
- Fukuda, H. (1981). Magnitude of suppression of binocular rivalry within the invisible pattern. *Perceptual & Motor Skills*, 53(2), 371–375.
- Gao, J. B., Billock, V. A., Merk, I., Tung, W. W., White, K. D., Harris, J. G. et al. (2006). Inertia and memory in ambiguous visual perception. *Cognitive Processing*, 7(2), 105–112.
- George, R. W. (1936). The significance of the fluctuations experienced in observing ambiguous figures and binocular rivalry. *Journal of General Psychology*, 15(1), 39–61.
- Gescheider, G. (1997) *Psychophysics. The fundamentals* (3rd ed.). Mahwah: Lawrence Erlbaum.
- Gilroy, L. A., & Blake, R. (2005). The interaction between binocular rivalry and negative afterimages. *Current Biology*, 15(19), 1740–1744.

- Goodale, M. A., & Milner, A. D. (1992). Separate visual pathways for perception and action. *Trends in Neurosciences*, 15(1), 20–25.
- Gray, K. L. H., Adams, W. J., & Garner, M. (2009). The influence of anxiety on the initial selection of emotional faces presented in binocular rivalry. *Cognition*, 113(1), 105–110.
- Hancock, S., & Andrews, T. J. (2007). The role of voluntary and involuntary attention in selecting perceptual dominance during binocular rivalry. *Perception*, 36(2), 288–298.
- Harris, J. J., Schwarzkopf, D. S., Song, C., Bahrami, B., & Rees, G. (2011). Contextual illusions reveal the limit of unconscious visual processing. *Psychological Science*, 22(3), 399–405.
- Hastorf, A. H., & Myro, G. (1959). The effect of meaning on binocular rivalry. *American Journal of Psychology*, 72(3), 393–400.
- Haynes, J. D., Deichmann, R., & Rees, G. (2005). Eye-specific effects of binocular rivalry in the human lateral geniculate nucleus. *Nature*, 438(7067), 496–499.
- Hofstoetter, C., Koch, C., & Kiper, D. C. (2004). Motion-induced blindness does not affect the formation of negative afterimages. *Consciousness and Cognition*, 13(4), 691–708.
- Hollins, M. (1980). The effect of contrast on the completeness of binocular rivalry suppression. *Perception & Psychophysics*, 27(6), 550–556.
- Hollins, M., & Hudnell, K. (1980). Adaptation of the binocular rivalry mechanism. *Investigative Ophthalmology & Visual Science*, 19(9), 1117–1120.
- Holmes, D. J., Hancock, S., & Andrews, T. J. (2006). Independent binocular integration for form and colour. *Vision Research*, 46(5), 665–677.
- Hong, S. W., & Blake, R. (2009). Interocular suppression differentially affects achromatic and chromatic mechanisms. *Attention, Perception, & Psychophysics*, 71(2), 403–411.
- Hupé, J. M., & Rubin, N. (2003). The dynamics of bi-stable alternation in ambiguous motion displays: A fresh look at plaids. *Vision Research*, 43(5), 531–548.
- Jalavisto, E., (1964) The phenomenon of retinal rivalry in the aged. *Gerontologia*, 49(1), 1–8.
- Jiang, Y., Costello, P., & He, S. (2007). Processing of invisible stimuli: Advantage of upright faces and recognizable words in overcoming interocular suppression. *Psychological Science*, 18(4), 349–355.
- Jiang, Y., Costello, P., Fang, F., Huang, M., & He, S. (2006). A gender-and sexual orientation-dependent spatial attentional effect of invisible images. *Proceedings of the National Academy of Sciences USA*, 103(45), 17048–17052.
- Kamphuisen, A. P., van Wezel, R. J., & van Ee, R. (2007). Inter-ocular transfer of stimulus cueing in dominance selection at the onset of binocular rivalry. *Vision Research*, 47(9), 1142–1144.
- Kanai, R., & Verstraten, F. A. (2005). Perceptual manifestations of fast neural plasticity: Motion priming, rapid motion aftereffect and perceptual sensitization. *Vision Research*, 45(35–36), 3109–3116.
- Kanai, R., Knapen, T. H., van Ee, R., & Verstraten, F. A. (2007). Disruption of implicit perceptual memory by intervening neutral stimuli. *Vision Research*, 47(20), 2675–2683.
- Kanai, R., Tsuchiya, N., & Verstraten, F. A. (2006). The scope and limits of top-down attention in unconscious visual processing. *Current Biology*, 16(23), 2332–2336.
- Kang, M. S. (2009). Size matters: A study of binocular rivalry dynamics. *Journal of Vision*, 9(1), 17. doi: 10.1167/9.1.17
- Kang, M. S., Heeger, D., & Blake, R. (2009). Periodic perturbations producing phase-locked fluctuations in visual perception. *Journal of Vision*, 9(2), 8. doi: 10.1167/9.2.8

- Keliris, G. A., Logothetis, N. K., & Tolias, A. S. (2010). The role of the primary visual cortex in perceptual suppression of salient visual stimuli. *Journal of Neuroscience*, 30(37), 12353–12365.
- Kihlstrom, J. F., Schacter, D. L., Cork, R. C., Hurt, C. A., & Behr, S. E. (1990). Implicit and explicit memory following surgical anesthesia. *Psychological Science*, 1(5), 303–306.
- Kim, C. Y., & Blake, R. (2005). Psychophysical magic: Rendering the visible 'invisible'. *Trends in Cognitive Sciences*, 9(8), 381–388.
- Klink, P. C., Brascamp, J. W., Blake, R., & van Wezel, R. J. (2010). Experience-driven plasticity in binocular vision. *Current Biology*, 20(16), 1464–1469.
- Klink, P. C., van Ee, R., & van Wezel, R. J. (2008a). General validity of Levelt's propositions reveals common computational mechanisms for visual rivalry. *PLoS ONE*, 3(10), e3473. doi: 10.1371/journal.pone.0003473
- Klink, P. C., van Ee, R., Nijs, M. M., Brouwer, G. J., Noest, A. J., & van Wezel, R. J. (2008b). Early interactions between neuronal adaptation and voluntary control determine perceptual choices in bistable vision. *Journal of Vision*, 8(5), 16. doi: 10.1167/8.5.16
- Knapen, T., van Ee, R., & Blake, R. (2007). Stimulus motion propels traveling waves in binocular rivalry. *PLoS ONE*, 2, e739. doi: 10.1371/journal.pone.0000739
- Kohn, H. (1960). Some personality variables associated with binocular rivalry. *Psychological Record*, 10, 9–13.
- Kolb, F. C., & Braun, J. (1995). Blindsight in normal observers. *Nature*, 377(6547), 336–338.
- Kovács, I., Papathomas, T. V., Yang, M., & Fehér, A. (1996). When the brain changes its mind: Interocular grouping during binocular rivalry. *Proceedings of the National Academy of Sciences USA*, 93(26), 15508–15511.
- Lack, L. (1978). *Selective attention and the control of binocular rivalry*. The Hague: Mouton.
- Lange-Malecki, B., Creutzfeldt, O. D., & Hinse, P. (1985). Haploscopic colour mixtures with and without contours in subjects with normal and disturbed binocular vision. *Perception*, 14(5), 587–600.
- Lee, S.-H., & Blake, R. (2004). A fresh look at interocular grouping during binocular rivalry. *Vision Research*, 44(10), 983–991.
- Lee, S.-H., Blake, R., & Heeger, D. J. (2005). Traveling waves of activity in primary visual cortex during binocular rivalry. *Nature Neuroscience*, 8(1), 22–23.
- Lehky, S. R. (1995). Binocular rivalry is not chaotic. *Proceedings of the Royal Society of London B: Biological Sciences*, 259(1354), 71–76.
- Lehky, S. R., & Blake, R. (1991). Organization of binocular pathways: Modeling and data related to rivalry. *Neural Computation*, 3(1), 44–53.
- Lehmkuhle, S. W., & Fox, R. (1975). Effect of binocular rivalry suppression on the motion after-effect. *Vision Research*, 15(7), 855–859.
- Leopold, D. A., & Logothetis, N. K. (1996). Activity changes in early visual cortex reflect monkeys' percepts during binocular rivalry. *Nature*, 379(6565), 549–553.
- Leopold, D. A., Wilke, M., Maier, A., & Logothetis, N. K. (2002). Stable perception of visually ambiguous patterns. *Nature Neuroscience*, 5(6), 605–609.
- Levelt, W. J. M. (1966). The alternation process in binocular rivalry. *British Journal of Psychology*, 57(3–4), 225–238.
- Levelt, W. J. M. (1967). Note on the distribution of dominance times in binocular rivalry. *British Journal of Psychology*, 58(1), 143–145.
- Li, D. F., Freeman, A. W., & Alais, D. (2005). Contrast sensitivity of form and motion discrimination during binocular rivalry. *Vision Research*, 45(10), 1255–1263.

- Lin, Z., & He, S. (2009). Seeing the invisible: The scope and limits of unconscious processing in binocular rivalry. *Progress in Neurobiology*, 87(4), 195–211.
- Ling, S., & Blake, R. (2009). Suppression during binocular rivalry broadens orientation tuning. *Psychological Science*, 20(11), 1348–1355.
- Ling, S., Hubert-Wallander, B., & Blake, R. (2010). Detecting contrast changes in invisible patterns during binocular rivalry. *Vision Research*, 50(23), 2421–2429.
- Liu, L., Tyler, C. W., & Schor, C. M. (1992). Failure of rivalry at low contrast: Evidence of a supra-threshold binocular summation process. *Vision Research*, 32(8), 1471–1479.
- Logothetis, N. K., Leopold, D. A., & Sheinberg, D. L. (1996). What is rivalling during binocular rivalry? *Nature*, 380(6575), 621–624.
- Long, G. M., Toppino, T. C., & Mondin, G. W. (1992). Prime time: Fatigue and set effects in the perception of reversible figures. *Perception & Psychophysics*, 52(6), 609–616.
- Mamassian, P., & Goutcher, R. (2005). Temporal dynamics in bistable perception. *Journal of Vision*, 5(4), 7. doi:10.1167/5.4.7
- Marcel, A. J. (1983). Conscious and unconscious perception: Experiments on visual masking and word recognition. *Cognitive Psychology*, 15(2), 197–237.
- Merikle, P. M., & Reingold, E. M. (1992). Measuring unconscious perceptual processes. In R. F. Bornstein & T. S. Pittman (Eds.), *Perception without awareness, cognitive, clinical and social perspectives* (pp. 55–80). New York: Guilford Press.
- Miller, S. M., Hansell, N. K., Ngo, T. T., Liu, G. B., Pettigrew, J. D., Martin, N. G. et al. (2010). Genetic contribution to individual variation in binocular rivalry rate. *Proceedings of the National Academy of Sciences USA*, 107(6), 2664–2668.
- Mitchell, J. F., Stoner, G. R., & Reynolds, J. H. (2004). Object-based attention determines dominance in binocular rivalry. *Nature*, 429(6990), 410–413.
- Montaser-Kouhsari, L., Moradi, F., Zandvakili, A., & Esteky, H. (2004). Orientation-selective adaptation during motion-induced blindness. *Perception*, 33(2), 249–254.
- Moradi, F., Koch, C., & Shimojo, S. (2005). Face adaptation depends on seeing the face. *Neuron*, 45(1), 169–175.
- Moreno-Bote, R., Rinzel, J., & Rubin, N. (2007). Noise-induced alternations in an attractor network model of perceptual bi-stability. *Journal of Neurophysiology*, 98(3), 1125–1139.
- Moreno-Bote, R., Shpiro, A., Rinzel, J., & Rubin, N. (2010). Alternation rate in perceptual bistability is maximal at and symmetric around equi-dominance. *Journal of Vision*, 10(11), 1. doi:10.1167/10.11.1
- Mueller, T. J., & Blake, R. (1989). A fresh look at the temporal dynamics of binocular rivalry. *Biological Cybernetics*, 61(3), 223–232.
- Murata, T., Matsui, N., Miyauchi, S., Kakita, Y., & Yanagida, T. (2003). Discrete stochastic process underlying perceptual rivalry. *Neuroreport*, 14(10), 1347–1352.
- Nagamine, M., Yoshino, A., Yamazaki, M., Obara, M., Sato, S., Takahashi, Y. et al. (2007). Accelerated binocular rivalry with anxious personality. *Physiology & Behavior*, 91(1), 161–165.
- Nawrot, M., & Blake, R. (1991). The interplay between stereopsis and structure from motion. *Perception & Psychophysics*, 49(3), 230–244.
- Ngo, T. T., Miller, S. M., Liu, G. B., & Pettigrew, J. D. (2000). Binocular rivalry and perceptual coherence. *Current Biology*, 10(4), R134–R136.
- Nguyen, V. A., Freeman, A. W., & Alais, D. (2003). Increasing depth of binocular rivalry suppression along two visual pathways. *Vision Research*, 43(19), 2003–2008.
- Nguyen, V. A., Freeman, A. W., & Wenderoth, P. (2001). The depth and selectivity of suppression in binocular rivalry. *Perception & Psychophysics*, 63(2), 348–360.

- Nichols, D.F., & Wilson, H.R. (2009). Stimulus specificity in spatially-extended interocular suppression. *Vision Research*, 49(16), 2110–2120.
- Noest, A.J., van Ee, R., Nijs, M.M., & van Wezel, R.J. (2007). Percept-choice sequences driven by interrupted ambiguous stimuli: A low-level neural model. *Journal of Vision*, 7(8), 10. doi:10.1167/7.8.10
- Norman, H.F., Norman, J.F., & Bilotta, J. (2000). The temporal course of suppression during binocular rivalry. *Perception*, 29(7), 831–841.
- Ooi, T.L., & He, Z.J. (1999). Binocular rivalry and visual awareness: The role of attention. *Perception*, 28(5), 551–574.
- Ooi, T.L., & He, Z.J. (2006). Binocular rivalry and surface-boundary processing. *Perception*, 35(5), 581–603.
- Ooi, T.L., & Loop, M.S. (1994). Visual suppression and its effect upon color and luminance sensitivity. *Vision Research*, 34(22), 2997–3003.
- O'Shea, R.P., & Crassini, B. (1981a). Interocular transfer of the motion after-effect is not reduced by binocular rivalry. *Vision Research*, 21(6), 801–804.
- O'Shea, R.P., & Crassini, B. (1981b). The sensitivity of binocular rivalry suppression to changes in orientation assessed by reaction-time and forced-choice techniques. *Perception*, 10(3), 283–293.
- O'Shea, R.P., Parker, A., La Rooy, D., & Alais, D. (2009). Monocular rivalry exhibits three hallmarks of binocular rivalry: Evidence for common processes. *Vision Research*, 49(7), 671–681.
- O'Shea, R.P., Sims, A.J., & Govan, D.G. (1997). The effect of spatial frequency and field size on the spread of exclusive visibility in binocular rivalry. *Vision Research*, 37(2), 175–183.
- Pastukhov, A., & Braun, J. (2008). A short-term memory of multi-stable perception. *Journal of Vision*, 8(13), 7. doi:10.1167/8.13.7
- Pastukhov, A., & Braun, J. (2011). Cumulative history quantifies the role of neural adaptation in binocular rivalry. *Journal of Vision*, 11(10), 12. doi:10.1167/11.10.12
- Pearson, J., & Brascamp, J. (2008). Sensory memory for ambiguous vision. *Trends in Cognitive Sciences*, 12(9), 334–341.
- Pearson, J., & Clifford, C.W. G. (2004). Determinants of visual awareness following interruptions during rivalry. *Journal of Vision*, 4(3), 6. doi:10.1167/4.3.6
- Pearson, J., & Clifford, C.W. G. (2005a). Mechanisms selectively engaged in rivalry: Normal vision habituates, rivalrous vision primes. *Vision Research*, 45(6), 707–714.
- Pearson, J., & Clifford, C.W. G. (2005b). Suppressed patterns alter vision during binocular rivalry. *Current Biology*, 15(23), 2142–2148.
- Pearson, J., Clifford, C.W. G., & Tong, F. (2008). The functional impact of mental imagery on conscious perception. *Current Biology*, 18(13), 982–986.
- Pettigrew, J.D., & Miller, S.M. (1998). A 'sticky' interhemispheric switch in bipolar disorder? *Proceedings of the Royal Society of London B: Biological Sciences*, 265(1411), 2141–2148.
- Piazza, M., Izard, V., Pinel, P., Bihan, D.L., & Dehaene, S. (2004). Tuning curves for approximate numerosity in the human intraparietal sulcus. *Neuron*, 44(3), 547–555.
- Sandberg, K., Timmermans, B., Overgaard, M., & Cleeremans, A. (2010). Measuring consciousness: Is one measure better than the other? *Consciousness and Cognition*, 19(4), 1069–1078.
- Schall, J.D., Nawrot, M., Blake, R., & Yu, K. (1993). Visually guided attention is neutralized when informative cues are visible but unperceived. *Vision Research*, 33(15), 2057–2064.
- Shannon, R.W., Patrick, C.J., Jiang, Y., Bernat, E., & He, S. (2011). Genes contribute to the switching dynamics of bistable perception. *Journal of Vision*, 11(3), 8. doi:10.1167/11.3.8

- Sheppard, B. M., & Pettigrew, J. D. (2006). Plaid motion rivalry: Correlates with binocular rivalry and positive mood state. *Perception*, 35(2), 157–169.
- Sheth, B. R., & Pham, T. (2008). How emotional arousal and valence influence access to awareness. *Vision Research*, 48(23–24), 2415–2424.
- Shimojo, S., & Nakayama, K. (1990). Real world occlusion constraints and binocular rivalry. *Vision Research*, 30(1), 69–80.
- Shin, K., Stolte, M., & Chong, S. C. (2009). The effect of spatial attention on invisible stimuli. *Attention, Perception & Psychophysics*, 71(7), 1507–1513.
- Shpiro, A., Moreno-Bote, R., Rubin, N., & Rinzel, J. (2009). Balance between noise and adaptation in competition models of perceptual bistability. *Journal of Computational Neuroscience*, 27(1), 37–54.
- Silver, M. A., & Logothetis, N. K. (2004). Grouping and segmentation in binocular rivalry. *Vision Research*, 44(14), 1675–1692.
- Smith, E. L., Levi, D. M., Harwerth, R. S., & White, J. M. (1982). Color vision is altered during the suppression phase of binocular rivalry. *Science*, 218(4574), 802–804.
- Somekh, D. E., & Wilding, J. M. (1973). Perception without awareness in a dichoptic viewing situation. *British Journal of Psychology*, 64(3), 339–349.
- Stanley, J., Carter, O., & Forte, J. (2011). Color and luminance influence, but can not explain, binocular rivalry onset bias. *PLoS ONE*, 6(5), e18978. doi: 10.1371/journal.pone.0018978
- Stein, T., Senju, A., Peelen, M. V., & Sterzer, P. (2011). Eye contact facilitates awareness of faces during interocular suppression. *Cognition*, 119(2), 307–311.
- Sterzer, P., Hilgenfeldt, T., Freudenberg, P., Bermpohl, F., & Adli, M. (2011). Access of emotional information to visual awareness in patients with major depressive disorder. *Psychological Medicine*, 41(8), 1–10.
- Stuit, S. M., Cass, J., Paffen, C. L., & Alais, D. (2009). Orientation-tuned suppression in binocular rivalry reveals general and specific components of rivalry suppression. *Journal of Vision*, 9(11), 17. doi: 10.1167/9.11.17
- Suzuki, S., & Grabowecky, M. (2002). Evidence for perceptual “trapping” and adaptation in multistable binocular rivalry. *Neuron*, 36(1), 143–157.
- Suzuki, S., & Grabowecky, M. (2007). Long-term speeding in perceptual switches mediated by attention-dependent plasticity in cortical visual processing. *Neuron*, 56(4), 741–753.
- Tong, F., Meng, M., & Blake, R. (2006). Neural bases of binocular rivalry. *Trends in Cognitive Sciences*, 10(11), 502–511.
- Tsuchiya, N., & Koch, C. (2005). Continuous flash suppression reduces negative afterimages. *Nature Neuroscience*, 8(8), 1096–1101.
- Tsuchiya, N., Koch, C., Gilroy, L. A., & Blake, R. (2006). Depth of interocular suppression associated with continuous flash suppression, flash suppression, and binocular rivalry. *Journal of Vision*, 6(10), 1068–1078. doi: 10.1167/6.10.6
- Tsuchiya, N., Moradi, F., Felsen, C., Yamazaki, M., & Adolphs, R. (2009). Intact rapid detection of fearful faces in the absence of the amygdala. *Nature Neuroscience*, 12(10), 1224–1225.
- Ukai, K., Ando, H., & Kuze, J. (2003). Binocular rivalry alternation rate declines with age. *Perceptual and Motor Skills*, 97(2), 393–397.
- van Boxtel, J. J., Tsuchiya, N., & Koch, C. (2010). Opposing effects of attention and consciousness on afterimages. *Proceedings of the National Academy of Sciences USA*, 107(19), 8883–8888.
- van der Zwan, R., & Wenderoth, P. (1994). Psychophysical evidence for area V2 involvement in the reduction of subjective contour tilt aftereffects by binocular rivalry. *Visual Neuroscience*, 11(4), 823–830.

- van der Zwan, R., Wenderoth, P., & Alais, D. (1993). Reduction of a pattern-induced motion aftereffect by binocular rivalry suggests the involvement of extrastriate mechanisms. *Visual Neuroscience*, 10(4), 703–709.
- van Ee, R. (2005). Dynamics of perceptual bi-stability for stereoscopic slant rivalry and a comparison with grating, house-face, and Necker cube rivalry. *Vision Research*, 45(1), 29–40.
- van Ee, R. (2009). Stochastic variations in sensory awareness are driven by noisy neuronal adaptation: Evidence from serial correlations in perceptual bistability. *Journal of the Optical Society of America A: Optics, Image Science, and Vision*, 26(12), 2612–2622.
- Wade, N. J. (1975). Monocular and binocular rivalry between contours. *Perception*, 4(1), 85–95.
- Wade, N. J., & de Weert, C. M. (1986). Aftereffects in binocular rivalry. *Perception*, 15(4), 419–434.
- Wade, N. J., & Wenderoth, P. (1978). The influence of colour and contour rivalry on the magnitude of the tilt after-effect. *Vision Research*, 18(7), 827–835.
- Wade, N. J., de Weert, C. M., & Swanston, M. T. (1984). Binocular rivalry with moving patterns. *Perception & Psychophysics*, 35(2), 111–122.
- Walker, P. (1975). Stochastic properties of binocular rivalry alternations. *Perception & Psychophysics*, 18, 467–473.
- Walker, P. (1978). Orientation-selective inhibition and binocular rivalry. *Perception*, 7(2), 207–214.
- Walker, P., & Powell, D. J. (1979). The sensitivity of binocular rivalry to changes in the nondominant stimulus. *Vision Research*, 19(3), 247–249.
- Wallach, H., & O'Connell, D. N. (1953). The kinetic depth effect. *Journal of Experimental Psychology*, 45(4), 205–217.
- Watanabe, K., Paik, Y., & Blake, R. (2004). Preserved gain control for luminance contrast during binocular rivalry suppression. *Vision Research*, 44(26), 3065–3071.
- Weber, E. H. (1834). *De pulsu, resorptione, auditu et tactu. Annotiones anatomicae et physiologicae*. Leipzig: Koehler.
- Weiskrantz, L. (1986) *Blindsight: A case study and implications*. Oxford: Oxford University Press.
- Wheatstone, C. (1838). Contributions to the physiology of vision – Part the first. On some remarkable, and hitherto unobserved, phenomena of binocular vision. *Philosophical Transactions of the Royal Society of London*, 128, 371–395.
- White, K. D., Petry, H. M., Riggs, L. A., & Miller, J. (1978). Binocular interactions during establishment of McCollough effects. *Vision Research* 18(9), 1201–1215.
- Wiesenfelder, H., & Blake, R. (1990). The neural site of binocular rivalry relative to the analysis of motion in the human visual system. *Journal of Neuroscience*, 10(12), 3880–3888.
- Wiesenfelder, H., & Blake, R. (1991). Apparent motion can survive binocular rivalry suppression. *Vision Research*, 31(9), 1589–1599.
- Wilson, H. R., Blake, R., & Lee, S. H. (2001). Dynamics of travelling waves in visual perception. *Nature*, 412(6850), 907–910.
- Wilson, H. R. (2007). Minimal physiological conditions for binocular rivalry and rivalry memory. *Vision Research*, 47(21), 2741–2750.
- Wolfe, J. M. (1983). Influence of spatial frequency, luminance, and duration on binocular rivalry and abnormal fusion of briefly presented dichoptic stimuli. *Perception*, 12(4), 447–456.
- Wolfe, J. M. (1984). Reversing ocular dominance and suppression in a single flash. *Vision Research*, 24(5), 471–478.

- Yang, E., Hong, S. W., & Blake, R. (2010). Adaptation aftereffects to facial expressions suppressed from visual awareness. *Journal of Vision*, 10(12), 24.
- Yang, E., Zald, D. H., & Blake, R. (2007). Fearful expressions gain preferential access to awareness during continuous flash suppression. *Emotion*, 7(4), 882–886.
- Yang, Y. H., & Yeh, S. L. (2011). Accessing the meaning of invisible words. *Consciousness and Cognition*, 20(2), 223–233.
- Yang, Y., Rose, D., & Blake, R. (1992). On the variety of percepts associated with dichoptic viewing of dissimilar monocular stimuli. *Perception*, 21(1), 47–62.
- Yoon, K. L., Hong, S. W., Joormann, J., & Kang, P. (2009). Perception of facial expressions of emotion during binocular rivalry. *Emotion*, 9(2), 172–182.
- Yu, K., & Blake, R. (1992). Do recognizable figures enjoy an advantage in binocular rivalry? *Journal of Experimental Psychology: Human Perception and Performance*, 18(4), 1158–1173.
- Zhou, Y. H., Gao, J. B., White, K. D., Merk, I., & Yao, K. (2004). Perceptual dominance time distributions in multistable visual perception. *Biological Cybernetics*, 90(4), 256–263.
- Zimba, L. D., & Blake, R. (1983). Binocular rivalry and semantic processing: Out of sight, out of mind. *Journal of Experimental Psychology: Human Perception and Performance*, 9(5), 807–815.

Investigating the structure and function of the brain

A methodological overview

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Our understanding of the inner workings of the human brain is increasing exponentially. This is due in no small part to the rapidly advancing technology that has evolved from the application of engineering to neuroscience. This chapter reviews some of the more influential tools that are in widespread use in research institutes throughout the world. Beginning with the basics of electrophysiology, a broad overview of the current methods for resolving and modulating neural activity in the fields of imaging and brain stimulation is presented. Special attention is paid to temporal and spatial resolution, i.e., the capacity of the technologies to resolve small detail in time and space. The chapter concludes with a discussion of technical obstacles and future directions.

Introduction

The application of engineering principles to neuroscience over the last century has resulted in an explosion of research that probes the complex inner workings of the human brain. Until relatively recently, the *structure* of an individual's brain as a whole could not be observed unless post-mortem. This changed with the advent of imaging tools – beginning with x-ray technology and leading to magnetic resonance imaging, enabling fine structures of the brain to be discerned in minute detail non-invasively. While in the past the *function* of the brain could be probed non-invasively with cognitive testing and the like, the field now has at its disposal a multitude of physiological measurement techniques that have the potential to tease out the complex biological mechanisms that contribute to human behavior. These state-of-the-art tools are becoming increasingly available to clinical and research institutions and as a result, the field of neuroscience is expanding rapidly.

Measuring the electrophysiology of the brain

Of all the tools in neuroscience, one of the most familiar to the general public is the electroencephalogram (EEG). It is often introduced by the media as the 'special cap that can measure brain waves', almost hinting at the possibility that it has the ability to read a person's mind. It may come as some surprise to many people, including EEG practitioners, that the first human EEG was devised by a German psychiatrist seeking to do just that. While serving in the Prussian army, Dr Hans Berger received a letter from his sister that detailed a recent dream in which her brother broke his leg falling from a horse. Coincidentally, Berger had fallen from his horse at around the time his sister sent the letter. Believing that the explanation for this unlikely event was telepathy, the doctor embarked on a series of experiments to uncover the carrier of the telepathic 'waves'. He reasoned that it was the electromagnetic forces generated by the brain that were responsible for transmitting the information to his sister. Using a string galvanometer, Berger measured the voltage fluctuations occurring at the scalp, and successfully proved that they were not the result of deviations of blood pressure or changes in skin conductivity. These experiments continued for five years, and in 1929 he published his research, stating "The electroencephalogram represents a continuous curve with continuous oscillations in which...one can distinguish larger first order waves with an average duration of 90 milliseconds and smaller second order waves of an average duration of 35 milliseconds. The larger deflections measure at most 150 to 200 microvolts..." It was the weakness of the signal, 10,000 times smaller than an AA battery, which convinced Berger that his telepathic hypothesis could not be true. Furthermore, Berger reasoned that in order to propagate, neuron voltage changes would need a conductor, and because air is a particularly poor conductor these currents would not go beyond the scalp (Millett, 2001).

Ever since Berger's experiments, neuroscientists have sought to understand how the signal measured by the EEG is generated by the brain. Countless experiments have been conducted in an attempt to correlate the patterns of oscillations in the EEG with the behavior observed in the individual. The field of EEG research had a slow start, mainly due to the difficulties involved in understanding the mechanism by which the signal is produced. Indeed, this question remains heavily debated to this day. The systems underlying the neuronal generators are complex, as is the electrical transfer of that signal from the cortex to the recording site in its journey through the cerebrospinal fluid (CSF), skull, and scalp. Because the origin of the signal is the firing of the neurons themselves, the EEG has exquisite temporal resolution, affording it a considerable advantage over other neuroimaging techniques. It is mainly for this reason that despite its age, EEG continues to be a valuable tool in human neuroscience and consciousness research.

The findings of physicist James Clerk Maxwell may have given Hans Berger hope in his search for a telepathic carrier of brain waves. Although Berger was discouraged by the weak electrical currents he measured and their potential for propagation through air, Maxwell's equations of electromagnetism identify that the dynamic nature of the electrical signal results in a magnetic transmission that would extend beyond the scalp. Unfortunately the signal is incredibly weak, in the order of a billionth of the strength of the Earth's magnetic field. Using the relatively recently developed technique of magnetoencephalography, it is possible to measure these fields. The magnetoencephalogram (MEG) signal has a higher spatial resolution than the EEG due to the capability of the magnetic field to pass almost unmodified through the various tissues before exiting the scalp. This advantage comes with a price, with MEG systems costing many times more than the far more technically simple EEG. This has resulted in relatively few MEG studies and an abundance of EEG studies that have been conducted since Hans Berger first embarked on his search for a telepathic carrier signal.

EEG: From brain to scalp

The original non-invasive recording technique derived by Berger more than 80 years ago is still, in essence, practised today. Rather than galvanometers, the signal can now be measured at multiple scalp locations using extremely sensitive amplifiers and is stored in digital format as opposed to ink and paper. This allows the practitioner to take full advantage of the real-time measurement of changes in neural activity, with an almost endless array of different offline analysis techniques. In contrast, the far more recent technique of functional magnetic resonance imaging (fMRI) offers superb spatial resolution but because the signal is derived primarily from the hemodynamic response to the fuel requirements of neural activity, it is a considerably more indirect measurement.

While only a few EEG electrodes are required to determine whether the brain is alive or dead, considerably more recording sites are necessary in order to attempt to localize the source of a certain pattern of activity. Furthermore, increasing the number of electrodes is only useful to a point, as electrodes in very close proximity will essentially read the same extracellular potential. With a spatial resolution of approximately 10 cm², source localization in EEG is a thorny problem and even today there are only limited solutions. The difficulty arises from the electrical properties of the tissues involved, namely the resistive, capacitive and inductive characteristics of the neural tissue, cell membranes, glia, blood vessels, dura, skull, muscle and skin. These tissues essentially distort and filter, both spatially and temporally, the original local field potentials (LFPs)

of the neurons resulting in a signal that has little resemblance to the patterns of activity that generated it. The signal is highly influenced by activity at superficial layers and the contribution by the deepest regions of the brain is very small. While there are methods for reconciling this bias, the scaling of these signals remains one of the major limitations of EEG compared to fMRI.

The changing signal measured by EEG and MEG is a reflection of the activity of large numbers of synchronized neurons. The aggregation of LFPs in extracellular space contribute to a 'mean field' that is large enough to propagate through to the scalp. Essentially, the EEG and MEG signal is an indication of the 'average' behavior of the underlying interacting neurons. Like almost all cells in the human body, neurons have a distribution of electrically charged ions that is kept in check by the cell membrane, resulting in a potential difference of around 60mV. In this way, the neuron exhibits a polarity and behaves similarly to a small battery. When we describe a neuron as firing, we are referring to the rapid changes in ion concentrations that are associated with the depolarising of this potential difference, giving rise to a propagating signal – the *action potential*. Neurons are capable of firing several hundred times per second, however it is not this signal that is measured directly by EEG, rather it is the effect of this firing. The inhibitory or excitatory effect of the neurotransmitter released at the synapse of a neuron can last for tens of milliseconds – a far longer lasting effect than an action potential, even if it is very much smaller in amplitude. These low frequency signals are able to pass through the tissue to the scalp far more effectively than the high frequency action potentials. When large numbers of neurons are firing in a synchronous manner, the field potentials summate, and a signal is generated that is sufficiently strong to be detected at the scalp. The measurement of this signal at multiple points on the head opens up a huge array of different analyses that can elucidate the temporospatial characteristics of brain activity.

The utility of EEG in vision research can be observed in a study conducted by Lansing in 1964 that used visual evoked potentials (VEPs) during binocular rivalry (Lansing, 1964; see also chapter by Sterzer, this volume). Electrodes were placed on the midline at the parietal/occipital cortex and the left eye was presented with a flickering light (6–8 pulses/sec), giving rise to a rhythmic brain response at the same frequency – a series of VEPs. This technique can be described as *physiological labeling by frequency tagging* and is highly useful in EEG research. The right eye was presented with a solid red visual stimulus that could be regulated in its intensity, enabling the investigator to shift perceptual dominance from left to right. The subject was instructed to indicate with a choice of two buttons whether the left or the right stimulus was dominant. As the intensity of the right-eye red stimulus was increased, perceptual dominance shifted away from the

left side (as indicated by the subject) and the VEP resulting from the flickering light was observed to reduce in amplitude markedly. An extension to the original Lansing EEG study can be observed in research conducted by Brown and Norcia (1997) which used the same technique of frequency tagging, however in this case, each eye was presented with a grating that oscillated at a unique frequency. The amplitude of the VEPs at each frequency could then be filtered and extracted, giving two time varying signals that represented the size of the neural response to each eye. These signals could then be compared with the subject's report (by button press) of whether the left grating was dominant, the right grating was dominant, or whether the stimuli were fused. The oscillating EEG signals were found to be positively correlated ('moving together') when the stimuli were fused and negatively correlated ('in opposition') when rivalry was occurring (Figure 1). This correspondence allows the individual's perceptual state to be directly assessed electrophysiologically, without the reliance upon subject participation via self-report. These two studies elegantly demonstrate that although the scalp measured oscillations are but a representation of the actual electrophysiological process of high frequency neuron firing, they are still extremely useful in investigating complex neural processes.

Although EEG is both a relatively old technology and a cheap and simple method of neuroimaging (especially when compared to magnetic resonance imaging), it is still an extremely important tool in neuroscience. Some of the most important insights into the inner workings of the brain have been discovered using EEG. Many people are familiar with the term 'brain waves' and some have heard of the idea of an 'alpha state' or 'theta wave' (Figure 2). These terms refer to the "fundamental" frequencies that are measured by EEG, namely delta (1–4 Hz), theta (4–8 Hz), alpha (8–12 Hz), beta (13–30 Hz), and gamma (30–70 Hz). As discussed above, these are representative of the firing of large groups of synchronized neurons. While the functional significance of these frequencies is not fully understood, they are believed to be integral to sleep cycles (e.g., delta/theta), waking cycles (alpha/beta/gamma), attentional demands (alpha), and emotional and cognitive processes (beta) (Ray & Cole, 1985). These EEG frequencies are of particular interest in clinical applications, especially in the investigation of epilepsy (Lesser, 2009) and behavioral states during sleep/wake cycles (Hobson, 2005). Recent studies combining EEG and single-cell recordings within the cortex during quiescent states (anesthesia, sleep and quiet wakefulness) have demonstrated that a significant driver of our "typical" EEG low frequencies is the slow oscillations of intracellular membrane potentials. Furthermore, when the brain moves into a more active conscious state, there is a significant reduction in the power of the slow EEG waves and single cell-recorded membrane-potential

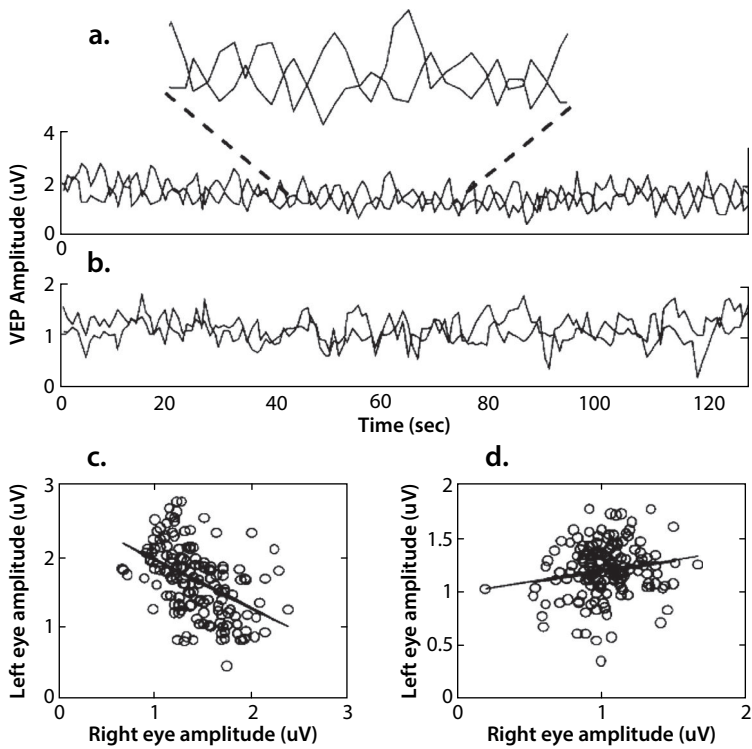


Figure 1. EEG and rivalry. Electrophysiological signal associated with binocular rivalry (a) or fusion (b) of two half-images in a single subject. In (a), part of the signal is magnified to demonstrate that the signals alternate in dominance over time. The correlations between the amplitudes of each eye are given for rivalry (c) and fusion (d) demonstrating a negative correlation when undergoing rivalry (reprinted by permission from Elsevier Ltd: *Vision Res*, Brown & Norcia, 1997, 37: 2401–2408).

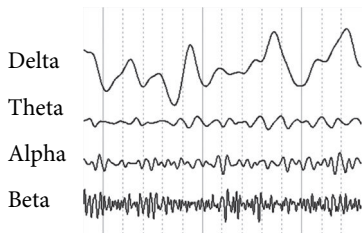


Figure 2. Electroencephalogram (EEG). Typical frequency bands of interest: 1. Delta (1–4Hz), 2. Theta (4–8Hz), 3. Alpha (8–12Hz), 4. Beta (13–30Hz). These bands are believed to be integral to sleep cycles (e.g., delta/theta), waking cycles (alpha/beta), attentional demands (alpha), and emotional and cognitive processes (beta).

fluctuations (Crochet & Petersen, 2006; Metherate, Cox, & Ashe, 1992; Poulet & Petersen, 2008). It appears likely that the humble EEG signal will contribute to a recognisable neural “signature” of consciousness (for at least one sense of “consciousness”), that may also be clinically invaluable in determining vegetative states (Boly et al., 2011).

Magnetoencephalography

The electrical currents resulting from neural activity give rise to incredibly small magnetic fluctuations that require highly specialized equipment to measure at the scalp level (Hämäläinen, Hari, Ilmoniemi, Knuutila, & Lounasmaa, 1993). These are termed *superconducting quantum interference devices*, commonly known as SQUIDS. Capable of measuring fields one thousand times smaller than those generated by the brain, SQUIDS must be cooled to a temperature approaching absolute zero in order to maintain their superconducting properties. This is typically achieved using an expensive liquid helium cooling system, and consequently MEG is beyond the financial reach of most institutions.

What do you get for your money? While EEG and MEG are closely related, and are measuring the same neuronal currents, MEG is a complementary tool rather than a direct replacement. The advantages are that (1) MEG does not require direct contact with the patient’s head, (2) it does not require a reference signal for comparison, (3) there is less cross-talk between channels (Nunez, 1995), and (4) it is capable of resolving rapid neural firing (e.g., 600 Hz somatosensory evoked fields; Curio et al., 1994). MEG differs from EEG in that MEG is only sensitive to tangential currents while EEG reflects currents from all orientations; however it is differentially influenced by currents perpendicular to the scalp surface. Although the MEG signal is not blurred by the tissue layers in between (meninges, skull, scalp etc.), it is relatively insensitive to deep brain activity due to the rapid decay of the magnetic field. EEG does not have this restriction – because the brain is an excellent conductor, the electrical signal is propagated with less attenuation than the MEG signal over greater distances at the cost of spatial resolution. For this reason, tasks such as the monitoring of brainstem activity are more easily achieved with EEG.

A study by Srinivasan and colleagues (Srinivasan, Russell, Edelman, & Tononi, 1999) takes advantage of the reduced cross-talk of the MEG signal when examining binocular rivalry. Using the previously discussed technique of frequency tagging a dichoptic image, the authors investigated perceptual dominance. They suggested that both local and global synchronization of neural activity was associated with perceptual dominance at occipital, temporal, and frontal regions. By examining

the coherence of widely separated sensors, the authors speculated that perceptual *non-dominance* might be regulated by active suppression from frontal regions. However, the certainty of this observation was limited by one of the disadvantages of MEG – that it is primarily sensitive to activity along sulcal walls. If activity along opposite sulcal walls is phase locked, the fields will effectively cancel. This highlights the advantage of combining two or more neuroimaging techniques in order to gain a more complete picture of the underlying brain activity. Although this particular study was challenged by further research suggesting that the synchronization was limited to oscillators in primary visual cortex (V1) (Kamphuisen, Bauer, & van Ee, 2008), the technique remains a valid and useful tool for investigating neural function.

MEG has not been applied as widely as EEG, but has still managed to make contributions to neuroscience research. One area that has benefited, for example, is the neuroscience of pain. Single cells in the brain have been identified that can give a binary response indicating whether there is a painful stimulus or not. However, cells have been recently identified in the thalamus and periaqueductal grey region which indicate the *intensity* of the pain by the duration of their output. This “signature” of pain might be useful as feedback to deep brain stimulation (DBS) treatment of pain, which currently stimulates neurons regardless of the level of pain experienced by the patient. Using MEG during different stages of DBS, the network of structures involved in pain relief could be elucidated (Kringelbach et al., 2007). MEG has also been used to investigate functional reorganization that can occur in the somatosensory cortex following acute pain in amputees (Soros et al., 2001). Interestingly, MEG has also revealed that the *perception* of pain in others results in a reduction in activity in somatosensory cortex (Cheng, Yang, Lin, Lee, & Decety, 2008), a subtle change that was not possible to observe using fMRI. With MEG becoming more accessible with time, it will no doubt become an invaluable tool in neuroscience research.

Source localization

There is currently no imaging technique that can measure neural activity accurately in both time and space. The neuroimaging techniques of EEG and MEG both share the advantage of having exquisite temporal resolution, however they also share one fundamental disadvantage – they have poor spatial resolution. Signals measured at the scalp level are representative of not only the neural activity directly beneath, but a gestalt of the electromagnetic fields generated by all the neural activity of the brain. The situation is not hopeless though – the fields that contribute to the signal measured at a certain point on the scalp vary in their

strength according to their distance from the measuring point. By way of example, synchronized neural activity in the frontal cortex will only be a minor contributor to the signal measured in the occipital cortex.

This simplistic approach to the problem of *source localization* can be extended upon by way of theoretical models. Large groups of neurons exhibiting synchronized neural activity will generate directed synaptic current that can be measured at the scalp level. These signal generators are modelled by *current dipoles*. Each current dipole can be assigned a location, orientation, and magnitude. Electrophysiological source imaging (ESI) is a technique that links the activity of these theoretical models (current dipoles) with the signal measured at the scalp. ESI is concerned with two approaches – the *forward model* and the *inverse model*. The forward model entails the modeling of brain sources and the brain tissue in order to estimate the contribution of those sources to the measurement made at the scalp level. Conversely, the inverse model begins with the scalp measurement and attempts to locate the generators of that signal in the brain (using the forward model) – a considerably more complex task. The problem of applying the inverse model requires constraints to be imposed and a raft of assumptions in order to obtain a unique solution. While these methods can be problematic when estimating the contributions made by deep structures (including temporal lobe structures and orbitofrontal regions (Hämäläinen et al., 1993), there is increasing evidence that they can provide reasonable estimates (Groening et al., 2009; Thornton et al., 2010; Vulliemoz et al., 2009).

Using source localization methods, Britz and colleagues (Britz, Landis, & Michel, 2009; Britz, Pitts, & Michel, 2011; Britz, Van De Ville, & Michel, 2010) have investigated the origins of the EEG signal generated with respect to *EEG microstates* associated with binocular rivalry. EEG microstates refer to brief (fraction of a second) intervals in which the electric field measured at the scalp is in a relatively stable state and are thought to be representative of the global state of the brain (Lehmann, 1989; Lehmann, Ozaki, & Pal, 1987). The research identified activity localized in the right inferior parietal cortex as preceding perceptual reversals and that perceptual stability was associated with generators in inferior temporal regions. These findings were in general agreement with previous fMRI research (Lumer & Rees, 1999) and single-cell recordings (Leopold & Logothetis, 1996). Source localization techniques are improving at a great pace, with increasingly complex and accurate models of electromagnetic interactions being developed.

Transcranial magnetic stimulation

Transcranial magnetic stimulation (TMS) is a method for measuring and modulating cortical excitability and has been in use in its present form since 1985 (Barker, Jalinous, & Freeston, 1985). Typically, the technique centers on the application of magnetic pulses to the scalp, either singularly or in pairs (single- and paired-pulse TMS) or in trains (repetitive TMS), in order to activate the cortex (Figure 3). Repetitive TMS (rTMS) is increasingly used as an alternative treatment for major depressive disorder and, to a lesser extent, the treatment and investigation of autism and schizophrenia. As it is non-invasive and painless, it is a popular tool in neuroscience research. It uses a rapidly changing large current through a metal coil to generate a transient magnetic field. This magnetic field can pass relatively unimpeded through the scalp, skull, and meninges through to the cortex, inducing an electrical ionic current that is parallel but in the opposite direction to the direction of the current in the coil (Figure 4). The volume of cortical tissue that the induced current passes through at a significant strength is determined by the amount of current passed through the coil (typically in the kilo-ampere range), the coil's shape and size, and the frequency and duration of the magnetic pulse delivered (Anand & Hotson, 2002). Typically, peak magnetic field strength is around 2 Tesla (T) at the surface of the coil and around 0.5 T at the level of the cortex.

There are three main categories of coil that are used in TMS research. The circular coil is the most basic shape, they are typically 14 cm in diameter and with a 100 μ s rise time of the electrical pulse, they will generate a field of 1.5–2 T decaying with the cube of the distance. The peak field strength is around the circumference of the coil and can activate neurons that are 1.5–2 cm below the scalp (Epstein, Schwartzberg, Davey, & Sudderth, 1990; Rudiak & Marg, 1994). A figure-of-8 coil is typically comprised of two 7–9 cm coils and is used for more focal stimulation with the peak field strength generated at the crossing of the coils. Finally the double-cone coil is comprised of two coils (typically 12 cm in diameter) combined at an angle of 90–100 deg. The coil is positioned with the two “wings” on either side of the skull and resulting in a more powerful magnetic field that can induce current in deeper parts of the brain. Often this is used to target the leg area of the human primary motor cortex (M1) located relatively deeply in the interhemispheric fissure at 3–4 cm depth from the scalp (Terao & Ugawa, 2002).

The most common method of using TMS to study human brain neurophysiology is with the use of single pulses to the motor cortex at a frequency of less than 1 Hz. TMS has very high temporal resolution and reasonable spatial resolution. A single pulse at high intensity with a coil will typically result in a motor evoked potential (MEP) at the resting contralateral upper extremity, allowing inferences to be made regarding the threshold of populations of neurons



Figure 3. Repetitive TMS. TMS is delivered to the subject's left motor cortex using a figure-of-8 liquid-cooled coil. This is a typical setup used for delivering therapeutic repetitive stimulation.

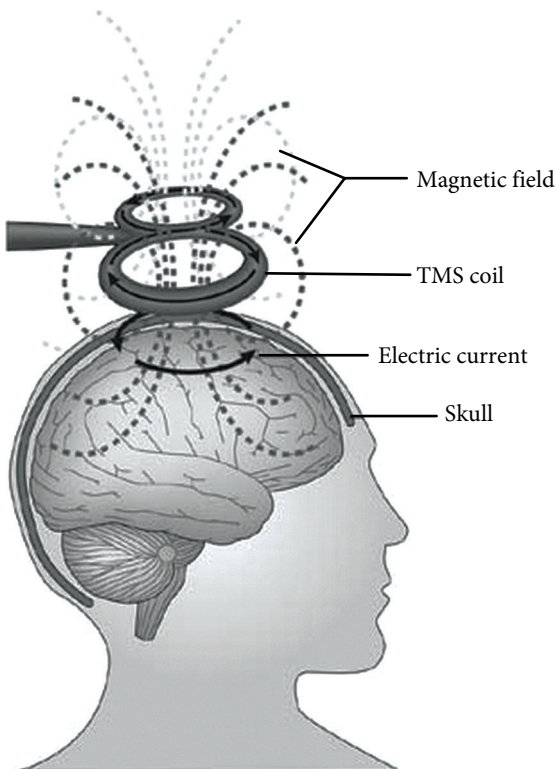


Figure 4. TMS mechanism. Each pulse of TMS involves a large current passing through a metal coil, resulting in a magnetic field that is capable of passing through the skull to the cortex. This magnetic field induces a current that can activate neural elements painlessly and non-invasively (reprinted by permission from Macmillan Publishers Ltd: *Nat Rev Neurosci*, Ridding & Rothwell, 2007, 8: 559–567).

and their related corticospinal conduction times (Anand & Hotson, 2002). The MEP is dependent upon the temporal summation of successive descending volleys that are required to cause resting spinal motor neurons to discharge. The size of the MEP is increased and the threshold required for evoking an MEP is reduced by activating the muscle by voluntary contraction and is associated with an increase of the cerebral blood flow to the contralateral motor cortex (Dettmers et al., 1996). The resting motor threshold (RMT) of a population of motor cortex neurons can be measured in terms of the TMS intensity required to generate an MEP in a resting muscle. Factors that modulate this threshold include the density of motor neurons located within the electrical field generated by the TMS and the membrane excitability of those neurons as confirmed by studies on sodium and calcium channels (Ziemann, Lonnecker, Steinhoff, & Paulus, 1996). The required TMS intensity increases as the distance (measured by MRI) between the coil location on the scalp and the surface of the motor cortex increases (McConnell et al., 2001). Anatomical differences in this distance are one factor contributing to difference in RMT between individuals. Typically the strength of the magnetic field falls by half at a distance of 4–5 cm from the coil surface (Edgley, Eyre, Lemon, & Miller, 1990; Hess, Mills, Murray, & Schrieffer, 1987) meaning that structures deeper than the base of the central sulcus such as the basal ganglia or thalamus are generally not stimulated. In terms of the white and grey matter of which the cerebral cortex is comprised, the white matter is of higher resistance and is typically not activated during TMS (Edgley et al., 1990).

Single-pulse TMS is a valuable tool for measuring change in the excitability of the motor system. Firstly the “hot spot” is located by determining the active scalp position for the target muscle by exploratory TMS. This method has been determined to be superior to using standard anatomical markers for determining the most appropriate location for the TMS coil (Conforto, Z’Graggen, Kohl, Rosler, & Kaelin-Lang, 2004). Typically as a baseline measure, the RMT is measured by determining the lowest TMS output intensity required to induce an MEP in a relaxed muscle with an amplitude of at least 50 μ V in 50% of trials (Rossini et al., 1994). Motor threshold is modulated by drugs that block voltage-gated sodium channels as opposed to drugs that alter GABA (γ -aminobutyric acid) or glutamate transmission, and therefore most likely reflects the level of neuronal membrane excitability (Chen, 2000). The size of the MEP evoked by TMS at a given intensity reflects this excitability (Rossini et al., 1994).

In the application of rTMS, the repeated stimulation of neurons can progressively change their activity over time. High-frequency rTMS (stimulation at >1 Hz and typically 5–20 Hz) has been shown to increase cortical excitability (reduced local activation threshold), while low frequency stimulation (typically 1 Hz) has the opposite effect, decreasing cortical excitability. With the benefit

of a measurable MEP, these effects can be readily observed at M1, however the modulation of excitability by rTMS frequency is not as well established at other cortical regions. Furthermore, individuals may vary in their response to different frequencies. A single session of rTMS may result in transient effects on local cortical excitability that are measurable for up to one hour, while in therapeutic applications, repeated sessions over time appear to have some form of additive effect. While research has focused upon the local effects of rTMS stimulation, it is possible that the effects of rTMS are not primarily local but result instead from the strengthening of connectivity between the local area stimulated and the areas to which the activated neurons connect. By combining TMS and brain imaging techniques such as EEG, connectivity between remote areas of the cortex can be investigated, including the potential to drive oscillatory activity by rTMS (for a review see Driver, Blankenburg, Bestmann, & Ruff, 2010). The ability of TMS to depolarize neurons by an external stimulus allows it to be used as a method of temporarily disrupting normal brain activity. TMS used in this fashion has often previously been referred to as evoking a “virtual lesion”, however this description does it a disservice. The abundance of TMS research into cognitive processes has revealed that the effects are more complex and subtle than previously thought (Silvanto & Muggleton, 2008). While TMS is often used to disrupt perception and behavior by stimulating *during* the perceptual/cognitive process, it also appears that TMS delivered *prior* to the onset of a cognitive process has the potential to facilitate (or inhibit) it. This phenomenon points to a *state-dependent* effect of TMS. The relatively broad TMS region of activation results in a change in excitability of not only neurons that are involved in the cognitive process under investigation, but also functionally distinct populations of neurons. This potentially leads to differential effects from varying the intensity of the TMS, dependent upon whether the region is in an active or suppressed state. TMS parameters delivered when the region is in a “normal state” may impair behavior, but may induce behavioral facilitations if the region is in an adapted or suppressed state (Schwarzkopf, Silvanto, & Rees, 2011). The disruptive and modulatory properties of TMS have been used in various investigations of visual perception, including research into visual extinction and neglect resulting from stroke (Battelli, Alvarez, Carlson, & Pascual-Leone, 2009; Cazzoli, Muri, Hess, & Nyffeler, 2010; Oliveri & Caltagirone, 2006; Oliveri et al., 1999) as well as binocular rivalry (Carmel, Walsh, Lavie, & Rees, 2010; Miller et al., 2000; Zaretskaya, Thielscher, Logothetis, & Bartels, 2010; see also chapters by Sterzer, and Ngo, Barsdell, Law & Miller, this volume).

Due to the size of the magnetic field to which the subject is exposed through TMS, safety studies have sought to investigate the possibility of electrical injury to the brain (for a review see Anand & Hotson, 2002). Evidence of injury has been sought via altered EEG, disruptions in hormone levels, cardiovascular function,

and long lasting changes in cognitive, perceptual, or motor functions. Apart from some positive cognitive effects, no negative effects have been documented (Bridgers & Delaney, 1989; Chokroverty et al., 1995; Yamada, Tamaki, Wakano, Mikami, & Transfeldt, 1995). The auditory stimulus resulting from the large currents required by TMS may result in an increase in the hearing threshold in rabbits (Counter, Borg, Lofqvist, & Brismar, 1990), however human studies have reported no adverse effects (Pascual-Leone et al., 1992). Single-pulse TMS in healthy adults is considered to be safe, the only side effects resulting from continual scalp muscle contraction which may lead to a transient headache or slight discomfort in the scalp at the stimulation site. No short- or long-term pathology has been found in safety studies in normal adult subjects (for a review see Anand & Hotson, 2002). If the appropriate safety guidelines are followed, the likelihood of an epileptic seizure during rTMS is remote, and even less so when administering single-pulse TMS (Classen et al., 1995; Hufnagel & Elger, 1991). As a result of these studies, TMS safety guidelines (Rossi, Hallett, Rossini, & Pascual-Leone, 2009) err on the side of caution and advise against the administration of any form of TMS to individuals with a family history of epilepsy.

Magnetic resonance imaging

Structural imaging

With the advent of magnetic resonance imaging (MRI) in the 1970s, it became possible to create three dimensional images that could clearly resolve the three fundamental constituents of the brain – grey matter, white matter and CSF. The contrast between white and grey matter was particularly useful as it enabled a host of new measurements that could be made on brain anatomy, particularly in the analysis of *volumetrics* and *morphology* (Figure 5). Using MRI scanners with strong magnetic fields (3 T or more), the brain can be revealed with sub-millimetre resolution. Cortical structures can be identified and manually ‘traced’ on each slice of the MRI by a skilled operator allowing accurate measurements of structural properties such as volume that can be used in region of interest (ROI) analyses. Hippocampal volumes, for example, have been investigated extensively in major depressive disorder and schizophrenia (Maller et al., 2012). While manual tracing is considered the ‘gold-standard’ for volumetrics, it is a time consuming process and efforts have been directed toward algorithms for extracting structural information. An alternative approach to ROI-based analysis is the technique of voxel-based morphometry. The MRI scans for each individual are aligned and normalized to a standard template by morphing the brain via a spatial transformation, or to put

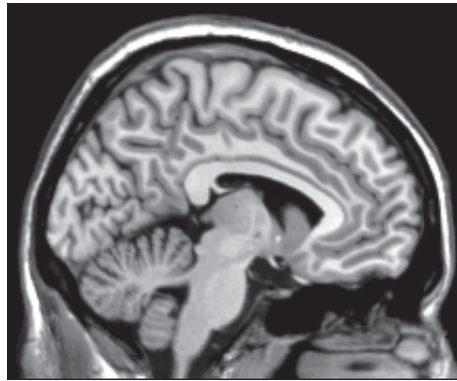


Figure 5. Magnetic resonance imaging. Sagittal slice of a standard structural scan demonstrating the contrast between white matter, grey matter, and cerebrospinal fluid.

it more simply, a process of warping, squashing, and stretching. Each voxel (i.e., three-dimensional pixel) may then be compared across individuals and groups via a technique called statistical parametric mapping. This method was designed as an attempt to allow small structural differences to be isolated while controlling for the problem of multiple comparisons (Ashburner & Friston, 2000; Friston, 1995, 1997). Further computational techniques have been developed that can intelligently segment the brain into grey matter, white matter, and CSF, allowing quantifications such as ratios of grey to white matter, degree of atrophy, extent of gyrification or folding, and asymmetries between left and right hemispheres. These values could be correlated with behavior, enabling new insights into the functional properties of brain structures and their role in neuropathology.

MRI can be used to perform diffusion tensor imaging (DTI), a technique that measures the preferred direction of the diffusion of water molecules along white matter fiber tracts. Water molecules will travel along the confines of the myelinated fiber tracts within the white matter of the brain, along with the extracellular space separating them, analogous to the movement of water molecules in the fibers of a stalk of celery. The most commonly used measurement proxy for white matter connections is the fractional anisotropy (FA) parameter. The FA value ranges from 0 to 1 and is a scalar measure of how well defined the direction of the diffusion of water molecules is within a given voxel. This is thought to reflect the extent of myelination and the thickness of the axons. In order to explore structural connections in the brain, the FA values can be used to perform diffusion tensor tractography (DTT). Typically, tractography algorithms are initiated from a 'seed' voxel, and with each new voxel encountered, the pathway grows, as long as certain conditions are met, e.g., the FA value is high enough, and the angle subtended by

the pathway (“tract”) is not unnaturally acute. This process is repeated, creating a map of pathways that is an approximation of the gross neuroanatomical orientation of the white matter fiber tracts (Figure 6). By parcellating the brain into many small volumes and systematically performing DTT on each pair of these volumes, a structural connectivity map of the brain can be realized.

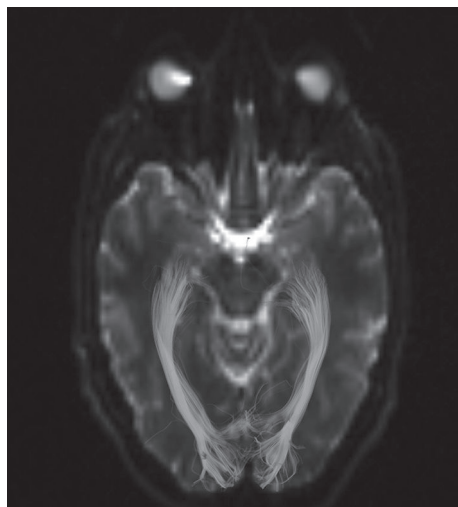


Figure 6. DTI tractography. Diffusion-weighted axial slice at the level of occipital cortex with subject's eyes visible at the top of the image. Superimposed tractography of bilateral optic radiation demonstrates connections between V1 and regions that include parts of the thalamus.

Using DTI and brain morphology measurements, the role of the underlying brain structure in human visual perception has been assessed in a rivalry framework. Kanai and colleagues (Kanai, Bahrami, & Rees, 2010) examined cortical thickness, gray-matter density, and white-matter integrity in the superior parietal lobe (SPL) of individuals who had completed a bistable motion illusion task. These structural properties accounted for inter-individual variability in perceptual alternation rate whereby faster rivalry rate was associated with larger values on the structural measures. The findings complemented previous studies demonstrating the effects of aging, brain damage and mood disorders on rivalry rate. More specifically, bipolar disorder, which has a strong genetic contribution (McGuffin et al., 2003), has been associated with slow binocular rivalry (Pettigrew & Miller, 1998; see chapter by Ngo et al., this volume) as well as cortical thinning (Lyoo et al., 2006), in agreement with the correlation found between SPL thickness and switch rate in controls (Kanai et al., 2010). Consistent with these findings, in healthy controls

a strong genetic contribution has been shown for individual variation in rivalry rate (Miller et al., 2010) and also for individual structural variations in grey and white matter morphology (Hulshoff Pol et al., 2006).

Functional imaging

Within the same magnetic resonance framework that enabled incredible structural images of the brain to be produced, the technique of fMRI was conceived. Early in its development, it became apparent that this would be a very important tool for the functional mapping of the human brain, beautifully demonstrated when defining the boundaries of the visual cortex (Engel et al., 1994). By taking advantage of the very different magnetic properties of oxygenated (diamagnetic) and de-oxygenated (paramagnetic) hemoglobin, the amplitudes of individual voxels in an fMRI scan are proportional to the level of localized oxygenated hemoglobin. At the heart of the fMRI technique is the *blood oxygen level dependent* (BOLD) signal, and the premise that the measured BOLD signal is coupled to neural function. The basic hypothesis is that the brain's response to neural function is to supply the region with additional blood in order to deliver the required fuel, i.e., oxygen and glucose. The signal measured during fMRI is modulated by this response and for this reason the temporal resolution of fMRI is poor. It is important to note that the precise nature of this coupling of BOLD and neural function is a subject of much conjecture. It is presumed that there are various aspects of neural function to which the BOLD response relates such as action potentials, neurotransmitter cycling, the behavior of neuroglia, and both excitatory and inhibitory post-synaptic potentials. The general consensus that is emerging proposes that the BOLD signal reflects the synaptic input, particularly the release of glutamate (Friston, 2008), to clusters of neurons as opposed to the spiking output. The glutamate release triggers astrocytes resulting in vasodilatory signals and consequently a change in the BOLD signal (Nair, 2005). Hemodynamic response is also modulated by other physiological processes and states, for example the response to stimulants such as caffeine, the age of the subject, disease (especially those influencing the circulatory system such as diabetes), as well as levels of respiration and hydration. For this reason, it is not entirely accurate to link fMRI signals directly to "neural activity". Even with this caveat in mind, the BOLD signal can still convey a wealth of neurophysiological information. A study by Mukamel and colleagues demonstrated that neural firing rates as measured by single-unit recordings of the auditory cortex correlate very strongly with the BOLD signal when presented with identical auditory stimuli (Mukamel et al., 2005). On a larger scale, correlations with the LFP (such as that measured by EEG) can be observed, with research

suggesting that the relationships between alpha, beta, and gamma power might be represented by the amplitude and latency components of the BOLD signal (Magri, Schridde, Murayama, Panzeri, & Logothetis, 2012).

What can fMRI tell us about binocular rivalry? The frequency “tagging” of visual stimuli used in EEG studies will not be useful in fMRI studies because the response being measured relies on the relatively slow moving hemodynamic system. However, visual stimuli can be tagged in fMRI using differences in *contrast*. Low contrast gratings will elicit a response of lower magnitude in the visual cortex than high contrast gratings (Heeger, Huk, Geisler, & Albrecht, 2000). Using low and high contrast gratings presented dichoptically enabled Polonsky and colleagues (Polonsky, Blake, Braun, & Heeger, 2000) to compare the response in V1 with higher visual cortices (V2–V5). By using fMRI, the previous EEG and MEG studies that had been hampered by the localization limitations of these modalities could be improved upon. The findings suggested that V1 has a larger role in rivalry than the previous single-cell studies had suggested, challenging the view that higher visual regions are dominant in modulating rivalry. This method of ‘tagging’ was used in another fMRI study (Wunderlich, Schneider, & Kastner, 2005), which found that rivalry was modulated even earlier than V1 at the lateral geniculate nucleus. This research highlights one of the major advantages of fMRI – the ability to assess small structures located deep in the brain. A large body of research has correlated region specific activation, such as the fusiform face area (FFA) with perceptual states during stimulus presentation (e.g., Muckli et al., 2002; Sterzer & Rees, 2008). A study by Tong and colleagues using visual stimuli of a house and a face revealed that the pattern of activity of the FFA and the parahippocampal place area was modulated by the *perception* of the stimuli rather than the retinal stimulation itself (Tong, Nakayama, Vaughan, & Kanwisher, 1998). Further research has demonstrated that patterns of activation as measured by fMRI can be categorized correctly by a computer into the corresponding perceptual state of the individual using a machine-learning algorithm (e.g., Haynes & Rees, 2005). The authors concluded that “it is therefore possible to predict the dynamically changing time course of subjective experience with only brain activity”. fMRI studies of rivalry are discussed in further detail in the chapter by Sterzer (this volume).

It is difficult to overstate the contribution that fMRI has made to neuroscience. Although the physiological origins of the measured signal are a proxy for the underlying neural activity, its exquisite spatial resolution and tolerable temporal resolution more than make up for this limitation. This is especially true in the communication of research findings in human behavior to the public – the ability to visually demonstrate which parts of the brain are being “lit up” is extremely powerful. Clinically, fMRI is a very useful technique, especially in the

field of neurosurgery as procedures for tumors or epilepsy often carry a risk to postoperative cognitive function. Surgery in the left temporal or frontal lobes, for example, can jeopardize language function. Consequently, prior to tissue removal, fMRI can be used to identify regions that should be avoided in order to preserve language function. This application is a testament to the spatial accuracy that fMRI offers to neuroscience research.

Future focus points

The trade-off between spatial and temporal resolution is a stumbling block in the advance of our understanding of brain function. With fMRI in one corner and EEG/MEG in the other, the obvious question is: can we combine them? Simultaneous EEG/fMRI is relatively straightforward to achieve with specialized equipment to control for electromagnetic artefact, however the interpretation of the measurements has not been as straightforward (Laufs, Daunizeau, Carmichael, & Kleinschmidt, 2008). Establishing the transfer function between BOLD and EEG remains a difficult problem, with some studies arguing that BOLD is EEG frequency dependent while others suggest it reflects the total power in the EEG signal (Rosa, Kilner, Blankenburg, Josephs, & Penny, 2010). Simultaneous MEG/fMRI remains an unresolved technological challenge due to magnetic interference, however studies have been conducted comparing MEG and fMRI that have been consecutively measured (Auranen et al., 2009). It is also possible to conduct TMS during both EEG (Fitzgerald, 2010) and fMRI (Ziemann, 2011), allowing the real-time imaging of the modulatory effect of different TMS paradigms and the disruption of neural responses during tasks.

A popular research topic in recent times is the assessment of functional and structural connectivity using EEG, MEG, fMRI, and DTI. EEG and fMRI studies typically analyze specific brain regions that demonstrate task-related positive changes in the neural activity compared to a baseline state such as the resting state. Recently however, there has been renewed interest in the resting state itself, and in those brain regions where there is greater neural activity than is present during the task. This set of brain regions is thought to constitute an organized network that describes a “default mode of brain function”. There is now considerable research underway in examining resting state fMRI and how it can contribute to determining the functional connectivity of an individual brain. By mapping the correlations in activity between brain regions, detailed maps can be derived of complex neural systems, describing an individual’s functional connectivity. It is also possible to systematically determine the structural connections between each volume and every other volume (via DTI) to establish

an individual's structural connectivity. Rather than examining only structural and functional connections between a small number of large brain volumes, computational technology is now enabling the investigation of hundreds or even thousands of very small brain volumes. It is then possible to systematically determine the structural connections between each volume and every other volume yielding both a two dimensional structural map and a functional map of an individual's neural connectivity. These maps, known as *connectomes* (Sporns, 2012), are just the beginning. By employing a branch of mathematics known as graph theory (Bullmore & Sporns, 2009), the networks of structures that have been identified can be analyzed in a host of different ways. By examining the pattern of edges (structural or functional connections) between nodes (brain regions), it is possible to quantitatively measure global brain characteristics such as segregation (the degree of clustering of nodes), centrality (the importance or influence of nodes), and integration (the efficiency of the communication between nodes) (Sporns, Tononi, & Edelman, 2000).

Neuroscience has a host of powerful tools at its disposal that have the ability to assess the structure and function of the brain at millimetre and millisecond resolution. With technological progression, engineering obstacles at both hardware and software levels are overcome at an incredible rate. Techniques for uncovering the secrets of the human brain are becoming more affordable, efficient, and less invasive, and the result has been an explosion of published research in recent years. With the ability to combine and integrate technologies to overcome spatial and temporal limitations, this will no doubt continue unimpeded.

References

- Anand, S., & Hotson, J. (2002). Transcranial magnetic stimulation: neurophysiological applications and safety. *Brain and Cognition*, 50(3), 366–386.
- Ashburner, J., & Friston, K. J. (2000). Voxel-based morphometry – the methods. *Neuroimage*, 11(6), 805–821.
- Auranen, T., Nummenmaa, A., Vanni, S., Vehtari, A., Hämäläinen, M. S., Lampinen, J. et al. (2009). Automatic fMRI-guided MEG multidipole localization for visual responses. *Human Brain Mapping*, 30(4), 1087–1099.
- Barker, A. T., Jalinous, R., & Freeston, I. L. (1985). Non-invasive magnetic stimulation of human motor cortex. *Lancet*, 325(8437), 1106–1107.
- Battelli, L., Alvarez, G. A., Carlson, T., & Pascual-Leone, A. (2009). The role of the parietal lobe in visual extinction studied with transcranial magnetic stimulation. *Journal of Cognitive Neuroscience*, 21(10), 1946–1955.
- Berger, H. (1929). Über das Elektrenkephalogramm des Menschen. *Archiv für Psychiatrie und Nervenkrankheiten*, 87(1), 527–570.

- Boly, M., Garrido, M. I., Gosseries, O., Bruno, M. A., Boveroux, P., Schnakers, C. et al. (2011). Preserved feedforward but impaired top-down processes in the vegetative state. *Science*, 332(6031), 858–862.
- Bridgers, S. L., & Delaney, R. C. (1989). Transcranial magnetic stimulation: An assessment of cognitive and other cerebral effects. *Neurology*, 39(3), 417–419.
- Britz, J., Landis, T., & Michel, C. M. (2009). Right parietal brain activity precedes perceptual alternation of bistable stimuli. *Cerebral cortex*, 19(1), 55–65.
- Britz, J., Pitts, M. A., & Michel, C. M. (2011). Right parietal brain activity precedes perceptual alternation during binocular rivalry. *Human Brain Mapping*, 32(9), 1432–1442.
- Britz, J., Van De Ville, D., & Michel, C. M. (2010). BOLD correlates of EEG topography reveal rapid resting-state network dynamics. *Neuroimage*, 52(4), 1162–1170.
- Brown, R. J., & Norcia, A. M. (1997). A method for investigating binocular rivalry in real-time with the steady-state VEP. *Vision Research*, 37(17), 2401–2408.
- Bullmore, E., & Sporns, O. (2009). Complex brain networks: Graph theoretical analysis of structural and functional systems. *Nature Reviews Neuroscience*, 10(3), 186–198.
- Carmel, D., Walsh, V., Lavie, N., & Rees, G. (2010). Right parietal TMS shortens dominance durations in binocular rivalry. *Current Biology*, 20(18), R799–R800.
- Cazzoli, D., Muri, R. M., Hess, C. W., & Nyffeler, T. (2010). Treatment of hemispatial neglect by means of rTMS – a review. *Restorative Neurology and Neuroscience*, 28(4), 499–510.
- Chen, R. (2000). Studies of human motor physiology with transcranial magnetic stimulation. *Muscle & Nerve*, 23(Suppl 9), S26–S32.
- Cheng, Y., Yang, C. Y., Lin, C. P., Lee, P. L., & Decety, J. (2008). The perception of pain in others suppresses somatosensory oscillations: A magnetoencephalography study. *Neuroimage*, 40(4), 1833–1840.
- Chokroverty, S., Hening, W., Wright, D., Walczak, T., Goldberg, J., Burger, R. et al. (1995). Magnetic brain stimulation: Safety studies. *Electroencephalography and Clinical Neurophysiology*, 97(1), 36–42.
- Classen, J., Witte, O. W., Schlaug, G., Seitz, R. J., Holthausen, H., & Benecke, R. (1995). Epileptic seizures triggered directly by focal transcranial magnetic stimulation. *Electroencephalography and Clinical Neurophysiology*, 94(1), 19–25.
- Conforto, A. B., Z'Graggen, W. J., Kohl, A. S., Rosler, K. M., & Kaelin-Lang, A. (2004). Impact of coil position and electrophysiological monitoring on determination of motor thresholds to transcranial magnetic stimulation. *Clinical Neurophysiology*, 115(4), 812–819.
- Counter, S. A., Borg, E., Lofqvist, L., & Brismar, T. (1990). Hearing loss from the acoustic artifact of the coil used in extracranial magnetic stimulation. *Neurology*, 40(8), 1159–1162.
- Crochet, S., & Petersen, C. C. (2006). Correlating whisker behavior with membrane potential in barrel cortex of awake mice. *Nature Neuroscience*, 9(5), 608–610.
- Curio, G., Mackert, B. M., Burghoff, M., Koetitz, R., Abraham-Fuchs, K., & Harer, W. (1994). Localization of evoked neuromagnetic 600 Hz activity in the cerebral somatosensory system. *Electroencephalography and Clinical Neurophysiology*, 91(6), 483–487.
- Dettmers, C., Ridding, M. C., Stephan, K. M., Lemon, R. N., Rothwell, J. C., & Frackowiak, R. S. (1996). Comparison of regional cerebral blood flow with transcranial magnetic stimulation at different forces. *Journal of Applied Physiology*, 81(2), 596–603.
- Driver, J., Blankenburg, F., Bestmann, S., & Ruff, C. C. (2010). New approaches to the study of human brain networks underlying spatial attention and related processes. *Experimental Brain Research*, 206(2), 153–162.

- Edgley, S. A., Eyre, J. A., Lemon, R. N., & Miller, S. (1990). Excitation of the corticospinal tract by electromagnetic and electrical stimulation of the scalp in the macaque monkey. *Journal of Physiology*, 425(1), 301–320.
- Engel, S. A., Rumelhart, D. E., Wandell, B. A., Lee, A. T., Glover, G. H., Chichilnisky, E. J. et al. (1994). fMRI of human visual cortex. *Nature*, 369(6481), 525.
- Epstein, C. M., Schwartzberg, D. G., Davey, K. R., & Sudderth, D. B. (1990). Localizing the site of magnetic brain stimulation in humans. *Neurology*, 40(4), 666–670.
- Fitzgerald, P. B. (2010). TMS-EEG: A technique that has come of age? *Clinical Neurophysiology*, 121(3), 265–267.
- Friston, K. (2008). Neurophysiology: The brain at work. *Current Biology*, 18(10), R418–R420.
- Friston, K. J. (1995). Commentary and opinion: II. Statistical parametric mapping: Ontology and current issues. *Journal of Cerebral Blood Flow and Metabolism*, 15(3), 361–370.
- Friston, K. J. (1997). Testing for anatomically specified regional effects. *Human Brain Mapping*, 5(2), 133–136.
- Groening, K., Brodbeck, V., Moeller, F., Wolff, S., van Baalen, A., Michel, C. M. et al. (2009). Combination of EEG-fMRI and EEG source analysis improves interpretation of spike-associated activation networks in paediatric pharmacoresistant focal epilepsies. *Neuroimaging*, 46(3), 827–833.
- Hämäläinen, M., Hari, R., Ilmoniemi, R. J., Knuutila, J., & Lounasmaa, O. V. (1993). Magnetoencephalography—theory, instrumentation, and applications to noninvasive studies of the working human brain. *Reviews of Modern Physics*, 65(2), 413–497.
- Haynes, J. D., & Rees, G. (2005). Predicting the stream of consciousness from activity in human visual cortex. *Current Biology*, 15(14), 1301–1307.
- Heeger, D. J., Huk, A. C., Geisler, W. S., & Albrecht, D. G. (2000). Spikes versus BOLD: What does neuroimaging tell us about neuronal activity? *Nature Neuroscience*, 3(7), 631–633.
- Hess, C. W., Mills, K. R., Murray, N. M., & Schrieffer, T. N. (1987). Magnetic brain stimulation: Central motor conduction studies in multiple sclerosis. *Annals of Neurology*, 22(6), 744–752.
- Hobson, J. A. (2005). Sleep is of the brain, by the brain and for the brain. *Nature*, 437(7063), 1254–1256.
- Hufnagel, A., & Elger, C. E. (1991). Responses of the epileptic focus to transcranial magnetic stimulation. *Electroencephalography and Clinical Neurophysiology Supplement*, 43, 86–99.
- Hulshoff Pol, H. E., Schnack, H. G., Posthuma, D., Mandl, R. C., Baare, W. F., van Oel, C. et al. (2006). Genetic contributions to human brain morphology and intelligence. *Journal of Neuroscience*, 26(40), 10235–10242.
- Kamphuisen, A., Bauer, M., & van Ee, R. (2008). No evidence for widespread synchronized networks in binocular rivalry: MEG frequency tagging entrains primarily early visual cortex. *Journal of Vision*, 8(5), 4. doi: 10.1167/8.5.4
- Kanai, R., Bahrami, B., & Rees, G. (2010). Human parietal cortex structure predicts individual differences in perceptual rivalry. *Current Biology*, 20(18), 1626–1630.
- Kringelbach, M. L., Jenkinson, N., Green, A. L., Owen, S. L., Hansen, P. C., Cornelissen, P. L. et al. (2007). Deep brain stimulation for chronic pain investigated with magnetoencephalography. *Neuroreport*, 18(3), 223–228.
- Lansing, R. W. (1964). Electroencephalographic correlates of binocular rivalry in man. *Science*, 146(3649), 1325–1327.

- Laufs, H., Daunizeau, J., Carmichael, D. W., & Kleinschmidt, A. (2008). Recent advances in recording electrophysiological data simultaneously with magnetic resonance imaging. *Neuroimage*, 40(2), 515–528.
- Lehmann, D. (1989). Brain electrical mapping of cognitive functions for psychiatry: Functional micro-states. *Psychiatry Research*, 29(3), 385–386.
- Lehmann, D., Ozaki, H., & Pal, I. (1987). EEG alpha map series: Brain micro-states by space-oriented adaptive segmentation. *Electroencephalography and Clinical Neurophysiology*, 67(3), 271–288.
- Leopold, D. A., & Logothetis, N. K. (1996). Activity changes in early visual cortex reflect monkeys' percepts during binocular rivalry. *Nature*, 379(6565), 549–553.
- Lesser, R. P. (2009). Epilepsy: Does continuous EEG monitoring improve seizure control? *Nature Reviews Neurology*, 5(11), 581–582.
- Lumer, E. D., & Rees, G. (1999). Covariation of activity in visual and prefrontal cortex associated with subjective visual perception. *Proceedings of the National Academy of Sciences USA*, 96(4), 1669–1673.
- Lyoo, I. K., Sung, Y. H., Dager, S. R., Friedman, S. D., Lee, J. Y., Kim, S. J. et al. (2006). Regional cerebral cortical thinning in bipolar disorder. *Bipolar Disorders*, 8(1), 65–74.
- Magri, C., Schridde, U., Murayama, Y., Panzeri, S., & Logothetis, N. K. (2012). The amplitude and timing of the BOLD signal reflects the relationship between local field potential power at different frequencies. *Journal of Neuroscience*, 32(4), 1395–1407.
- Maller, J. J., Daskalakis, Z. J., Thomson, R. H., Daigle, M., Barr, M. S., & Fitzgerald, P. B. (2012). Hippocampal volumetrics in treatment-resistant depression and schizophrenia: The devil's in de-tail. *Hippocampus*, 22(1), 9–16.
- McConnell, K. A., Nahas, Z., Shastri, A., Lorberbaum, J. P., Kozel, F. A., Bohning, D. E. et al. (2001). The transcranial magnetic stimulation motor threshold depends on the distance from coil to underlying cortex: A replication in healthy adults comparing two methods of assessing the distance to cortex. *Biological Psychiatry*, 49(5), 454–459.
- McGuffin, P., Rijsdijk, F., Andrew, M., Sham, P., Katz, R., & Cardno, A. (2003). The heritability of bipolar affective disorder and the genetic relationship to unipolar depression. *Archives of General Psychiatry*, 60(5), 497–502.
- Metherate, R., Cox, C. L., & Ashe, J. H. (1992). Cellular bases of neocortical activation: modulation of neural oscillations by the nucleus basalis and endogenous acetylcholine. *Journal of Neuroscience*, 12(12), 4701–4711.
- Miller, S. M., Hansell, N. K., Ngo, T. T., Liu, G. B., Pettigrew, J. D., Martin, N. G. et al. (2010). Genetic contribution to individual variation in binocular rivalry rate. *Proceedings of the National Academy of Sciences USA*, 107(6), 2664–2668.
- Miller, S. M., Liu, G. B., Ngo, T. T., Hooper, G., Riek, S., Carson, R. G. et al. (2000). Interhemispheric switching mediates perceptual rivalry. *Current Biology*, 10(7), 383–392.
- Millett, D. (2001). Hans Berger: From psychic energy to the EEG. *Perspectives in Biology and Medicine*, 44(4), 522–542.
- Muckli, L., Kriegeskorte, N., Lanfermann, H., Zanella, F. E., Singer, W., & Goebel, R. (2002). Apparent motion: Event-related functional magnetic resonance imaging of perceptual switches and states. *Journal of Neuroscience*, 22(9), RC219.
- Mukamel, R., Gelbard, H., Arieli, A., Hasson, U., Fried, I., & Malach, R. (2005). Coupling between neuronal firing, field potentials, and fMRI in human auditory cortex. *Science*, 309(5736), 951–954.

- Nair, D. G. (2005). About being BOLD. *Brain Research Reviews*, 50(2), 229–243.
- Nunez, P. L. (1995). *Neocortical dynamics and human EEG rhythms*. New York: Oxford University Press.
- Oliveri, M., & Caltagirone, C. (2006). Suppression of extinction with TMS in humans: From healthy controls to patients. *Behavioural Neurology*, 17(3–4), 163–167.
- Oliveri, M., Rossini, P. M., Traversa, R., Cicinelli, P., Filippi, M. M., Pasqualetti, P. et al. (1999). Left frontal transcranial magnetic stimulation reduces contralesional extinction in patients with unilateral right brain damage. *Brain*, 122(9), 1731–1739.
- Pascual-Leone, A., Cohen, L. G., Shotland, L. I., Dang, N., Pikus, A., Wassermann, E. M. et al. (1992). No evidence of hearing loss in humans due to transcranial magnetic stimulation. *Neurology*, 42(3), 647–651.
- Pettigrew, J. D., & Miller, S. M. (1998). A ‘sticky’ interhemispheric switch in bipolar disorder? *Proceedings of the Royal Society of London B: Biological Sciences*, 265(1411), 2141–2148.
- Polonsky, A., Blake, R., Braun, J., & Heeger, D. J. (2000). Neuronal activity in human primary visual cortex correlates with perception during binocular rivalry. *Nature Neuroscience*, 3(11), 1153–1159.
- Poulet, J. F., & Petersen, C. C. (2008). Internal brain state regulates membrane potential synchrony in barrel cortex of behaving mice. *Nature*, 454(7206), 881–885.
- Ray, W. J., & Cole, H. W. (1985). EEG alpha activity reflects attentional demands, and beta activity reflects emotional and cognitive processes. *Science*, 228(4700), 750–752.
- Rosa, M. J., Kilner, J., Blankenburg, F., Josephs, O., & Penny, W. (2010). Estimating the transfer function from neuronal activity to BOLD using simultaneous EEG-fMRI. *Neuroimage*, 49(2), 1496–1509.
- Rossi, S., Hallett, M., Rossini, P. M., & Pascual-Leone, A. (2009). Safety, ethical considerations, and application guidelines for the use of transcranial magnetic stimulation in clinical practice and research. *Clinical Neurophysiology*, 120(12), 2008–2039.
- Rossini, P. M., Barker, A. T., Berardelli, A., Caramia, M. D., Caruso, G., Cracco, R. Q. et al. (1994). Non-invasive electrical and magnetic stimulation of the brain, spinal cord and roots: Basic principles and procedures for routine clinical application. Report of an IFCN committee. *Electroencephalography and Clinical Neurophysiology*, 91(2), 79–92.
- Rudiak, D., & Marg, E. (1994). Finding the depth of magnetic brain stimulation: A re-evaluation. *Electroencephalography and Clinical Neurophysiology*, 93(5), 358–371.
- Schwarzkopf, D. S., Silvanto, J., & Rees, G. (2011). Stochastic resonance effects reveal the neural mechanisms of transcranial magnetic stimulation. *Journal of Neuroscience*, 31(9), 3143–3147.
- Silvanto, J., & Muggleton, N. G. (2008). New light through old windows: moving beyond the “virtual lesion” approach to transcranial magnetic stimulation. *Neuroimage*, 39(2), 549–552.
- Soros, P., Knecht, S., Bantel, C., Imai, T., Wusten, R., Pantev, C. et al. (2001). Functional reorganization of the human primary somatosensory cortex after acute pain demonstrated by magnetoencephalography. *Neuroscience Letters*, 298(3), 195–198.
- Sporns, O. (2012). From simple graphs to the connectome: Networks in neuroimaging. *Neuroimage*, 62(2), 881–886.
- Sporns, O., Tononi, G., & Edelman, G. M. (2000). Theoretical neuroanatomy: Relating anatomical and functional connectivity in graphs and cortical connection matrices. *Cerebral Cortex*, 10(2), 127–141.

- Srinivasan, R., Russell, D. P., Edelman, G. M., & Tononi, G. (1999). Increased synchronization of neuromagnetic responses during conscious perception. *Journal of Neuroscience*, 19(13), 5435–5448.
- Sterzer, P., & Rees, G. (2008). A neural basis for percept stabilization in binocular rivalry. *Journal of Cognitive Neuroscience*, 20(3), 389–399.
- Terao, Y., & Ugawa, Y. (2002). Basic mechanisms of TMS. *Journal of Clinical Neurophysiology*, 19(4), 322–343.
- Thornton, R. C., Rodionov, R., Laufs, H., Vulliemoz, S., Vaudano, A., Carmichael, D. et al. (2010). Imaging haemodynamic changes related to seizures: comparison of EEG-based general linear model, independent component analysis of fMRI and intracranial EEG. *Neuroimage*, 53(1), 196–205.
- Tong, F., Nakayama, K., Vaughan, J. T., & Kanwisher, N. (1998). Binocular rivalry and visual awareness in human extrastriate cortex. *Neuron*, 21(4), 753–759.
- Vulliemoz, S., Thornton, R., Rodionov, R., Carmichael, D. W., Guye, M., Lhatoo, S. et al. (2009). The spatio-temporal mapping of epileptic networks: Combination of EEG-fMRI and EEG source imaging. *Neuroimage*, 46(3), 834–843.
- Wunderlich, K., Schneider, K. A., & Kastner, S. (2005). Neural correlates of binocular rivalry in the human lateral geniculate nucleus. *Nature Neuroscience*, 8(11), 1595–1602.
- Yamada, H., Tamaki, T., Wakano, K., Mikami, A., & Transfeldt, E. E. (1995). Effect of transcranial magnetic stimulation on cerebral function in a monkey model. *Electroencephalography and Clinical Neurophysiology*, 97(2), 140–144.
- Zaretskaya, N., Thielscher, A., Logothetis, N. K., & Bartels, A. (2010). Disrupting parietal function prolongs dominance durations in binocular rivalry. *Current Biology*, 20(23), 2106–2111.
- Ziemann, U. (2011). Transcranial magnetic stimulation at the interface with other techniques: A powerful tool for studying the human cortex. *Neuroscientist*, 17(4), 368–381.
- Ziemann, U., Lonnecker, S., Steinhoff, B. J., & Paulus, W. (1996). The effect of lorazepam on the motor cortical excitability in man. *Experimental Brain Research*, 109(1), 127–135.

The neuron doctrine of binocular rivalry

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Ever since Horace Barlow (1972) proposed his neuron doctrine for perceptual psychology, the holy grail for neurophysiologists has been to find individual neurons or groups of neurons whose firing correlates with specific percepts or even a state of mind or consciousness. Binocular rivalry is a particularly attractive paradigm for this approach because a stable visual stimulus causes an ever-changing subjective perceptual experience. The publication of Blake's neural theory of binocular rivalry (Blake, 1989) inspired numerous attempts to identify neurons in various areas along the central visual pathways whose firing rate might signal dominance or suppression. Collectively these studies have shown that depending on the type of stimulus, rivalry is resolved at both lower and higher levels in the visual system.

Introduction to single-cell recording

The mind has no direct access to the outside world but all sensory experiences are translated by transduction processes in the sense organs into electrical impulses traveling along nerve fibers. Since Adrian (1928) first proposed that action potentials are the principal means of communication between neurons, the recording of electrical signals from single neurons in the nervous system has been the gold standard of neuroscientists trying to figure out how the brain works. The first single-cell recording studies in the visual system were performed on retinal ganglion cells by Hartline and Granit in the late 1930s and then by Kuffler and Barlow in the early 1950s, made possible through the development of microelectrodes which had been pioneered by Granit (Granit & Svaetichin, 1939).

While the earliest microelectrodes were glass micropipettes filled with an electrolyte solution similar to extracellular fluid, David Hubel (1957) developed tungsten microelectrodes for his pioneering work on the cat visual cortex. He used

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tungsten wire of 125 μm diameter pointed by electropolishing, and insulated up to a few millimeters from the tip with a vinyl lacquer. The borosilicate glass-coated platinum-plated tungsten microelectrode developed by Merrill and Ainsworth (1972) has since become a standard tool of neurophysiologists. Depending on the size of the exposed tip and the impedance, electrodes will either pick up action potentials produced by a single neuron nearby (with electrode impedances of 1.5 $\text{M}\Omega$ or more) or multi-unit activity (for impedances of $<1 \text{ M}\Omega$). Compared with intracellular recordings where the size of an action potential is in the order of 100 mV (against resting membrane potential), extracellularly recorded signals are much smaller, typically only 0.1 mV. First, this means that signals need to be amplified and band pass filtered in order to distinguish them from electrical noise. Second, as there is no certainty from which neuron(s) the signals originated, a method of discriminating between spikes (action potentials) from different cells is vital if single-unit recording is desired. Historically, discrimination tended to be based simply on the amplitude of the first peak of the bi-phasic spikes, visualized on an oscilloscope screen (and made audible via a loudspeaker). This discrimination can be implemented electronically using a Schmitt trigger or window discriminator for example. More recently, various methods of spike sorting have been developed which all rely on the fact that each neuron's extracellularly recorded action potentials have a characteristic and relatively stable shape that depends primarily on the distance from and orientation relative to the electrode tip (Gold, Henze, Koch, & Buzsáki, 2006).

Spike sorting entails the grouping of action potentials into clusters based on the similarity of their shapes. Probably the simplest method is template matching which requires the user to determine a characteristic spike shape for each cluster and then assign all other spikes to one of those templates (Gerstein & Clark, 1964). This is not practical for a larger number of recording channels; moreover, the shape of a neuron's spike may change in the course of a longer recording session. In contrast, current spike sorting techniques are largely unsupervised. The detection of spike events using an amplitude threshold is followed by extraction of features of the spike shape in a multidimensional space. This can be done using principal component analysis (Abeles & Goldstein, 1977) or, more commonly now, wavelet analysis (Letelier & Weber, 2000; Quiroga, Nadasdy, & Ben-Shaul, 2004). The final step is cluster cutting, the grouping of spikes with the same features into clusters. This can be done manually in a two-dimensional feature space (Gray, Maldonado, Wilson, & McNaughton, 1995), or preferably automatically, employing Bayesian algorithms for example (Lewicki, 1994) or expectation maximization procedures (Harris, Henze, Csicsvari, Hirase, & Buzsáki, 2000).

To some extent, spike detection methods have lagged behind significant advances in electrode design. Instead of single-channel electrodes, many researchers

are now using tetrodes consisting of four microelectrodes wires, insulated to near the tips, closely twisted together (Gray et al., 1995; Wilson & McNaughton, 1993). Because the spikes of individual neurons will typically be picked up by more than one of the four electrodes and will look slightly different on each channel, they can be distinguished more reliably through spike sorting. For independent multiple-channel recordings, a variety of multi-electrode devices are now in use, including multi-pronged electrodes, electrodes with several recording sites along the shaft ("Michigan probes"; Drake, Wise, Farraye, Anderson, & BeMent, 1988), or large rectangular multi-electrode arrays ("Utah arrays"; Nordhausen, Rousche, & Normann, 1994). In principle, single neurons can be recorded on each channel of these devices using spike sorting, but their power stems from the ability to record the responses of a large number of cells to a given stimulus at the same time, which in turns allows for analysis of spatial patterns of response as well as temporal correlations.

Relating single-cell responses to perception

While recording from various types of cells in the vertebrate retina has taught us a lot about the sophisticated processing of visual information that goes on at that level, few would argue that visual perception and visual awareness arise from retinal activity. The first paper to relate the spiking activity of individual neurons to a behaviorally relevant output was "What the frog's eye tells the frog's brain" by Lettvin and colleagues (Lettvin, Maturana, McCulloch, & Pitts, 1959). In this classic paper, the authors describe four basic types of neurons in the optic tectum (equivalent to the mammalian superior colliculus) that underpin a frog's visually guided behavior, namely contrast detectors, convexity detectors, moving edge detectors and dimming detectors, and finish by stating that their "operations thus have much more the flavor of perception than of sensation, if that distinction has any meaning now... We have been tempted, for example, to call the convexity detectors 'bug perceivers.'" The pioneering studies by Hubel and Wiesel (1962) on cat primary visual cortex (V1) showed that the mammalian visual cortex contains 'feature detectors' too, in this case orientation and contrast edge detectors, as well as disparity detectors (Barlow, Blakemore, & Pettigrew, 1967). But can one actually prove that the firing of individual cortical neurons is relevant for perception? In his "neuron doctrine for perceptual psychology", Barlow (1972) postulated this as the first dogma: "To understand nervous function one needs to look at interactions at a cellular level, rather than either a more macroscopic or microscopic level". He formulated four more dogmas on how neuronal firing relates to subjective perception. The second dogma states that a sensory experience should be represented by

a minimum number of active cells, a strategy that has become known as sparse coding (Olshausen & Field, 2004). Third, the trigger features detected by neurons should be matched to patterns of stimulation through an experience-dependent developmental process. Fourth, perception should correspond to the activity of a small number of high-level neurons responding to more complex stimulus patterns. Finally, the higher a neuron's firing rate, the more likely its trigger feature is present (Barlow, 1972).

In the majority of neurophysiological studies, researchers are concerned only with firing rates, but it is well recognized that information can also be transmitted through variations in the firing pattern. For instance, cells may switch between a burst firing mode and spiking at regular intervals; in the thalamus these modes are linked with different states of sleep and arousal (Steriade, 2005). In addition, populations of neurons may synchronize their firing in response to a particular stimulus, and this has been proposed as a mechanism to encode perceptual grouping and to solve the binding problem (Singer, 1999). Synchrony may also play a role in which interpretation reaches perceptual consciousness during the viewing of ambiguous figures, and this will be discussed later. In addition, neurons may also communicate electrically, via gap junctions, and chemically, via neuromodulators, but the implications of these means of communication for the representation of information remain largely unclear.

Regarding the representation of objects or concepts in the brain, in his neuron doctrine for perceptual psychology Barlow (1972) proposed 'cardinal cells' as an intermediate between the two possible extremes introduced by Sherrington (1941), namely the 'pontifical cell, ...the climax of the whole system of integration' vs. a 'million-fold democracy whose each unit is a cell'. The search for dedicated neurons that respond selectively to very specific stimuli has played a prominent role in attempts to link the hardware of the brain to perception, consciousness and the mind. Perhaps the greatest success story in that respect has been the identification of face selective neurons in the macaque inferotemporal cortex (Gross, Rocha-Miranda, & Bender, 1972; Perrett, Rolls, & Caan, 1982). Moreover, in the human medial temporal lobe (in particular the hippocampus), neurons have been identified that respond not only selectively to a particular person's face but also, for example, the name of the person in writing, implying that these neurons encode a concept or abstract entity (Quiroga, Reddy, Kreiman, Koch, & Fried, 2005). Nevertheless, these are not quite 'grandmother cells' in the sense of Jerome Lettvin's term, coined in the late 1960s to refer to "a neuron that would respond only to a specific, complex, and meaningful stimulus, that is, to a single percept or even a single concept" (Gross, 2002). The study does not claim the existence of single neurons coding uniquely for discrete percepts because it is likely that (a) these cells would have responded to other persons as well and (b) other cells

would have responded to the same person (Quiroga et al., 2005). In this context it should be noted that analysis of responses to a necessarily limited set of stimuli may lead to the false impression of grandmother cell-type selectivity.

These observations on single-cell responses are intriguing but provide only qualitative correlational evidence linking neuronal firing with perception. However, the fifth dogma of Barlow's neuron doctrine for perceptual psychology (relating a neuron's firing rate to the likelihood of its trigger feature being present) suggests a quantitative relationship that has been tested particularly successfully with respect to pattern motion detection in area MT (or V5) of the macaque superior temporal sulcus (Parker & Newsome, 1998). Here, responses of single neurons to arrays of moving dots, a proportion of which move coherently in one direction while the others move in random directions, has been compared with the subject's ability to judge the direction of coherent motion. Plotting the firing rate of an MT neuron against the percentage of dots moving in that neuron's preferred directions yields a sigmoid 'neurometric' function, while plotting the percentage of correct judgements of the trained monkey against the coherence level gives a psychometric function which is also a sigmoid. Neural performance and psychophysical performance are remarkably well matched in terms of the sensitivity (i.e., threshold) and slope of the two functions (Britten, Shadlen, Newsome, & Movshon, 1992; Newsome, Britten, & Movshon, 1989), although on a trial-by-trial basis the correlation between the activity of single MT neurons and the monkey's behavior is weaker, suggesting that behavioral choice is based on the pooling of responses of a number of neurons (Britten, Newsome, Shadlen, Celebrini, & Movshon, 1996; Shadlen, Britten, Newsome, & Movshon, 1996). Probably the most convincing evidence for a causal relationship between neuronal firing and a perceptual or behavioral consequence comes from a study showing that increasing the firing rate of a cluster of neurons preferring a particular direction of motion by means of microstimulation, shifted the psychometric function and increased the frequency with which the subject reported perceiving that direction of motion (Salzman, Britten, & Newsome, 1990). Of particular relevance to the topic of this book is the discovery that MT neurons also respond to perceptually ambiguous structure-from-motion stimuli in a manner that correlates with perception (Grunewald, Bradley, & Andersen, 2002; Parker, Krug, & Cumming, 2002). In that study, the impression of a three-dimensional rotating cylinder arises from two planes of dots on a computer screen moving in opposite directions. Without an additional cue as to which set of dots belongs to the front or the rear surface, the direction of rotation of the cylinder, clockwise or counter-clockwise, is ambiguous, but adding a disparity (depth) signal to one set of dots disambiguates it. Similar to the detection of coherent motion, the behavioral choice (i.e., perceptual judgement) of the subject can be predicted on the basis of the firing of a subset of neurons in MT

whose neurometric function in turn depends on the sign and amount of disparity added to the stimulus (Parker et al., 2002). Notably, with zero disparity a physically unchanging stimulus can be interpreted in two different ways, and the subject's perceptual judgement can be shown to depend on the firing of the neuronal "decision pool" (Parker et al., 2002).

Single-cell investigations of binocular rivalry

If we are to apply Barlow's neuron doctrine to binocular rivalry, then there are two questions that need answering: (1) where in the brain does the firing of neurons stop to be directly related to the (unchanging) physical properties of the dichoptic stimulus and where does it start to reflect the fluctuating subjective perception, and (2) which cells are responsible for the switching between the two rival percepts? I shall return to the latter question later, however most research has been concerned with the former. As outlined above, this question first became experimentally accessible in the 1960s when Hubel and Wiesel published their seminal papers on receptive fields of neurons in primary visual cortex (Hubel & Wiesel, 1962, 1968). Indeed, when Colin Blakemore started work as a PhD student with Horace Barlow, he initially proposed to study responses in V1 to rival dichoptic stimuli before being persuaded to examine the responses to the more natural fusible stimuli (C. Blakemore, personal communication); this work led to the discovery of disparity selective cells in V1 (Barlow et al., 1967). Nevertheless, an interest in the neural substrate of binocular rivalry remained, and in line with the prevailing view in the 1970s and 1980s of rivalry as a bottom-up integration of information from the two eyes, Blakemore and colleagues suggested that binocular interactions in the lateral geniculate nucleus (LGN), which had been shown to be almost exclusively inhibitory (Sanderson, Darian-Smith, & Bishop, 1969), might account for binocular rivalry (Blakemore, Iversen, & Zangwill, 1972).

The first direct electrophysiological investigation of neural responses to rival dichoptic stimuli was carried out by Varela and Singer (1987), who recorded from neurons in the A laminae (which receive the principal retinofugal projection) of the LGN in cats (which were anesthetized, like in other studies on cats discussed below). They induced a steady-state response by continuously presenting a drifting grating to the dominant eye and then intermittently showed a second grating to the non-dominant eye. They reported that this second stimulus caused response suppression which was of long latency and, crucially, depended on the orientation and direction of movement of the two stimuli being different, just as one would expect of 'binocular rivalry detectors'. Furthermore, these binocular interactions appeared to depend on intact corticothalamic feedback (Varela et al.,

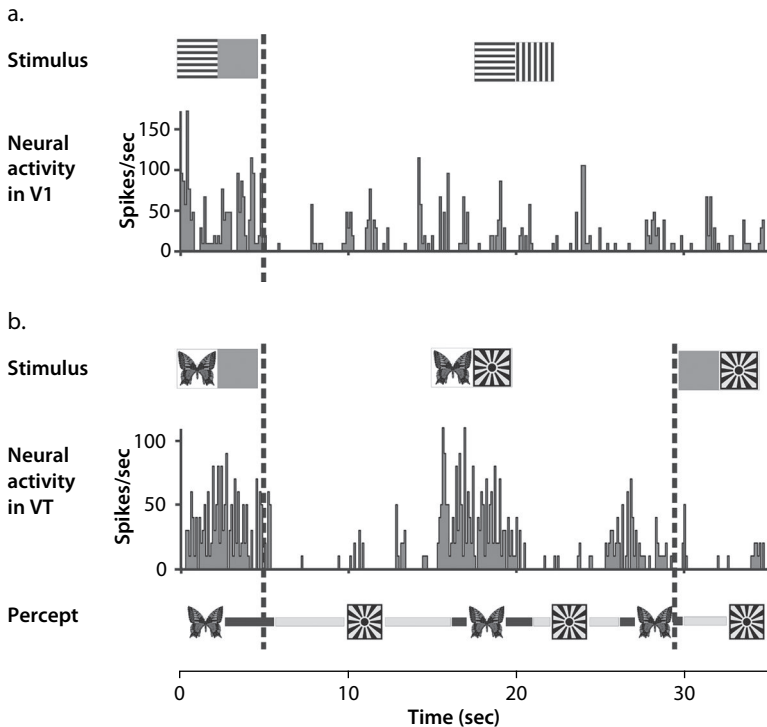


Figure 1. Typical single-cell responses to rival binocular stimuli. (a) Response of a binocular complex cell in cat V1. The cell is first stimulated through the dominant eye alone with a grating of optimal (horizontal) orientation, causing a strong response. After 5 sec (dotted line), an orthogonally oriented (vertical) grating appears in the non-dominant eye. Suppression sets in quite rapidly (< 100 msec) and is strongest for the first few seconds, although the response is tonically reduced (typically by about 40%) for the entire period of rival binocular exposure. Suppression has a shorter latency in V1 than in IT (where latencies are ~ 200 msec), so it cannot be the result of feedback inhibition. (b) Response of a macaque IT neuron and the animal's perceptual report. The cell responds best to a butterfly stimulus and not at all to the sunburst. The dotted vertical lines mark changes in the physical stimulus. A long period of rival stimulation is preceded by monocular presentation of the butterfly alone and is followed by a short period of the sunburst alone, in the other eye. During these monocular epochs, the monkey's perceptual reports (indicated by the icons and bars below) match the activity of the neuron, showing that the animal reports its perception accurately. After the onset of the rival presentation, the cell is suppressed and the animal's perception switches from butterfly to sunburst. Subsequently, the neuron fires only just before and during two epochs when the monkey indicates perception of the cell's preferred stimulus (reprinted by permission from Elsevier Ltd: *Current Biology*, Sengpiel, 1997, 7: R447–R450).

1987). However, just a year earlier, Ohzawa and Freeman (1986a) had carried out a detailed quantitative study of binocular responses in cat V1, and concluded that presenting an orthogonal-to-optimum grating to the non-dominant eye had no effect whatsoever (at least in simple cells) on the responses to an optimally oriented grating presented to the dominant eye; among complex cells some exceptional cases of suppression with orthogonal grating pairs were described (Ohzawa & Freeman, 1986b). In contrast, Logothetis and Schall (1989), recording from area MT in awake behaving monkeys presented with dichoptic gratings drifting in opposite directions, found that for a minority of cells the response strength correlated positively with the perceptual report of the subject, i.e., these cells fired more action potentials when their preferred direction of movement was perceptually dominant than when it was suppressed. Curiously, for a similar number of cells the correlation was negative (Logothetis & Schall, 1989).

It was against this background that Richard Harrad, Colin Blakemore and I decided to study responses in cat LGN and V1 to rival stimuli (Sengpiel, Blakemore, & Harrad, 1995a). We employed a stimulus paradigm similar to that of Varela and Singer because we reasoned that with asynchronous onset of the dichoptic stimuli, we would have a better chance of uncovering any rivalry-related neuronal responses. It had been reported before that the sudden onset of a rival stimulus in one eye reliably captures dominance from a stimulus already present in the other eye, a phenomenon known as flash suppression (Wolfe, 1984). Recording from LGN neurons, we found that responses to binocular stimuli were almost invariably lower than responses to monocular stimuli presented to the dominant eye alone, but contrary to the report by Varela and Singer (1987), this interocular suppression was just as strong for fusible as for rival stimuli (Sengpiel et al., 1995a). Monocular cells in layer 4 of V1 behaved similarly. [In this context, monocular cells in the sense of Hubel and Wiesel (1962) are those in which a direct, excitatory response to stimulation of the classical receptive field can only be elicited through one eye.] In contrast, responses of binocular neurons (i.e., those that could be excited through either eye) clearly differed between fusible and rival binocular stimuli, exhibiting facilitation beyond the dominant-eye monocular response for the former and suppression below that level for the latter (Figure 1a). Specifically, we found that the transition from facilitation to suppression occurred at an interocular orientation difference of about 22° , close to the value of 30° at which, in humans, fusion gives way to rivalry (Braddick, 1979). Similarly, for iso-oriented dichoptic gratings, suppression was observed when their spatial frequencies differed by more than 0.5–1.0 octaves (Sengpiel, Freeman, & Blakemore, 1995b). Surprisingly, suppression by iso-oriented gratings can occur even for spatial frequencies within the excitatory tuning curve of the cell, capable of exciting

the cell when presented monocularly. In those cases, interocular suppression is actually non-selective for orientation, leading us to suggest that the response of V1 neurons to dichoptic stimuli is the sum of a facilitatory component that is specific for fusible stimuli and an inhibitory component that lacks specificity and becomes apparent for rival stimuli (Sengpiel et al., 1995b). The strength of suppression during binocular rivalry is measured in terms of the contrast threshold increment in various detection or discrimination tasks, and increments of around 0.3–0.5 log units have typically been reported (Fox & Check, 1966, 1968; Wales & Fox, 1970). When we measured the effect of rival stimulus presentations on neuronal contrast response functions, we found that on the one hand response amplitudes were reduced across all contrasts (an effect called response gain control), and on the other hand response curves were shifted to higher contrasts (contrast gain control) on average by a factor of 1.49, or 0.17 log units (Sengpiel, Baddeley, Freeman, Harrad, & Blakemore, 1998). Response gain control was predominantly observed in layer 4, whereas cells in other layers mainly exhibited contrast gain control (Sengpiel et al., 1998). All in all, interocular suppression in cat V1 exhibited many striking similarities with human binocular rivalry (Table 1).

Table 1. Comparison of interocular suppression in cat V1 with human rivalry

Parameter	Binocular rivalry	Interocular suppression
Threshold for loss of fusion, interocular orientation difference	30° (Braddick, 1979)	22° (Sengpiel et al., 1995a)
Threshold for loss of fusion, interocular spatial frequency difference	0.4 octaves (Blakemore, 1970)	0.5–1 octave (Sengpiel et al., 1995b)
Dependence of strength of inhibition on interocular orientation difference	none (Blake & Lema, 1978)	none (Sengpiel et al., 1995b)
Spatial extent of exclusive stimulus visibility / of suppression field	scaled with eccentricity (Blake, O'Shea, & Mueller, 1992)	similar to receptive field (Sengpiel, Bonhoeffer, Freeman, & Blakemore, 2001)
Increase of contrast threshold for stimulus detection / response in the suppressed eye	0.3–0.5 log units (Fox & Check, 1966, 1968; Wales & Fox, 1970)	0.17 log units (Sengpiel et al., 1998)
Temporal pattern of inhibition	intermittent (phase durations Γ distributed) (Fox & Herrmann, 1967)	tonic (with onset transient) (Sengpiel et al., 1995a; Leopold & Logothetis, 1996)

Why had the robust interocular suppression that we found to be exhibited by a large percentage of V1 neurons not been reported before, for example, by Ohzawa and Freeman (1986b)? It seems likely that our mode of stimulation, introducing a rival stimulus in one eye against the background of an ongoing response to a stimulus continuously present in the other eye played a key role. Indeed, we found that presentation of a rival stimulus pair with simultaneous onset resulted in much less suppression of the binocular response below the level of the dominant-eye monocular response (Sengpiel & Blakemore, 1994).

What we did not observe in V1 (except perhaps in one or two cells) was the characteristic stochastic fluctuation between suppressed and non-suppressed states with rival stimuli. This might have been due to the fact our subjects were anesthetized, or simply because there are no 'rivalry detector neurons' in V1.

Studies on awake behaving monkeys appear to favor the latter explanation. On the one hand, there is no evidence of rivalry related responses in the LGN (Lehky & Maunsell, 1996). On the other hand, the percentage of cells whose responses correlate with the monkeys' perceptual report increases throughout the hierarchy of cortical areas in both the ventral and dorsal streams (Figure 2). Logothetis and colleagues trained monkeys to press one of two levers to indicate which percept was dominant during the viewing of rival dichoptic stimuli; the accuracy of the report was verified by interspersing rival stimulus presentations with physically alternating stimuli, one being the recorded cell's preferred stimulus and the other a non-preferred one (see Figure 1b). In areas V1 and V2, about 18% of cells modulated their firing rate in a way that was related to the monkey's perception, while in area V4 this figure was 38% (Leopold & Logothetis, 1996) and in the inferior temporal cortex (IT) it was as high as 90% (Sheinberg & Logothetis, 1997). Very few monocular cells were found to modulate their firing rate in this way (Leopold & Logothetis, 1996). It is worth noting that a similar progressive increase in correlation between neuronal activity and perceptual judgments across cortical areas has been described for somatosensory areas of the parietal lobe and premotor areas of the frontal lobe (de Lafuente & Romo, 2006).

Taken together, the single-cell recording studies on (anesthetized) cats and (awake behaving) monkeys suggest that, although certain information about the presence of rival stimuli in the two eyes is encoded in the firing of neurons at the earliest stages of binocular convergence, we must look in higher visual areas for rivalry detectors, neurons whose firing corresponds closely to the subject's conscious visual experience. However, two very different sets of results call this interpretation into question. First, although a recent electrophysiological study on macaque V1 using tetrodes confirmed that only a minority (20%) of neurons in their firing reflect the perceived visual stimulus and these cells exhibited perceptual modulations substantially weaker compared with physically changing stimuli,

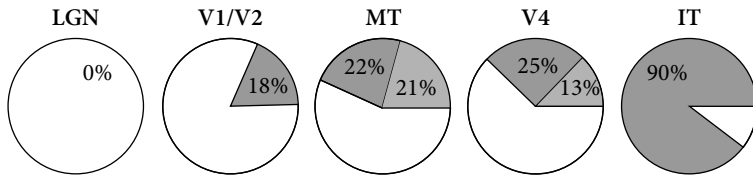


Figure 2. Correlation of neuronal firing with the monkey's perceptual report in different visual areas. The dark grey sectors indicate the percentage of neurons whose firing rate is positively correlated with the monkey's perceptual report of whether the neuron's preferred stimulus is dominant or suppressed during rivalry. The light grey sectors indicate the percentage of neurons whose firing is anti-correlated with the perceptual report (i.e., lower firing rate when the cell's preferred stimulus is present). The firing of the remaining cells is not correlated with the monkey's percept. For recordings from LGN (Lehky et al., 1996), V1/V2 and V4 (Leopold & Logothetis, 1996), monkeys were stimulated with orthogonal drifting gratings. For MT recordings, monkeys were shown two horizontal gratings drifting in opposite directions (Logothetis & Schall, 1989) while for IT recordings more complex visual object stimuli (see Figure 1b) were used (Sheinberg & Logothetis, 1997).

Keliris, Logothetis and Tolias (2010), in contrast with the earlier study by Leopold and Logothetis (1996), reported that equal numbers of monocular and binocular cells exhibited such perceptual modulations. Notably, Keliris and colleagues (2010) employed a flash suppression stimulus paradigm similar to our study on cat V1 (Sengpiel et al., 1995a). In addition to single-cell responses, they also found that at a similar percentage of sites, the power of the local field potential (LFP) showed moderate perceptual modulations during viewing of rival stimuli.

Second, several human fMRI studies have revealed clear blood oxygen level dependent (BOLD) signal modulation in V1 and even the LGN during binocular rivalry. The first one, by Polonsky, Blake, Braun and Heeger (2000), employed a low-contrast vertical red grating presented to one eye and a high-contrast horizontal green grating presented to the other eye; the signature of rivalry was the attenuation of the BOLD signal when the subject perceived the low-contrast vertical grating and increase in BOLD signal when the high-contrast horizontal grating was dominant. The modulations in V1 activity during rivalry amounted to 55% of those evoked by physically alternating the two monocular images without rivalry. Interestingly, the rivalry-related modulations in V1 activity were similar to those observed in the higher visual areas V2, V3, and V4v (Polonsky et al., 2000). Even more astonishing is the report by Wunderlich, Schneider and Kastner (2005) who, using the same stimulus paradigm of high- and low-contrast gratings as Polonsky et al. (2000), found that in 3 out of 5 subjects rivalry-related response modulation in the LGN was of the same magnitude as for physical stimulus alternations.

There are a number of possible explanations for the disagreement between the monkey electrophysiological data and human fMRI studies regarding the role of early visual areas in binocular rivalry. There may be a species difference regarding where perceptual ambiguities are resolved or a difference in the origin of the recorded signal. A recent electrophysiological study of spiking activity and LFPs in monkey V1 and V2 has shed light on this issue (Wilke, Logothetis, & Leopold, 2006). It has been demonstrated that (in monkeys) LFPs correlate more closely with BOLD signal measured in fMRI than do single- and multi-unit spiking responses (Logothetis, Pauls, Augath, Trinath, & Oeltermann, 2001). Wilke et al. (2006) found that low-frequency (9–30 Hz) LFP power is more closely related to the representation of stimulus visibility than spiking or gamma frequency (30–50 Hz) LFP activity in V1 and V2, while in V4 both spiking and gamma frequency LFPs exhibited perception-related modulation. The discrepancies between single-unit activity and LFPs during rivalry led Keliris et al. (2010) to conclude that

the possibility remains that perception may be strongly reflected in more elaborate aspects of activity in V1 circuits (e.g., specific neuronal subtypes) or perceptual states might have a modulatory role on more intricate aspects of V1 firing patterns (e.g., synchronization), not necessarily altering the firing rates of single cells or the LFP power dramatically. (p. 12353)

A third possible explanation for the discrepancies between the single-cell and fMRI data is an influence of attention or post-decision feedback on responses in early visual areas. Because this may well be sub-threshold in terms of action potentials, it will likely be more evident in LFP and BOLD signals. The role of attention has been discussed controversially since the earliest studies of binocular rivalry, with Wheatstone (1838) stating that “it does not appear to be in the power of the will to determine the appearance of either of [two rivalling] letters”, and Helmholtz (1910) claiming that he could retain one or the other image of a rival pair at will. The general consensus now is that “voluntary control over binocular rivalry is possible, yet limited” (Paffen & Alais, 2011). There is also agreement that both endogenous (voluntary) and exogenous (involuntary) attention can modulate binocular rivalry. However, while until very recently it has been thought that withdrawing attention slows down but does not stop perceptual alternation in binocular rivalry (Paffen & Alais, 2011), evidence has now been presented that diverting attention may halt rivalry altogether (Zhang, Jamison, Engel, He, & He, 2011). In modeling terms, attention is likely to enhance the effective contrast of the competing images in a top-down manner, while adaptation of neuronal responses in early visual cortex reduces the effective contrast of the dominant stimulus in a bottom-up fashion (Paffen & Alais, 2011; see below).

Effects of binocular rivalry on neuronal firing patterns

The majority of single-unit studies implicitly assume that the information conveyed by a neuron's spiking activity is primarily or exclusively captured by changes in firing rate over time, depending on stimuli presented (Barlow, 1972). A question that has long puzzled visual neuroscientists and that has been debated controversially is how the firing of thousands of neurons in response to a multitude of features and elements in a visual scene enables us to segment that scene and to recognize individual objects. Temporal binding of the firing of neurons responding to the same object has been proposed as a solution to this problem (von der Malsburg, 1981, 1995), specifically by means of precise synchronization of firing (Singer, 1993, 1999), although others have objected to this hypothesis both on conceptual grounds and with regard to experimental evidence (Shadlen & Movshon, 1999). To give an example, if a single long contour (the edge of an object) simultaneously sweeps across the overlapping receptive fields of two V1 neurons with similar orientation preference, then their action potentials will be synchronized but if two contours separately sweep across the two receptive fields the firing will not be synchronized (Engel, König, & Singer, 1991). It has even been proposed that phenomenal awareness and consciousness are characterized by the dynamic binding of feature-specific cells into functionally coherent cell assemblies (Singer, 2001). As binocular rivalry reflects changing perceptual states in the face of unchanging external stimuli, one might expect to find a signature of dominance and suppression of one or the other stimulus representation in the extent to which populations of neurons synchronize their activity. In order to address this question, Fries, Roelfsema, Engel, König and Singer (1997) studied the responses in V1 of awake strabismic cats to rival stimuli; in these animals the alternating perceptual dominance of one or the other of two drifting grating stimuli could be objectively determined by monitoring the animal's optokinetic nystagmus. Indeed, neurons responding to the perceptually dominant grating displayed increased synchronization of firing in the gamma-frequency range, while those responding to the suppressed grating exhibited reduced synchronization compared with the response to monocularly presented gratings (Fries et al., 1997). In a follow-up study, Fries, Schroder, Roelfsema, Singer and Engel (2002) employed the flash suppression paradigm of staggered stimulus presentation to the two eyes, as well as stimulus pairs of highly different contrasts which biases rivalry in favor of the higher-contrast stimulus, and found similar effects on gamma-frequency synchronization depending on whether the stimulus that the recorded neurons responded to was perceptually dominant or suppressed. Therefore, synchronization of neuronal activity may be a necessary condition for the generation of perceptual states and awareness of sensory stimuli (Engel, Fries, König, Brecht, & Singer, 1999).

Interestingly, increased synchronization in correlation with conscious perception has been reported not only among pairs of neurons or recording sites within a single cortical area in animal studies, but also between numerous areas of the human visual cortex, both within one cortical hemisphere and across hemispheres, as revealed by magnetoencephalography (Srinivasan, Russell, Edelman, & Tononi, 1999).

Correlation with percept vs. correlation with switch mechanism

So far we have exclusively considered the question of which neurons' firing might be considered a neural correlate of a subject's perceptual state during binocular rivalry, and not the question of which cells are responsible for the switching between the two rival percepts, an apparently stochastic process (Fox & Herrmann, 1967). In fact, these need not necessarily be two separate populations of neurons; if as the evidence reviewed above suggests, rivalry is a "bottom-up" process that involves at least to some extent neurons at the earliest stages of binocular convergence, it is quite possible or even likely that no external gating is required at that stage. Instead, models of the switching assume the operation of an autonomous oscillator involving reciprocal inhibition between populations of monocular neurons, resulting in alternating blockage of signals from the two eyes (Lehky & Blake, 1991; Matsuoka, 1984; Mueller, 1990). In electronics terms, the binocular integration circuit may be implemented as an astable multivibrator (Lehky, 1988). Alternatively, congruent and conflicting stimuli may have different effects on the relative timing of action potentials in V1. In the model proposed by Lumer (1998), congruent stimulation of both eyes results in synchronization of discharges among binocular neurons in V1, while conflicting stimulation causes asynchronous firing. This asynchrony then produces rival response suppression later on in the visual pathway. Neither of these models has been tested directly in single-unit recordings, although increased gamma-band synchrony has been reported to precede switching of perceptual states in human binocular rivalry (Doesburg, Kitajo, & Ward, 2005). It is also worth noting that single-pulse transcranial magnetic stimulation (TMS) applied to the occipital (i.e., early visual) cortex increases the likelihood of a change in perceptual state (Pearson, Tadin, & Blake, 2007).

If, on the other hand, rivalry involves competition between two mutually exclusive interpretations of a visual scene that may each be represented by the firing of neurons in different cortical areas, an external switching mechanism is likely to be involved, such as one driven by attention or other top-down feedback mechanisms (see above). Visual attention involves both the thalamus as a 'gateway to the cortex' (McAlonan, Cavanaugh, & Wurtz, 2008) as well as early visual cortical areas (e.g.,

Silver, Ress, & Heeger, 2007), and in particular parietal cortex (for a review see e.g., Bisley & Goldberg, 2010). There is now plenty of evidence in humans showing that parietal cortex plays an important part in binocular rivalry. Lumer and colleagues were the first to demonstrate that activity in the frontoparietal cortex is specifically associated with perceptual transitions during rivalry (Lumer, Friston, & Rees, 1998). More recently, repetitive TMS of the right superior parietal cortex was shown to shorten the periods of stimulus dominance, indicating that normal function of right parietal cortex stabilizes the current perceptual state during rivalry (Carmel, Walsh, Lavie, & Rees, 2010). In contrast, Zaretskaya and colleagues found that repetitive TMS over the right intraparietal sulcus prolonged the periods of stable percepts (Zaretskaya, Thielscher, Logothetis, & Bartels, 2010).

A very different view of how switches between perceptual states are mediated is offered by Miller and colleagues (Miller et al., 2000). They proposed that one of the two rival percepts is represented by one cortical hemisphere, and vice versa for the other, and that the switching of perceptual states is mediated by switching between the hemispheres, perhaps controlled by a subcortical oscillator located in the brainstem. They found that right-ear caloric vestibular stimulation (which activates left temporo-parietal cortex and other left-sided structures such as insular and anterior cingulate cortex) shifted the relative dominance of two rivaling grating stimuli (Miller et al., 2000). In addition, they found that a single TMS pulse applied to the left temporo-parietal cortex will disrupt dominance of the stimulus adopted by that hemisphere.

Taken together, the studies reviewed above provide some good clues on where to look for neurons whose firing might correlate with and even cause perceptual alternations during rivalry, but up to now no single-cell recordings have been made in the target areas in humans.

Conclusions

Single-cell recording studies carried out in the last 20 years or so have gone a long way to backing up a neuron doctrine of binocular rivalry. It is now widely accepted that there is no single mechanism underlying binocular rivalry and no single site in the brain where perceptual ambiguities are resolved (Andrews, Sengpiel, & Blakemore, 2005; Blake & Logothetis, 2002). Instead, it seems that for simple stimuli such as gratings, early visual areas such as LGN, V1 and V2 play an important role while for more complex objects, for example faces vs. houses, activity reflecting the subject's perceptual state is more likely to be found in higher visual areas, primarily in the temporal lobe. However, one caveat regarding this view is that it is difficult to determine if neural correlates of rivalry appear at a given cortical level

because those stimuli are optimized for the brain region under study (e.g., gratings in V1/V2 and objects in IT), or if rivalry truly emerges in a single, higher cortical area like IT, with the effects fed back to bias the responses of earlier areas.

In terms of Barlow's neuron doctrine, neurophysiological studies have shown that the firing of certain individual neurons and of populations of neurons is correlated with the percept rather than the physical stimulus, but a causal relationship between neuronal activity and perceptual state has not been demonstrated yet. For instance, no quantitative comparison has been made between neurometric and psychometric functions as for MT neurons and the discrimination of direction of motion (Newsome et al., 1989), or a trial-by-trial analysis of neuronal firing rate vs. the likelihood of the monkey to choose the recorded neuron's preferred stimulus, as Barlow's fifth dogma would suggest and as demonstrated for MT by Britten et al. (1996). Even more compelling proof of a causal relationship would be evidence that microstimulation of a cluster of neurons responding to one of a rival pair of stimuli can influence the probability with which the monkey reports this stimulus as being dominant, as has been shown for MT (Salzman et al., 1990). Finally, another intriguing open question relates to the third dogma of Barlow's neuron doctrine: is our processing of rival stimuli and the corresponding neuronal responses subject to an experience-dependent process of maturation, or is it determined by genetic factors (Miller et al., 2010)? Electrophysiological investigations of binocular rivalry have taught us a lot about the neural basis of perception, visual awareness and consciousness, but more remains to be done.

References

- Abeles, M., & Goldstein, M. H., Jr. (1977). Multispike train analysis. *Proceedings of the IEEE*, 65(5), 762–773.
- Adrian, E. D. (1928). *The basis of sensation*. London: Christophers.
- Andrews, T. J., Sengpiel, F., & Blakemore, C. (2005). From contour to object-face rivalry: Multiple neural mechanisms resolve perceptual ambiguity. In D. Alais & R. Blake (Eds.), *Binocular rivalry* (pp. 187–211). Cambridge, MA: MIT Press.
- Barlow, H. B. (1972). Single units and sensation: A neuron doctrine for perceptual psychology? *Perception*, 1(4), 371–394.
- Barlow, H. B., Blakemore, C., & Pettigrew, J. D. (1967). The neural mechanism of binocular depth discrimination. *Journal of Physiology*, 193(2), 327–342.
- Bisley, J. W., & Goldberg, M. E. (2010). Attention, intention, and priority in the parietal lobe. *Annual Review of Neuroscience*, 33, 1–21.
- Blake, R. (1989). A neural theory of binocular rivalry. *Psychological Review*, 96(1), 145–167.
- Blake, R., & Lema, S. A. (1978). Inhibitory effect of binocular rivalry suppression is independent of orientation. *Vision Research*, 18(5), 541–544.
- Blake, R., & Logothetis, N. K. (2002). Visual competition. *Nature Reviews Neuroscience*, 3(1), 13–21.

- Blake, R., O'Shea, R. P., & Mueller, T. J. (1992). Spatial zones of binocular rivalry in central and peripheral vision. *Visual Neuroscience*, 8(5), 469–478.
- Blakemore, C. (1970). A new kind of stereoscopic vision. *Vision Research*, 10(11), 1181–1199.
- Blakemore, C., Iversen, S. D., & Zangwill, O. L. (1972). Brain functions. *Annual Review of Psychology*, 23, 413–456.
- Braddick, O. J. (1979). Binocular single vision and perceptual processing. *Proceedings of the Royal Society of London B: Biological Sciences*, 204(1157), 503–512.
- Britten, K. H., Newsome, W. T., Shadlen, M. N., Celebrini, S., & Movshon, J. A. (1996). A relationship between behavioral choice and the visual responses of neurons in macaque MT. *Visual Neuroscience*, 13(1), 87–100.
- Britten, K. H., Shadlen, M. N., Newsome, W. T., & Movshon, J. A. (1992). The analysis of visual motion: A comparison of neuronal and psychophysical performance. *Journal of Neuroscience*, 12(12), 4745–4765.
- Carmel, D., Walsh, V., Lavie, N., & Rees, G. (2010). Right parietal TMS shortens dominance durations in binocular rivalry. *Current Biology*, 20(18), R799–R800.
- de Lafuente, V., & Romo, R. (2006). Neural correlate of subjective sensory experience gradually builds up across cortical areas. *Proceedings of the National Academy of Sciences USA*, 103(39), 14266–14271.
- Doesburg, S. M., Kitajo, K., & Ward, L. M. (2005). Increased gamma-band synchrony precedes switching of conscious perceptual objects in binocular rivalry. *Neuroreport*, 16(11), 1139–1142.
- Drake, K. L., Wise, K. D., Farraye, J., Anderson, D. J., & BeMent, S. L. (1988). Performance of planar multisite microprobes in recording extracellular single-unit intracortical activity. *IEEE Transactions on Biomedical Engineering*, 35(9), 719–732.
- Engel, A. K., König, P., & Singer, W. (1991). Direct physiological evidence for scene segmentation by temporal coding. *Proceedings of the National Academy of Sciences USA*, 88(20), 9136–9140.
- Engel, A. K., Fries, P., König, P., Brecht, M., & Singer, W. (1999). Temporal binding, binocular rivalry, and consciousness. *Consciousness and Cognition*, 8(2), 128–151.
- Fox, R., & Check, R. (1966). Forced-choice form recognition during binocular rivalry. *Psychonomic Science*, 6(10), 471–472.
- Fox, R., & Check, R. (1968). Detection of motion during binocular rivalry suppression. *Journal of Experimental Psychology*, 78(3), 388–395.
- Fox, R., & Herrmann, J. (1967). Stochastic properties of binocular rivalry alternations. *Perception & Psychophysics*, 2(9), 432–436.
- Fries, P., Roelfsema, P. R., Engel, A. K., König, P., & Singer, W. (1997). Synchronization of oscillatory responses in visual cortex correlates with perception in interocular rivalry. *Proceedings of the National Academy of Sciences USA*, 94(23), 12699–12704.
- Fries, P., Schröder, J. H., Roelfsema, P. R., Singer, W., & Engel, A. K. (2002). Oscillatory neuronal synchronization in primary visual cortex as a correlate of stimulus selection. *Journal of Neuroscience*, 22(9), 3739–3754.
- Gerstein, G. L., & Clark, W. A. (1964). Simultaneous studies of firing patterns in several neurons. *Science*, 143(3612), 1325–1327.
- Gold, C., Henze, D. A., Koch, C., & Buzsáki, G. (2006). On the origin of the extracellular action potential waveform: A modeling study. *Journal of Neurophysiology*, 95(5), 3113–3128.
- Granit, R., & Svaetichin, G. (1939). Principles and technique of the electrophysiological analysis of colour reception with the aid of microelectrodes. *Upsala LäkareföreningsFörhandlingar*, 45(1–4), 161–177.

- Gray, C. M., Maldonado, P. E., Wilson, M., & McNaughton, B. (1995). Tetrodes markedly improve the reliability and yield of multiple single-unit isolation from multi-unit recordings in cat striate cortex. *Journal of Neuroscience Methods*, 63(1–2), 43–54.
- Gross, C. G. (2002). Genealogy of the “grandmother cell”. *Neuroscientist*, 8(12), 512–518.
- Gross, C. G., Rocha-Miranda, C. E., & Bender, D. B. (1972). Visual properties of neurons in inferotemporal cortex of the macaque. *Journal of Neurophysiology*, 35(1), 96–111.
- Grunewald, A., Bradley, D. C., & Andersen, R. A. (2002). Neural correlates of structure-from-motion perception in macaque V1 and MT. *Journal of Neuroscience*, 22(14), 6195–6207.
- Harris, K. D., Henze, D. A., Csicsvari, J., Hirase, H., & Buzsáki, G. (2000). Accuracy of tetrode spike separation as determined by simultaneous intracellular and extracellular measurements. *Journal of Neurophysiology*, 84(1), 401–414.
- Helmholtz, H. (1910). *Handbuch der physiologischen Optik* (3rd ed.; A. Gullstrand, J. von Kries, & W. Nagel, Eds.). Hamburg: Verlag von Leopold Voss.
- Hubel, D. H., & Wiesel, T. N. (1968). Receptive fields and functional architecture of monkey striate cortex. *Journal of Physiology*, 195(1), 215–243.
- Hubel, D. H., & Wiesel, T. N. (1962). Receptive fields, binocular interaction and functional architecture in the cat’s visual cortex. *Journal of Physiology*, 160(1), 106–154.
- Hubel, D. H. (1957). Tungsten microelectrode for recording from single units. *Science*, 125(3247), 549–550.
- Keliris, G. A., Logothetis, N. K., & Tolias, A. S. (2010). The role of the primary visual cortex in perceptual suppression of salient visual stimuli. *Journal of Neuroscience*, 30(37), 12353–12365.
- Lehky, S., & Maunsell, J. H. R. (1996). No binocular rivalry in the LGN of alert macaque monkeys. *Vision Research*, 36(9), 1225–1234.
- Lehky, S. R. (1988). An astable multivibrator model of binocular rivalry. *Perception*, 17(2), 215–228.
- Lehky, S. R., & Blake, R. (1991). Organization of binocular pathways: Modeling and data related to rivalry. *Neural Computation*, 3(1), 44–53.
- Leopold, D. A., & Logothetis, N. K. (1996). Activity changes in early visual cortex reflects monkeys’ percepts during binocular rivalry. *Nature*, 379(6565), 549–553.
- Letelier, J. C., & Weber, P. P. (2000). Spike sorting based on discrete wavelet transform coefficients. *Journal of Neuroscience Methods*, 101(2), 93–106.
- Lettvin, J. Y., Maturana, H. R., McCulloch, W. S., & Pitts, W. H. (1959). What the frog’s eye tells the frog’s brain. *Proceedings of the IRE*, 47(11), 1940–1951.
- Lewicki, M. S. (1994). Bayesian modeling and classification of neural signals. *Neural Computation*, 6(5), 1005–1030.
- Logothetis, N. K., & Schall, J. D. (1989). Neuronal correlates of subjective visual perception. *Science*, 245(4919), 761–763.
- Logothetis, N. K., Pauls, J., Augath, M., Trinath, T., & Oeltermann, A. (2001). Neurophysiological investigation of the basis of the fMRI signal. *Nature*, 412(6843), 150–157.
- Lumer, E. D. (1998). A neural model of binocular integration and rivalry based on the coordination of action-potential timing in primary visual cortex. *Cerebral Cortex*, 8(6), 553–561.
- Lumer, E. D., Friston, K. J., & Rees, G. (1998). Neural correlates of perceptual rivalry in the human brain. *Science*, 280(5371), 1930–1934.
- Matsuoka, K. (1984). The dynamic model of binocular rivalry. *Biological Cybernetics*, 49(3), 201–208.
- McAlonan, K., Cavanaugh, J., & Wurtz, R. H. (2008). Guarding the gateway to cortex with attention in visual thalamus. *Nature*, 456(7220), 391–394.
- Merrill, E. G. & Ainsworth, A. (1972). Glass-coated platinum-plated tungsten micro-electrodes. *Medical & Biological Engineering & Computing*, 10(5), 662–672.

- Miller, S. M., Liu, G. B., Ngo, T. T., Hooper, G., Riek, S., Carson, R. G. et al. (2000). Interhemispheric switching mediates perceptual rivalry. *Current Biology*, 10(7), 383–392.
- Miller, S. M., Hansell, N. K., Ngo, T. T., Liu, G. B., Pettigrew, J. D., Martin, N. G. et al. (2010). Genetic contribution to individual variation in binocular rivalry rate. *Proceedings of the National Academy of Sciences USA*, 107(6), 2664–2668.
- Mueller, T. J. (1990). A physiological model of binocular rivalry. *Visual Neuroscience*, 4(1), 63–73.
- Newsome, W. T., Britten, K. H., & Movshon, J. A. (1989). Neuronal correlates of a perceptual decision. *Nature*, 341(6237), 52–54.
- Nordhausen, C. T., Rousche, P. J., & Normann, R. A. (1994). Optimizing recording capabilities of the Utah Intracortical Electrode Array. *Brain Research*, 637(1–2), 27–36.
- Ohzawa, I., & Freeman, R. D. (1986a). The binocular organization of simple cells in the cat's visual cortex. *Journal of Neurophysiology*, 56(1), 221–242.
- Ohzawa, I., & Freeman, R. D. (1986b). The binocular organization of complex cells in the cat's visual cortex. *Journal of Neurophysiology*, 56(1), 243–259.
- Olshausen, B. A., & Field, D. J. (2004). Sparse coding of sensory inputs. *Current Opinion in Neurobiology*, 14(4), 481–487.
- Paffen, C. L., & Alais, D. (2011). Attentional modulation of binocular rivalry. *Frontiers in Human Neuroscience*, 5, 105.
- Parker, A. J., & Newsome, W. T. (1998). Sense and the single neuron: Probing the physiology of perception. *Annual Review of Neuroscience*, 21, 227–277.
- Parker, A. J., Krug, K., & Cumming, B. G. (2002). Neuronal activity and its links with the perception of multi-stable figures. *Philosophical Transactions of the Royal Society of London B: Biological Sciences*, 357(1424), 1053–1062.
- Pearson, J., Tadin, D., & Blake, R. (2007). The effects of transcranial magnetic stimulation on visual rivalry. *Journal of Vision*, 7(7), 2, 1–11. doi: 10.1167/7.7.2
- Perrett, D. I., Rolls, E. T., & Caan, W. (1982). Visual neurones responsive to faces in the monkey temporal cortex. *Experimental Brain Research*, 47(3), 329–342.
- Polonsky, A., Blake, R., Braun, J., & Heeger, D. J. (2000). Neuronal activity in human primary visual cortex correlates with perception during binocular rivalry. *Nature Neuroscience*, 3(11), 1153–1159.
- Quiroga, R. Q., Nadasdy, Z., & Ben-Shaul, Y. (2004). Unsupervised spike detection and sorting with wavelets and superparamagnetic clustering. *Neural Computation*, 16(8), 1661–1687.
- Quiroga, R. Q., Reddy, L., Kreiman, G., Koch, C., & Fried, I. (2005). Invariant visual representation by single neurons in the human brain. *Nature*, 435(7045), 1102–1107.
- Salzman, C. D., Britten, K. H., & Newsome, W. T. (1990). Cortical microstimulation influences perceptual judgements of motion direction. *Nature*, 346(6280), 174–177.
- Sanderson, K. J., Darian-Smith, I., & Bishop, P. O. (1969). Binocular corresponding receptive fields of single units in the cat dorsal lateral geniculate nucleus. *Vision Research*, 9(10), 1297–1303.
- Sengpiel, F., Baddeley, R. J., Freeman, T. C. B., Harrad, R., & Blakemore, C. (1998). Different mechanisms underlie three inhibitory phenomena in cat area 17. *Vision Research*, 38(14), 2067–2080.
- Sengpiel, F., & Blakemore, C. (1994). Interocular control of neuronal responsiveness in cat visual cortex. *Nature*, 368(6474), 847–850.
- Sengpiel, F., Blakemore, C., & Harrad, R. (1995a). Interocular suppression in the primary visual cortex: A possible neural basis of binocular rivalry. *Vision Research*, 35(2), 179–195.
- Sengpiel, F., Bonhoeffer, T., Freeman, T. C. B., & Blakemore, C. (2001). On the relationship between interocular suppression in the primary visual cortex and binocular rivalry. *Brain and Mind*, 2(1), 39–54.

- Sengpiel, F., Freeman, T. C. B., & Blakemore, C. (1995b). Interocular suppression in cat striate cortex is not orientation selective. *Neuroreport*, 6(16), 2235–2239.
- Shadlen, M. N., Britten, K. H., Newsome, W. T., & Movshon, J. A. (1996). A computational analysis of the relationship between neuronal and behavioural responses to visual motion. *Journal of Neuroscience*, 16(4), 1486–1510.
- Shadlen, M. N., & Movshon, J. A. (1999). Synchrony unbound: A critical evaluation of the temporal binding hypothesis. *Neuron*, 24(1), 67–77.
- Sheinberg, D. L., & Logothetis, N. K. (1997). The role of temporal cortical areas in perceptual organization. *Proceedings of the National Academy of Sciences USA*, 94(7), 3408–3413.
- Sherrington, C. S. (1941). *Man on his nature*. New York: Macmillan.
- Silver, M. A., Ress, D., & Heeger, D. J. (2007). Neural correlates of sustained spatial attention in human early visual cortex. *Journal of Neurophysiology*, 97(1), 229–237.
- Singer, W. (1993). Synchronization of cortical activity and its putative role in information processing and learning. *Annual Reviews in Physiology*, 55, 349–374.
- Singer, W. (1999). Neuronal synchrony: A versatile code for the definition of relations? *Neuron*, 24(1), 49–65.
- Singer, W. (2001). Consciousness and the binding problem. *Annals of the New York Academy of Sciences*, 929, 123–146.
- Srinivasan, R., Russell, D. P., Edelman, G. M., & Tononi, G. (1999). Increased synchronization of neuromagnetic responses during conscious perception. *Journal of Neuroscience*, 19(1), 5435–5448.
- Steriade, M. (2005). Sleep, epilepsy and thalamic reticular inhibitory neurons. *Trends in Neurosciences*, 28(6), 317–324.
- Varela, F. J., & Singer, W. (1987). Neuronal dynamics in the visual corticothalamic pathway revealed through binocular rivalry. *Experimental Brain Research*, 66(1), 10–20.
- von der Malsburg, C. (1981). The correlation theory of brain function. Internal report No. 81-2.
- von der Malsburg, C. (1995). Binding in models of perception and brain function. *Current Opinion in Neurobiology*, 5(4), 520–526.
- Wales, R., & Fox, R. (1970). Increment detection thresholds during binocular rivalry suppression. *Perception & Psychophysics*, 8(2), 90–94.
- Wheatstone, C. (1838). Contributions to the physiology of vision. – Part the first. On some remarkable, and hitherto unobserved, phenomena of binocular vision. *Philosophical Transactions of the Royal Society of London*, 128, 371–394.
- Wilke, M., Logothetis, N. K., & Leopold, D. A. (2006). Local field potential reflects perceptual suppression in monkey visual cortex. *Proceedings of the National Academy of Sciences USA*, 103(46), 17507–17512.
- Wilson, M. A., & McNaughton, B. L. (1993). Dynamics of the hippocampal ensemble code for space. *Science*, 261(5124), 1055–1058.
- Wolfe, J. M. (1984). Reversing ocular dominance and suppression in a single flash. *Vision Research*, 24(5), 471–478.
- Wunderlich, K., Schneider, K. A., & Kastner, S. (2005). Neural correlates of binocular rivalry in the human lateral geniculate nucleus. *Nature Neuroscience*, 8(11), 1595–1602.
- Zaretskaya, N., Thielscher, A., Logothetis, N. K., & Bartels, A. (2010). Disrupting parietal function prolongs dominance durations in binocular rivalry. *Current Biology*, 20(23), 2106–2111.
- Zhang, P., Jamison, K., Engel, S., He, B., & He, S. (2011). Binocular rivalry requires visual attention. *Neuron*, 71(2), 362–369.

Functional neuroimaging of binocular rivalry

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Binocular rivalry has intrigued researchers for over two centuries, but research into its neural mechanisms was until recently limited to behavioral and animal studies. The availability of functional magnetic resonance imaging since the 1990s has boosted the neuroscientific investigation of binocular rivalry in humans. Functional neuroimaging has revealed an involvement of all levels of the brain's visual processing hierarchy in rivalry dynamics, including early subcortical and cortical stages, functionally specialized visual areas, and non-sensory frontoparietal regions. Moreover, variants of binocular rivalry have helped to elucidate the neural fate of unconscious information during binocular rivalry suppression. The findings from neuroimaging research are integrated into a comprehensive view on how different processing stages interact to resolve perceptual conflict in the human brain.

Introduction

Binocular rivalry occurs when two conflicting images are presented to each of the two eyes: rather than merging into a mixture, the two images tend to rival for exclusive dominance. Perception typically alternates between the two images every few seconds. The first scientific description of this intriguing phenomenon is ascribed to Étienne-François Du Tour (Du Tour, 1760; see chapter by Wade & Ngo, this volume). He reported that, when presenting a disk of blue fabric to one eye and a disk of yellow fabric to the other eye, he did not see a mixture of blue and yellow colors, i.e., green. Instead, he experienced his perception to alternate between blue and yellow every few seconds in an unpredictable fashion. Such spontaneous perceptual alternations are a characteristic feature of binocular rivalry. It is therefore considered a form of multistable perception, which refers

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to a larger group of perceptual phenomena that are characterized by alternations between two or more perceptual states while the sensory input remains constant. Other well-known examples of multistable perception include the Necker cube, Rubin's face-vase illusion, and bistable apparent motion (for a recent review, see Sterzer, Kleinschmidt, & Rees, 2009b).

Binocular rivalry has fascinated many scientists over the last two centuries (see chapter by Wade & Ngo, this volume), but research into the underlying neural mechanisms has only recently become popular among visual and cognitive neuroscientists. The increasing interest in binocular rivalry can at least in part be attributed to the advent and widespread availability of functional magnetic resonance imaging (fMRI) in the 1990s, which has greatly extended the possibilities of studying the neural underpinnings of binocular rivalry in humans. Among the studies that have used modern neuroimaging techniques to investigate binocular rivalry, three major topics can be identified. First, binocular rivalry has become a standard tool for the study of the neural correlates of the contents of conscious perception. As perception fluctuates between two possible states while the actual sensory input remains the same, binocular rivalry – like other forms of multistable perception – provides an elegant way of dissociating the neural correlates of conscious perception from those associated with changes in visual stimulation. Second, binocular rivalry and recently developed variants of it have been used to study neural responses to stimuli that remain unconscious. Whenever one of the two rivaling images dominates conscious perception, the other respective image is suppressed from conscious awareness for several seconds, which offers the unique opportunity to study unconscious visual processing over prolonged periods of time. Third, binocular rivalry is an impressive example of the constructive nature of perception. As perception changes spontaneously every few seconds, binocular rivalry is an interesting tool to study the neural mechanisms that govern perceptual decisions in situations of ambiguous or conflicting sensory input. This chapter is structured to reflect these three major topics in neuroimaging research into binocular rivalry. A variety of methodologies have been used to study the neural correlates of bistable perception in humans, including functional magnetic resonance imaging, electroencephalography (EEG) and magnetoencephalography (MEG). As most studies discussed in this chapter used fMRI, this method and its limitations are briefly discussed in the following section (for a comprehensive review of neuroimaging methods, see chapter by Thomson & Fitzgerald, this volume).

fMRI as a tool to study binocular rivalry

Over the past two decades, fMRI has become a popular tool to study the neural correlates of binocular rivalry. fMRI is based on the measurement of a blood-oxygen level dependent (BOLD) signal, which is a component of the hemodynamic response that is associated with local neural activity (Heeger & Ress, 2002). The BOLD signal is essentially linearly correlated with spiking activity, that is, the action potentials recorded from neurons in the vicinity of electrodes used for direct electrophysiological measurements; and there is even a stronger correlation with local field potentials (LFPs) (Logothetis, Pauls, Augath, Trinath, & Oeltermann, 2001). LFPs represent the aggregate activity of a population of neurons located close to the electrode and are thought to reflect mainly synaptic activity associated with both input to and output from a cortical area. The BOLD signal might therefore reflect pre- and post-synaptic activity and hence the processing in an area more closely than multi-unit activity. One drawback of fMRI is that it does not measure neural activity directly and that it has a limited temporal resolution (in the range of seconds) due to the sluggishness of the hemodynamic response. Despite great technical improvements over the last years, fMRI has also limited spatial resolution (in the range of millimeters) and can therefore only measure signals that are generated by relatively large populations of neurons. However, the spatial resolution is still considerably better than that of other non-invasive methods such as EEG and MEG. The greatest strength of fMRI is its capacity to record activity from the entire brain essentially simultaneously, including deep subcortical brain structures. In contrast to single- or multi-unit recordings, fMRI therefore in principle does not require prior assumptions as to where activity is expected to occur.

Binocular rivalry and the neural correlates of consciousness

One of the greatest challenges when investigating the neural correlates of conscious perception of a sensory stimulus is to disentangle the neural processes that are uniquely linked with the contents of consciousness from those neural responses that are evoked by the sensory stimulus independently of consciousness. In this respect, binocular rivalry and other forms of multistable perception are particularly interesting experimental paradigms, as the contents of conscious perception alternate between two or more unique states while sensory stimulation remains constant. This allows for a dissociation of the neural correlates of consciousness from purely stimulus-driven responses (see also chapter by Klink, van Wezel, & van Ee, this volume).

A notion that is already implied in the term binocular rivalry is that the neural activity patterns originating from the two eyes are likely to compete for perceptual dominance at some level along the neural processing hierarchy. A way to find out at which levels such competition takes place, is to determine the degree to which neural activity correlates with perception at different processing levels. First evidence for percept-related activity fluctuations during binocular rivalry in visual cortex came from EEG recordings. When the two monocular images are flashed at distinct frequencies in order to tag EEG signals associated with the perception of either image, the power at the tagging frequency in occipital cortex corresponds to reported perceptual awareness (Brown & Norcia, 1997; Lansing, 1964; Lawwill & Biersdorf, 1968). Subsequent work using MEG suggested that such percept-related modulation of tagged frequency power extends beyond occipital cortex into parietal, temporal and frontal areas. Moreover, intra- and inter-hemispheric synchronization at the flicker frequency of the dominant image is enhanced, suggesting an increase in coordinated neural activity across large parts of the cortex as a correlate of conscious perception (Cosmelli et al., 2004; Srinivasan, Russell, Edelman, & Tononi, 1999; Tononi, Srinivasan, Russell, & Edelman, 1998). The latter conclusion was, however, recently questioned by phase analyses of percept-related MEG signals, which revealed that the spatially extended nature of the frequency tag was produced by a limited set of occipital sources most likely located in early visual cortex (Kamphuisen, Bauer, & van Ee, 2008). While EEG and MEG studies using frequency tagging during binocular rivalry have thus consistently provided evidence for percept-related neural activity modulations in visual cortex, the notion of widespread synchronization of cortical networks as a correlate of conscious perception remains controversial.

In the 1990s, fMRI became available as a further non-invasive neuroimaging technique. Despite the sluggishness of the BOLD response measured with fMRI, it has sufficient temporal resolution to track percept-related neural activity fluctuations during binocular rivalry. The detailed characterization of functionally specialized extrastriate visual areas with fMRI, as well as spatiotopic analyses of neural signals in retinotopic visual cortex (Serenio et al., 1995) and even in subcortical regions such as the lateral geniculate nucleus (LGN; Chen et al., 1998; Chen, Zhu, Thulborn, & Ugurbil, 1999) now offered the possibility to measure stimulus-specific activity fluctuations during binocular rivalry throughout all central levels of the visual processing hierarchy (see chapter by Price, this volume). One of the first fMRI studies investigating the neural underpinnings of binocular rivalry exploited the functional specialization for object categories in ventral occipitotemporal visual areas and presented a face stimulus to one eye and a house to the other eye (Tong, Nakayama, Vaughan, & Kanwisher, 1998). fMRI signal in the fusiform face area (FFA; Kanwisher, McDermott, & Chun, 1997) and the parahippocampal

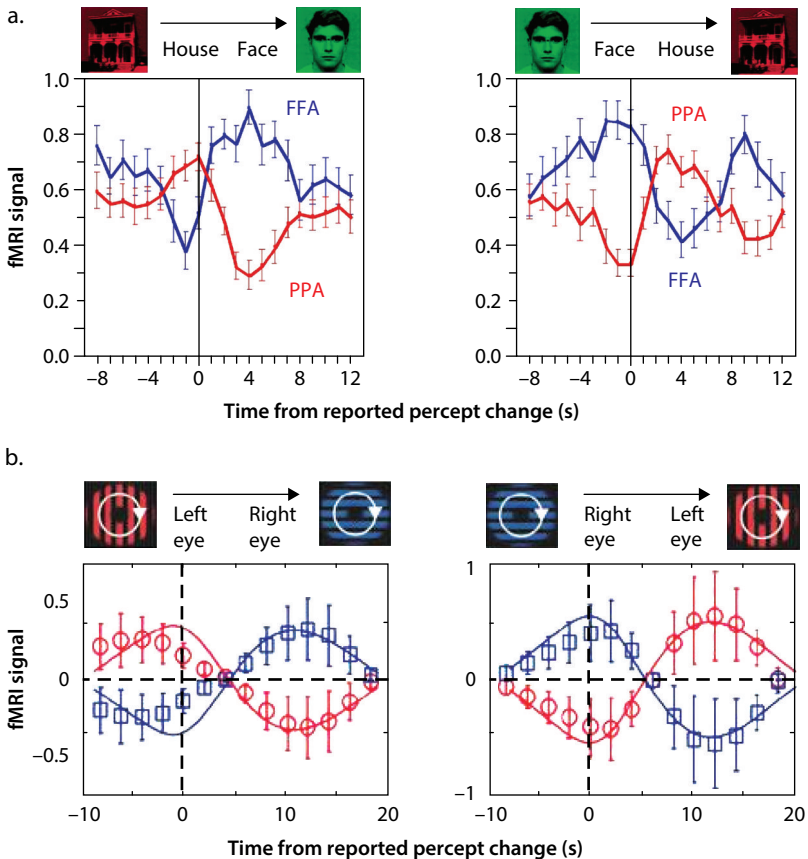


Figure 1. fMRI studies show percept-related signal fluctuations during binocular rivalry. (a) Depicted are averaged event-related fMRI signal timecourses from the FFA (blue line) and PPA (red line), time-locked to the reported percept changes during binocular rivalry between a face and a house stimulus. The fMRI signal in the FFA increases after changes towards face perception while PPA signal decreases (left panel). The reverse pattern is observed after changes towards house perception (right panel). Reproduced with permission from Tong et al. (1998). (b) The fMRI signal in the LGN fluctuates as a function of reported perceptual alternations during binocular rivalry of rotating orthogonal red and blue grating stimuli. LGN subregions that respond predominantly to signals originating from the right eye (blue line) show an increase in activity after changes towards the left-eye stimulus, while subregions reflecting signals from the left eye (red line) show a simultaneous decrease in activity (left panel). The reverse pattern is observed after the left eye-stimulus gains perceptual dominance (right panel). Reproduced with permission from Haynes et al. (2005). Note that the fMRI signal reflects a hemodynamic response that peaks with a delay of 4–6 seconds after the underlying neural activity changes.

place area (PPA; Epstein, Harris, Stanley, & Kanwisher, 1999), i.e., brain areas preferentially responding to face and house stimuli, respectively, closely reflected the observer's reported perception during binocular rivalry between face and house (see Figure 1a). Importantly, responses in these areas during binocular rivalry were as strong as those evoked by physical alternations between the face and the house. This was interpreted as an indication that rivalry is largely resolved at these advanced stages of visual processing. Analogously, in a more recent fMRI study perception of a face during binocular rivalry between a face and an abstract grating stimulus was also associated with enhanced activity in the FFA, and again the amplitudes of activity fluctuations during rivalry were similar to those during physical alternations of the stimuli (Sterzer & Rees, 2008).

Subsequent work also demonstrated strong effects of binocular rivalry on signals in primary visual cortex, V1 (Polonsky, Blake, Braun, & Heeger, 2000; Tong & Engel, 2001), with a close linkage between BOLD signals and the evolving spatiotemporal dynamics of rivalry perception (Lee, Blake, & Heeger, 2005). Moreover, fluctuating perception during binocular rivalry can be predicted for extended periods of time from BOLD signals in human V1 alone (Haynes & Rees, 2005) when information is accumulated across voxels using multi-voxel pattern analysis (Haynes & Rees, 2006; Norman, Polyn, Detre, & Haxby, 2006). Transcranial magnetic stimulation (TMS) over early visual cortex (V1) can induce perceptual alternations (Pearson, Tadin, & Blake, 2007), suggesting a causal role for fluctuations in V1 activity in influencing the outcome of rivalry. Similar to the fMRI findings in V1, even BOLD signals in the LGN correlate with the perception of observers during rivalry (see Figure 1b) (Haynes, Deichmann, & Rees, 2005; Wunderlich, Schneider, & Kastner, 2005). The finding of a tight association between perceptual fluctuations and neural activity at advanced levels of visual processing is in line with single-cell recordings in monkeys' inferotemporal cortex. In contrast, such electrophysiological measurements in V1 and LGN showed only weak if any correlation between perception and neural activity (see Leopold & Logothetis, 1999; and chapter by Sengpiel, this volume), thus contrasting with the above mentioned fMRI results in humans. Discrepancies between electrophysiological and fMRI studies may be related to the fact that neuronal spiking activity (as measured in earlier electrophysiological studies in monkeys) is less closely related to perceptual awareness than LFPs (Wilke, Logothetis, & Leopold, 2006). The latter in turn correlate more strongly with fMRI BOLD signals than spiking activity (Logothetis et al., 2001), thus underlining the usefulness of fMRI for studying neural correlates of perception. Moreover, context-dependent differences in the coupling between fMRI and electrophysiological signals in visual cortex may also explain apparent contradictions between studies. For instance, during conventional visual stimulus presentation, BOLD signals, LFPs and spiking activity are in good agreement.

During perceptual suppression, in contrast, only BOLD responses and low-frequency LFP power show decreases, whereas the spiking and high-frequency LFP power are unaffected (Maier et al., 2008). Finally, differences between species may also account for some of the discrepancies between electrophysiological studies in monkeys and fMRI in humans.

Neuroimaging has thus established that signals from the anatomically earliest visual processing stages up to the level of category-specific object processing correlate with conscious perception during binocular rivalry (see Tong, Meng, & Blake, 2006, for a review). These findings support the notion that neural activity even at the earliest central processing levels, while in itself not being sufficient for generating a conscious percept, is a prerequisite for visual information to reach consciousness (Lamme & Roelfsema, 2000; Pollen, 2003; Tong, 2003). Yet, a limitation for understanding the neural correlates of consciousness is that we still do not know exactly what is rivaling during binocular rivalry. On the basis of neuroimaging data, it cannot be decided whether the observed signal fluctuations at a given neural site reflect local competitive interactions between neuronal populations representing the two rivaling images, or whether they reflect the outcome of such competitive interactions at another level of processing. Conceivably, percept-related signal fluctuations in the FFA and PPA during face-house rivalry could reflect the outcome of competitive neuronal interactions between monocular processing channels in the LGN and V1 (*eye rivalry*), but they could also be due to rivalry between neuronal populations that encode the perceptual content (*pattern rivalry*). Conversely, the observation that fMRI signals at the level of the LGN concur with reported perception does not necessarily imply that rivalry between monocular processing channels is at the origin of perceptual alternations. Instead, an alternative explanation could be that top-down (eye-independent) modulation controls alternations between those lower-level afferent processes that are linked with a given percept. Current models of binocular rivalry propose a multi-level process involving competitive neural interactions at both monocular and binocular stages of the visual processing hierarchy (Tong et al., 2006; see also chapter by Wilson, this volume). To what extent the interactions at each level are involved in the resolution of binocular rivalry remains a challenging question for future research.

Neural processing of perceptually suppressed information during binocular rivalry

During binocular rivalry, one of the two rivaling images dominates conscious perception, while the other respective image is suppressed from awareness, which offers the opportunity to study neural signals associated with unconscious visual

processing. However, the assessment of awareness during binocular rivalry in its traditional form is complicated by the fact that it relies completely on subjective perceptual reports by the observer. Moreover, dominance of one image and suppression of the other image are not always complete (*piecemeal rivalry*) and transitions between perceptual states occur largely stochastically and thus unpredictably to both the observer and the experimenter. It is therefore difficult to reliably determine at which time an image is suppressed and whether it is fully suppressed from awareness. One variant of binocular rivalry that allows the experimenter to control perceptual dominance at least for brief periods of time is a technique called *flash suppression* (Wolfe, 1984): when one of the two rivaling images is presented first monocularly, followed by binocular presentation of the two images, the image presented first is invariably suppressed from awareness at the beginning of binocular presentation (see chapter by Brascamp & Baker, this volume). A further modification of this technique, *continuous flash suppression* (CFS), can be used to reliably suppress an image for several seconds or even minutes. For CFS, dynamic high-contrast Mondrian-like patterns are flashed to one eye, rendering low-contrast stimuli presented to the other eye invisible for extended periods of time (Tsuchiya & Koch, 2005). It should be mentioned that it is not yet clear whether CFS should be regarded as a variant of binocular rivalry that induces particularly strong suppression (Shimaoka & Kaneko, 2011), or whether CFS is supported by mechanisms distinct from binocular rivalry (Tsuchiya, Koch, Gilroy, & Blake, 2006). For the purpose of the present chapter, the terms CFS and binocular rivalry suppression are used interchangeably, following common practice (e.g., Lin & He, 2009).

The abovementioned observation that the amplitudes of percept-related fMRI signal fluctuations during binocular rivalry in high-level extrastriate visual areas are similar to those during actual stimulus alternations (see Figure 1a) (Tong et al., 1998) was initially interpreted as evidence for a resolution of rivalry at early levels, with no maintained representation of the suppressed stimulus at this advanced stage of processing. However, behaviorally the involvement of perceptual (rather than purely interocular) mechanisms is shown by persistence of rivalry when the monocular images are rapidly swapped between the eyes, preventing interocular competition (Logothetis, Leopold, & Sheinberg, 1996). Similarly, the ability of complementary patchworks of intermingled images presented to each eye to drive rivalry also speaks to an influence of perceptual mechanisms (Kovács, Papathomas, Yang, & Fehér, 1996). Moreover, binocular rivalry is affected by complex information contained in suppressed stimuli (e.g., Alais & Parker, 2006; Andrews & Blakemore, 1999; see also Blake & Logothetis, 2002; Tong et al., 2006, for reviews), indicating that information from binocularly suppressed stimuli is still processed at sufficiently advanced levels where this information can be extracted and represented (see also chapter by Bressler, Denison, & Silver, this volume).

Recent neuroimaging work has explicitly addressed the question of whether complex stimulus information is still represented at advanced stages of the visual processing hierarchy during binocular rivalry suppression. An important conceptual and methodological aspect of studies investigating such unconscious processing relates to the assessment of awareness, or in this case better *unawareness* of a stimulus (Pessoa, 2005; Snodgrass, 2004). According to *objective* criteria, an observer is unaware of a stimulus when performance in a 'forced-choice' task is at chance level. In contrast, *subjective* unawareness refers to the subjective report of an observer that a stimulus was not consciously perceived. Especially in the face of weak or noisy signals, observers might indicate to be unaware of target stimuli and thus appear to be unable to detect them, even though a trace of awareness was present but not reported, e.g., due to a conservative criterion for reporting awareness. Recent evidence even suggests that spatial attention induces conservative biases in subjective aspects of visual perception (Rahnev et al., 2011).

When discussing neuroimaging findings on unconscious information processing, it is therefore important to take into consideration whether objective or subjective measures were used for the assessment of unawareness. Objective measures may be too conservative when one seeks to identify neural correlates of *conscious* perception, because an observer may perform significantly above chance level in a forced-choice task but still not subjectively experience awareness of the target stimulus. For research questions that focus on *unconscious* neural processing, however, the use of forced-choice tasks that are optimally performed 'online' during the neuroimaging procedure should be regarded as the gold standard for a criterion- and bias-free assessment of unawareness (Pessoa, 2005).

Neuroimaging studies into the neural processing of complex visual information during binocular rivalry suppression have focused mainly on three questions: first, is visual information that is of special behavioral relevance and may therefore undergo preferential and automatic processing even in the absence of attention and even awareness, e.g., emotional information (for reviews see Pessoa, 2005; Vuilleumier, 2005), still processed under binocular rivalry suppression? Second, is complex stimulus information such as object category, no matter whether it is of particular behavioral relevance, represented in functionally specialized high-level visual areas during suppression? And finally, are there differences between such high-level visual areas, e.g., ventral and dorsal stream areas, regarding the degree to which suppressed information is processed?

With regard to the first question, whether emotional information is processed during binocular rivalry suppression, results from fMRI studies consistently indicate enhanced processing of emotional facial expressions. Williams et al. (2004) presented either faces with neutral, happy, or fearful expressions to one eye and houses to the other eye. Stimuli were presented only for a short, fixed duration

and the contrast and hue of the rivalrous images was manipulated so that just one image class was reliably perceived while the other image was suppressed. Activation in the FFA and PPA was increased for perceptually dominant versus suppressed faces and houses. In contrast, amygdala activation was increased in response to fearful versus neutral faces regardless of whether the face was dominant or suppressed, in line with the view that detection of emotional information proceeds automatically and does not require awareness (Vuilleumier, 2005). Similarly, during rivalry between a fearful face or a chair stimulus shown to one eye and a house stimulus (that was moving in order to ensure its dominance) to the other eye, activity in the amygdala was greater in response to suppressed fearful faces compared to chairs (Pasley, Mayes, & Schultz, 2004). No such response difference was observed in ventral visual cortex in this study, from which the authors concluded that a high-level cortical representation is not required for the discrimination of certain behaviorally relevant stimuli in the amygdala. It should be noted, however, that in these studies unawareness of the suppressed image was assessed either by using a one-back task that required participants to report repetitions of identical face or house stimuli (Williams, Morris, McGlone, Abbott, & Mattingley, 2004), or by instructing participants to press a button if at any point they perceived anything else but the dominant house stimulus (Pasley et al., 2004). As such methods do not reliably ensure objective unawareness of the suppressed stimuli, it cannot be ruled out that the observed response differences for suppressed faces may be at least in part be due to residual traces of stimulus awareness that went undetected by the tasks used.

In another fMRI study, CFS was used to render faces with fearful or neutral expressions invisible (Jiang & He, 2006). Here, a forced-choice task was used at least in behavioral pre- and post-scan sessions and showed that observers were unable to detect the suppressed stimuli, in addition to a subjective awareness assessment during fMRI scanning. Responses to invisible face stimuli in the FFA were strongly reduced relative to visible faces, but did not show differences between neutral and fearful expressions. In contrast, greater responses to fearful than to neutral faces were observed in the amygdala and in the superior temporal sulcus, a region previously implicated in the processing of changeable facial features such as expression or eye gaze (Haxby, Hoffman, & Gobbini, 2000). In a subsequent MEG study from the same group (Jiang et al., 2009), the amplitude of the M170, a face-specific signal thought to reflect face processing in ventral occipitotemporal cortex, was not significantly different for fearful and neutral faces. In contrast, a later signal along the superior temporal sulcus was specific for fearful expressions. Together, these neuroimaging studies of emotional face processing indicate that neither the category nor the emotional information of suppressed object stimuli seem to be represented in high-level ventral visual areas such as

the FFA. In contrast, both the amygdala and superior temporal sulcus show differential responses to fearful and neutral face stimuli. This is consistent with the notion of automatic processing of threat-signaling stimuli (Vuilleumier, 2005), which may thus bypass the visual processing stages at which binocular conflict is resolved, possibly via subcortical pathways.

The question remains whether object processing during binocular rivalry suppression is confined to emotionally relevant information, or whether other types of information may also survive suppression at early stages and be retained at advanced stages of visual processing. Moreover, just the absence of evidence for category-specific processing in specialized ventral visual areas during suppression (Pasley et al., 2004; Williams et al., 2004) cannot be taken as definite proof for the absence of such processing, as weak residual neural signals evoked by suppressed stimuli may have gone undetected by the neuroimaging methods used. Fang and He (2005) investigated neural responses to object stimuli suppressed by CFS in high-level areas pertaining to the ventral and dorsal streams of visual processing, respectively. Similar to the abovementioned studies (Pasley et al., 2004; Williams et al., 2004), they did not observe any category-specific fMRI responses to invisible images of faces or tools in ventral visual areas. In contrast, dorsal regions did show responses to suppressed stimuli that were only slightly reduced in amplitude relative to visible stimuli, but exclusively for images of tools. The authors concluded that indeed substantial information from the suppressed eye can escape competitive interactions at early processing levels and reach dorsal visual areas, but not ventral areas. In line with previous evidence from lesion studies in humans and from animal studies (Milner & Goodale, 1995), they interpreted these findings as support for a fundamental specialization of the visual system into a dorsal *vision-for-action/where* stream and a ventral *vision-for-perception/what* stream. According to this theory, dorsal areas are expected to form action-relevant representations for selected types of visual objects, e.g., tools and other man-made manipulable objects, even in the absence of awareness, while there are no such representations in ventral visual areas (see chapter by Price, this volume).

Findings from subsequent neuroimaging studies have provided partly diverging evidence that has questioned these conclusions. Using high-resolution fMRI study and multi-voxel pattern analysis to increase the sensitivity for distributed fMRI signals (Haynes & Rees, 2006; Norman et al., 2006) the fine-grained spatial activity patterns within the ventral areas FFA and PPA were shown to still contain information about the category of face and house stimuli even when reliably suppressed from conscious perception, as evidenced by a rigorous objective awareness assessment during fMRI scanning (Sterzer, Haynes, & Rees, 2008). Thus, the fine-grained spatial pattern of activity measured with fMRI in ventral visual areas encodes information about the identity of suppressed object stimuli.

Similarly, face-specific electromagnetic responses to binocularly suppressed stimuli are reduced in amplitude but still present in the human ventral visual pathway (Sterzer, Jalkanen, & Rees, 2009a). These results are consistent with more general findings of high-level processing for stimuli outside awareness in other paradigms (e.g., see Rees, 2007) and provide a possible neural basis for how complex stimulus features could contribute to the resolution of perceptual conflict even when suppressed. The processing of suppressed stimuli, however, does not seem to extend to semantic information (i.e., the relation between lexical units), as a recent EEG study found signals related to the semantic mismatch between a stimulus and the context in which it is presented to be absent when participants could not discriminate the meaning of suppressed words (Kang, Blake, & Woodman, 2011).

A recently published study also questioned the distinction between dorsal and ventral visual areas in the processing of suppressed object stimuli (Hesselmann & Malach, 2011). In this study participants had to detect, during CFS, images of tools. Despite their substantial difference in connectivity and neuroanatomical specialization, both ventral and dorsal stream areas revealed a similarly tight link to perceptual awareness, that is, strong fMRI signals for visible tools but a significant reduction of activity in the invisible condition. In other words, this study failed to replicate the previous finding (Fang & He, 2005) that specifically dorsal areas contain representations of manipulable objects during binocular rivalry suppression. Another interesting observation from this study is that CFS did not lead to a complete abolition of category-specific activity in response to invisible stimuli, as object category could still be decoded from fMRI signal patterns in lateral occipital cortex with multi-voxel pattern analyses, in line with the above-mentioned previous work (Sterzer et al., 2008). The divergent findings between the studies by Fang and He (2005) and Hesselmann and Malach (2011) may be explained by differences in study design, especially with respect to the behavioral assessment of unawareness. In the experiments of Fang and He, participants were asked to report whether they perceived any shape or object after 260 seconds of fMRI scanning while their task was to detect occasional size changes of the fixation point. Only a subset of participants performed a trial-wise forced-choice task in separate control experiments. In contrast, Hesselmann and Malach (2011) used an online trial-by-trial forced choice task which is likely to be a more conservative test for visibility given subjects can use any low level feature difference between target and masks to detect the target's presence. Because high-order visual areas specialized on object processing are extremely sensitive even to poorly visible low contrast images or object parts (Avidan et al., 2002; Lerner, Hendler, & Malach, 2002), it cannot be excluded, because of the relatively liberal assessment of unawareness during fMRI scanning, that responses to invisible tools in the study by Fang and He (2005) were at least in part due to occasional traces of residual

target visibility. In a further study that focused on the relationship between report type, subjective versus objective, and fMRI responses to face or tool stimuli during CFS, Hesselmann, Hebart and Malach (2011) replicated their previous finding of similar fMRI signal reductions in both ventral and dorsal visual areas when stimuli were invisible. In addition, they showed a dissociation between type of report and retinotopic vs high-level visual areas: subjective visibility effects in high-level visual areas were found even under equal objective performance. In contrast, no significant differences were found between correct and incorrect trials in these areas when subjective report was constant. On the other hand, objective performance was linked to the accuracy of multivariate pattern classification mainly in early visual areas, thus suggesting that subjective and objective reports tap cortical signals of different location and amplitude within the visual cortex (Hesselmann et al., 2011).

In summary, neuroimaging studies investigating the processing of suppressed visual information during binocular rivalry have shown repeatedly that object- or category-specific neural activity in high-level visual areas of the ventral stream is strongly reduced, but can be retrieved when sufficiently sensitive methods of data analysis are used, such as multi-voxel pattern analysis of fMRI data. It will be an important challenge for future research to determine to what degree such residual traces of object-related neural activity are relevant behaviorally, e.g., in that they influence the access of object information to awareness. While it seems established that suppressed emotional information is processed in the amygdala, research into a putative dissociation of ventral and dorsal stream areas in the processing of object information has not provided conclusive results yet. Possibly, dorsal areas are more sensitive than ventral areas to the presence of weak or noisy information, but responses in dorsal and ventral areas seem to be reduced to a similar degree when object stimuli are fully and objectively suppressed from awareness.

The constructive nature of visual perception: Neural mechanisms underlying perceptual changes during binocular rivalry

Perhaps the most intriguing feature of binocular rivalry is that perception changes spontaneously and unpredictably every few seconds. But these spontaneous perceptual alternations are not only a curious phenomenon, they make binocular rivalry an interesting tool to study the neural mechanisms that govern perceptual decisions in situations of ambiguous or conflicting sensory input (see also chapter by Wilson, this volume). As perception *re-organizes* every few seconds during ongoing binocular rivalry, measuring neural activity associated with perceptual transitions can help to elucidate the processes underlying such perceptual

reorganization. How these perceptual reorganizations are actually triggered has been matter of a long-standing debate (Blake & Logothetis, 2002; Sterzer et al., 2009b; Tong et al., 2006). As early as in the 19th century, Hermann von Helmholtz proposed that spontaneous perceptual transitions are caused by shifts in attention (Helmholtz, 1867), while Ewald Hering suggested that they are a consequence of sensory adaptation (Hering, 1920) (see chapter by Wade & Ngo, this volume). To date there is an ongoing debate about the question whether *high-level* mechanisms involving non-sensory brain regions have a causal role in triggering perceptual reorganizations; or whether perceptual fluctuations in binocular rivalry are mainly driven by *low-level* mechanisms such as adaptation of neuronal populations in sensory areas (Blake & Logothetis, 2002). In the following, studies that have helped to better understand the roles of *high-level* and *low-level* mechanisms in binocular rivalry and other forms of bistable perception are summarized and discussed in the context of this debate.

In an early fMRI study, Lumer, Friston and Rees (1998) measured neural activity associated with perceptual transitions during binocular rivalry. Event-related activations during perceptual transitions in this study were not confined to brain regions representing the sensory properties of the visual stimuli undergoing rivalry. They also included focal regions of the parietal cortex and lateral prefrontal cortex, similar to regions previously implicated in attentional selection (Corbetta & Shulman, 2002). Interestingly, such transient activity increases in frontoparietal regions associated with spontaneous alternations during rivalry are greater compared to stimulus-driven changes in perception (Lumer et al., 1998; for a recent replication, see Figure 2b; Zaretskaya, Thielscher, Logothetis, & Bartels, 2010). This could imply that these supra-modal brain regions are involved in generating perceptual reorganizations and thereby inducing perceptual transitions (Leopold & Logothetis, 1999; Sterzer et al., 2009b). Yet, such an interpretation cannot be based solely on the analysis of response amplitudes during perceptual transitions. Alternatively, enhanced activity increases in frontoparietal regions could reflect greater salience of spontaneous perceptual transitions, relative to stimulus-driven perceptual changes, while they are actually determined by neural processes at the level of visual cortex (e.g., adaptation). There is also evidence indicating that switch-related frontoparietal activations may be related to individual perceptual biases towards alternating rather than stable perception, at least during intermittent (rather than continuous; see below) presentation of bistable stimuli (Raemaekers, van der Schaaf, van Ee, & van Wezel, 2009). Furthermore, a recent study suggested that increased perceptual uncertainty and longer transition phases may also contribute to greater activity increases during spontaneous perceptual transitions in binocular rivalry relative to control conditions generating stimulus-driven perceptual changes (Knäpen, Brascamp, Pearson, van Ee, & Blake, 2011).

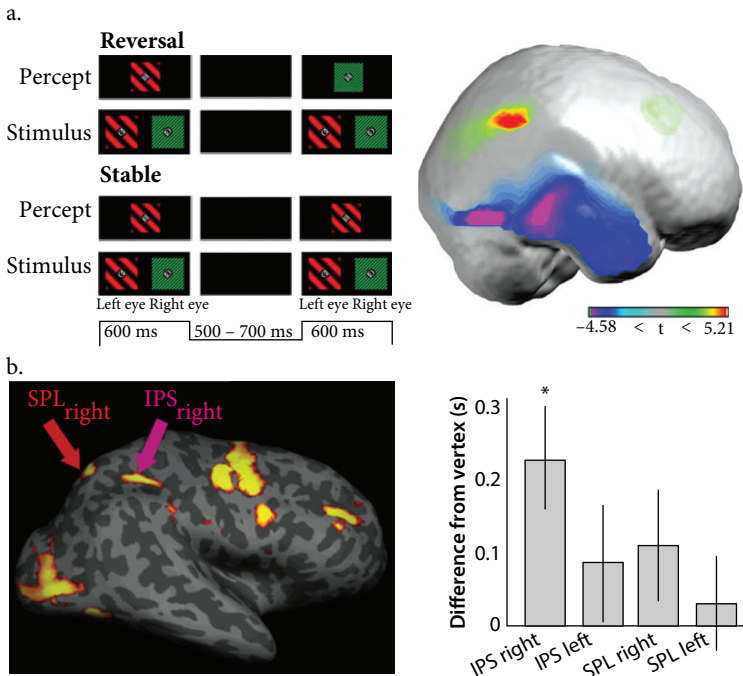


Figure 2. Evidence from EEG, fMRI and TMS for a role of right parietal cortex in perceptual reversals during binocular rivalry. (a) Rivaling stimuli were shown intermittently and observers reported their perception after each stimulus presentation. EEG in a 50 ms time-window preceding stimulus onset was analyzed as a function of whether perception reversed upon onset of a stimulus presentation or whether it remained stable (left panel). Source estimation showed greater responses in right inferior parietal cortex during reversals relative to stable trials (right panel, orange-red colors). Greater responses in stable relative to reversal trials were observed in ventral occipitotemporal regions (blue-violet colors). Reproduced with permission from Britz et al. (2011). (b) fMRI was used to localize in individual participants brain regions that showed greater responses during perceptual transitions during continuous binocular rivalry between a face and a house (left panel). Repetitive TMS was then used to disrupt the function of individually localized left or right intraparietal sulcus (IPS) and superior parietal lobule (SPL). Average dominance durations increased significantly only after applying TMS to right IPS (right panel), indicating an involvement of right IPS in destabilizing perception during binocular rivalry. Reproduced with permission from Zaretskaya et al. (2010).

In this study, participants were required to report both the onset and the offset of transitions during binocular rivalry, whenever transitions were not instantaneous. The authors compared transition-related increases in fMRI signal during rivalry with a control condition in which perceptual transitions were replayed with physically changing stimuli and transition periods that were matched in duration to those during rivalry. Using such a duration-matched control condition, this study failed to replicate the finding of greater transition-related activations during rivalry transitions previously reported by Lumer et al. (1998). Knapen et al. (2011) therefore concluded that at least a component of transition-related frontoparietal activation may reflect a response to perceptual transitions rather than their cause. While the evidence from the amplitude-based analysis of transition-related fMRI signals therefore remains inconclusive, chronometric analyses of fMRI and EEG signals and *virtual lesion* studies with TMS have recently helped to further elucidate the role of frontal and parietal regions in binocular rivalry.

Chronometric analyses of neural signals are concerned with the temporal aspects of brain activity, such as the latency or the temporal sequence of measured responses. Evidence from chronometric analyses of fMRI signals during binocular rivalry transitions is still lacking. Chronometry of fMRI signals associated with another form of bistable perception, bistable apparent motion, shows that transition-related activation of right prefrontal cortex precedes that of V5/MT during bistable perception, relative to externally induced perceptual changes (Sterzer & Kleinschmidt, 2007). It should be noted that conclusions from such chronometric analyses of fMRI signals – even when appropriately grounded in demonstrating a region-by-condition interaction (Sterzer & Kleinschmidt, 2007) that removes effects of local variations in neurovascular coupling – are still limited by our incomplete understanding of the relationship between neural activity and hemodynamic responses. The use of neurophysiological measures with a higher temporal resolution, such as EEG or MEG, may help to overcome this limitation. One problem with the measurement of neurophysiological signals related to rivalry transitions is that the analysis of these signals has to rely on subjective reports of the participants. Thus, both exact onset and the duration of the transitions (see Knapen et al., 2011) remain uncertain. This problem can be circumvented by presenting bistable stimuli intermittently instead of continuously. With brief stimulus presentations of 600–800 ms and interleaved blank screens of 400–600 ms duration, perceptual switches usually coincide with stimulus onsets (Orbach, Ehrlich, & Heath, 1963; Pitts & Britz, 2011). Neural activity can thus be analyzed in relation to the known time of stimulus onset, rather than the time of the behavioral report.

Using such intermittent presentation of binocular rivalry stimuli, a recent EEG study investigated EEG signals immediately preceding stimulus-onsets (Britz,

Pitts, & Michel, 2011). By applying distributed source localization methods, these authors found that the pre-stimulus activity occurring prior to perceptual reversals is generated in the right inferior parietal cortex (see Figure 2a). In contrast, stable perception was associated with greater activity predominantly in ventral occipitotemporal cortex, in line with an earlier fMRI study showing involvement of ventral visual areas in percept stabilization (Sterzer & Rees, 2008). Increased right inferior parietal activity preceding perceptual reversals had previously also been found with intermittent presentation of a Necker-cube like reversible figure (Britz, Landis, & Michel, 2009). The results from these two EEG studies thus suggest an involvement of the right inferior parietal cortex in perceptual reversals during intermittent presentation of multi-stable stimuli regardless of stimulus type. While the exact role of parietal cortex cannot be determined on the basis of these findings, the temporal precedence of the right inferior parietal signal renders this brain region an interesting candidate for a causal role of perceptual reversals during rivalry. The inferior parietal activation during continuous binocular rivalry observed earlier with fMRI (Lumer et al., 1998) and increased pre-stimulus activity in a similar region measured with EEG (Britz et al., 2009, 2011) may thus reflect a similar process. It should be noted, however, that it is not clear whether the mechanisms underlying perceptual reversals during intermittent presentation are truly identical to those under continuous stimulus presentation. The apparent discrepancy between the above-mentioned chronometric fMRI study showing temporal precedence of activity in right inferior frontal cortex (Sterzer & Kleinschmidt, 2007) and the two EEG studies implicating right inferior parietal cortex (Britz et al., 2009, 2011) in perceptual reversals could be due to differences in temporal resolution. As the fMRI signal is characterized by relatively poor temporal resolution, short onset differences in parietal activation between spontaneous and stimulus-driven reversals may simply not have been detectable in fMRI signals. Conversely, the EEG studies of Britz and colleagues limited their analyses to the time window 50 ms before stimulus onset. Earlier activity possibly occurring in prefrontal regions hence may have been missed in these analyses. One could therefore speculate that the two findings in right prefrontal cortex (fMRI) and right parietal cortex (EEG) may reflect parts of a cascade of neural events that precedes spontaneous reversals.

Temporal precedence is widely used as an indicator of causality, but such precedence does not provide direct evidence for a causal relationship between frontal and parietal activations and the occurrence of perceptual transitions during binocular rivalry. Complementary evidence for a causal role of frontal and parietal regions in controlling the rate of reversals during binocular rivalry comes from experiments that used TMS to interfere with cortical function (Figure 2b; see also chapter by Ngo, Barsdell, Law, & Miller, this volume). In an early TMS study

(Miller et al., 2000), single-pulse stimulation of left parietal cortex during binocular rivalry between a vertical and a horizontal grating disrupted perceptual transitions. When the TMS pulse was applied during a transition from the vertical to the horizontal grating percept, a shortened horizontal interval duration indicated reversion to the vertical percept. No such effect was observed when the TMS pulse was timed to occur at the opposite perceptual switch. The phase-specificity of this effect supports the notion that competition for awareness in binocular rivalry occurs between, rather than within, each brain hemisphere (interhemispheric switch hypothesis). More generally, this finding suggests that parietal cortex may indeed play a causal role in modulating perceptual transitions in binocular rivalry. Recently, a number of researchers have applied repetitive TMS to study the role of parietal cortex in binocular rivalry. In a study that used fMRI to individually localize four parietal regions correlated with perceptual transitions during binocular rivalry, disrupting the function of right intraparietal sulcus with low-frequency (2 Hz) repetitive TMS led to increased dominance durations and hence a stabilization of perception (Zaretskaya et al., 2010). While this finding is in line with the notion that right parietal cortex may play a role in destabilizing perception, another study recently reported that repetitive TMS over right superior parietal cortex shortened, rather than prolonged, binocular rivalry dominance durations (Carmel, Walsh, Lavie, & Rees, 2010). This latter finding suggests that right parietal cortex plays a role in stabilizing, rather than destabilizing the current perceptual state during rivalry. A possible solution to the apparent discrepancy between these two studies could be that different regions in parietal cortex may subserve different functions in regulating perceptual organization during binocular rivalry. Indeed, it has recently been shown that repetitive TMS of two distinct subregions of the superior parietal lobule has opposite effects on the alternation rate in the perception of a bistable motion stimulus (Kanai, Bahrami, & Rees, 2010; Kanai, Carmel, Bahrami, & Rees, 2011). Interestingly, this dissociation was paralleled by opposite associations of perceptual alternation rate with grey matter density in these subregions.

So far only one study has probed the putative causal role of frontal brain regions in triggering perceptual transitions in bistable perception using TMS (de Graaf, de Jong, Goebel, van Ee, & Sack, 2011). After repetitive TMS over dorsolateral prefrontal cortex, an effect on percept durations of a bistable motion stimulus was only observed when participants were instructed to voluntarily increase the alternation rate but not during passive viewing. The authors interpreted this finding as speaking for a causal role of prefrontal cortex in mediating voluntary control of perceptual alternations, but against a causal role in top-down modulation of *spontaneous* perceptual alternations in bistable perception. It should be noted, however, that previous neuroimaging studies implicated ventral

rather than dorsal prefrontal cortex in spontaneous perceptual transitions during binocular rivalry and bistable motion perception (Lumer et al., 1998; Sterzer & Kleinschmidt, 2007). The absence of a TMS effect on spontaneous alternation rates after dorsal prefrontal stimulation therefore cannot be taken generally as evidence against a causal role of frontal cortex in spontaneous perceptual transitions. In contrast to accumulating evidence from a number of recently published studies (Carmel et al., 2010; Kanai et al., 2010, 2011; Zaretskaya et al., 2010) no effects of superior parietal stimulation were observed by de Graaf et al. (2011). This absence of an effect could reflect differences in the experimental protocol, especially with respect to the exact location of the parietal regions stimulated with TMS.

Taken together, there is now empirical support for the notion that 'reorganizations of activity throughout the visual cortex, concurrent with perceptual reversals, are initiated by higher, largely non-sensory brain centers' (Leopold & Logothetis, 1999). fMRI, EEG and TMS have provided some evidence for a causal role of parietal brain regions in the modulation of perceptual alternations in binocular rivalry and other forms of bistable perception. Less evidence is available for the role of prefrontal regions, which thus awaits further clarification. But how exactly could the functional role of non-sensory brain regions in parietal and frontal cortices be conceptualized? Is the view that non-sensory brain regions are causally involved in triggering perceptual reorganizations compatible with the well-established notion that adaptation of neuronal populations in sensory areas are an important factor in bistable perception (Blake & Logothetis, 2002)? It is conceivable that non-sensory areas initiate perceptual reorganizations whenever the *balance of power* between neuronal populations coding for rivaling percepts in sensory cortices destabilizes due to adaptation or mutual inhibition. Alternatively, such putative destabilization in sensory cortices may serve as a salient event that activates frontoparietal regions in a feed-forward manner. Frontoparietal regions could in turn work to re-direct attention to the sensory input and initiate a re-evaluation of its current interpretation, eventually leading to a perceptual reversal (Knapen et al., 2011; Sterzer et al., 2009b). Irrespective of whether frontoparietal cortices are involved spontaneously or as a consequence of sensory destabilization, it seems likely that their functional role is not restricted to the mere detection of salient external events, but rather that it extends into a constructive process of evaluating sensory input for its perceptual significance. Given the evidence from empirical studies to date, it is thus plausible that non-sensory brain regions take an active part in inferential processes that give rise to the subjectively unitary and unambiguous conscious perception of the sensory input.

Conclusions

Neuroimaging studies have contributed to an improved understanding of several aspects of binocular rivalry. It is now firmly established that signals from the anatomically earliest visual processing stages up to the level of category-specific object processing correlate with conscious perception during binocular rivalry. This is consistent with current models of binocular rivalry that propose a multi-level process involving competitive neural interactions at multiple stages throughout the visual processing hierarchy. Neuroimaging has also contributed to our understanding of visual information processing in the absence of awareness. It has been demonstrated repeatedly that during binocular suppression of complex visual stimuli, object- or category-specific neural activity in high-level visual areas of the ventral stream is strongly reduced, but can be retrieved when sufficiently sensitive methods of data analysis are used. Finally, recent neuroimaging work has shaped our view on the constructive nature of vision that provides us with unitary perceptual experiences, despite the fact that the visual system is often faced with ambiguities or even conflicts in the sensory input. In contrast to previous views that explicitly contrast *low-level* (e.g., Blake, 1989) and *high-level* mechanisms (Leopold & Logothetis, 1999), current models now consider binocular rivalry to be the result of continuous multi-level interactions between processes at the earliest monocular levels, perceptual processing stages in higher-order visual areas, and non-sensory brain regions in frontal and parietal cortices (Sterzer et al., 2009b; Tong et al., 2006). Future research using neuroimaging methods to investigate binocular rivalry and related multistable phenomena should seek to provide a more detailed account of how these processes contribute to human consciousness.

References

- Alais, D., & Parker, A. (2006). Independent binocular rivalry processes for form and motion. *Neuron*, 52(5), 911–920.
- Andrews, T. J., & Blakemore, C. (1999). Form and motion have independent access to consciousness. *Nature Neuroscience*, 2(5), 405–406.
- Avidan, G., Harel, M., Hendler, T., Ben-Bashat, D., Zohary, E., & Malach, R. (2002). Contrast sensitivity in human visual areas and its relationship to object recognition. *Journal of Neurophysiology*, 87(6), 3102–3116.
- Blake, R. (1989). A neural theory of binocular rivalry. *Psychological Review*, 96(1), 145–167.
- Blake, R., & Logothetis, N. K. (2002). Visual competition. *Nature Reviews Neuroscience*, 3(1), 13–21.

- Britz, J., Landis, T., & Michel, C. M. (2009). Right parietal brain activity precedes perceptual alternation of bistable stimuli. *Cerebral Cortex*, 19(1), 55–65.
- Britz, J., Pitts, M. A., & Michel, C. M. (2011). Right parietal brain activity precedes perceptual alternation during binocular rivalry. *Human Brain Mapping*, 32(9), 1432–1442.
- Brown, R. J., & Norcia, A. M. (1997). A method for investigating binocular rivalry in real-time with the steady-state VEP. *Vision Research*, 37(17), 2401–2408.
- Carmel, D., Walsh, V., Lavie, N., & Rees, G. (2010). Right parietal TMS shortens dominance durations in binocular rivalry. *Current Biology*, 20(18), R799–R800.
- Chen, W., Kato, T., Zhu, X. H., Strupp, J., Ogawa, S., & Ugurbil, K. (1998). Mapping of lateral geniculate nucleus activation during visual stimulation in human brain using fMRI. *Magnetic Resonance in Medicine*, 39(1), 89–96.
- Chen, W., Zhu, X. H., Thulborn, K. R., & Ugurbil, K. (1999). Retinotopic mapping of lateral geniculate nucleus in humans using functional magnetic resonance imaging. *Proceedings of the National Academy of Sciences USA*, 96(5), 2430–2434.
- Corbetta, M., & Shulman, G. L. (2002). Control of goal-directed and stimulus-driven attention in the brain. *Nature Reviews Neuroscience*, 3(3), 201–215.
- Cosmelli, D., David, O., Lachaux, J. P., Martinerie, J., Garnero, L., Renault, B. et al. (2004). Waves of consciousness: Ongoing cortical patterns during binocular rivalry. *Neuroimage*, 23(1), 128–140.
- de Graaf, T. A., de Jong, M. C., Goebel, R., van Ee, R., & Sack, A. T. (2011). On the functional relevance of frontal cortex for passive and voluntarily controlled bistable vision. *Cerebral Cortex*, 21(10), 2322–2331.
- Du Tour, E.-F. (1760). Discussion d'une question d'optique. *Mémoires de Mathématique et de Physique, présentés à l'Académie Royale des Sciences, par divers Savans, & lus dans ses Assemblées*, 3, 514–530.
- Epstein, R., Harris, A., Stanley, D., & Kanwisher, N. (1999). The parahippocampal place area: Recognition, navigation, or encoding? *Neuron*, 23(1), 115–125.
- Fang, F., & He, S. (2005). Cortical responses to invisible objects in the human dorsal and ventral pathways. *Nature Neuroscience*, 8(10), 1380–1385.
- Haxby, J. V., Hoffman, E. A., & Gobbini, M. I. (2000). The distributed human neural system for face perception. *Trends in Cognitive Sciences*, 4(6), 223–233.
- Haynes, J.-D., Deichmann, R., & Rees, G. (2005). Eye-specific effects of binocular rivalry in the human lateral geniculate nucleus. *Nature*, 438(7067), 496–499.
- Haynes, J.-D., & Rees, G. (2005). Predicting the stream of consciousness from activity in human visual cortex. *Current Biology*, 15(14), 1301–1307.
- Haynes, J.-D., & Rees, G. (2006). Decoding mental states from brain activity in humans. *Nature Reviews Neuroscience*, 7(7), 523–534.
- Heeger, D. J., & Ress, D. (2002). What does fMRI tell us about neuronal activity? *Nature Reviews Neuroscience*, 3(2), 142–151.
- Helmholtz, H. (1867). *Handbuch der physiologischen Optik*. In G. Karsten (Ed.), *Allgemeine Encyclopädie der Physik*, Vol. 9. Leipzig: Leopold Voss.
- Hering, E. (1920). *Grundzüge der Lehre vom Lichtsinn*. Berlin: Julius Springer.
- Hesselmann, G., Hebart, M., & Malach, R. (2011). Differential BOLD activity associated with subjective and objective reports during “blindsight” in normal observers. *Journal of Neuroscience*, 31(36), 12936–12944.

- Hesselmann, G., & Malach, R. (2011). The link between fMRI-BOLD activation and perceptual awareness is "stream-invariant" in the human visual system. *Cerebral Cortex*, 21(12), 2829–2837.
- Jiang, Y., & He, S. (2006). Cortical responses to invisible faces: Dissociating subsystems for facial-information processing. *Current Biology*, 16(20), 2023–2029.
- Jiang, Y., Shannon, R. W., Vizueta, N., Bernat, E. M., Patrick, C. J., & He, S. (2009). Dynamics of processing invisible faces in the brain: Automatic neural encoding of facial expression information. *Neuroimage*, 44(3), 1171–1177.
- Kamphuisen, A., Bauer, M., & van Ee, R. (2008). No evidence for widespread synchronized networks in binocular rivalry: MEG frequency tagging entrains primarily early visual cortex. *Journal of Vision*, 8(5), 4. doi: 10.1167/8.5.4
- Kanai, R., Bahrami, B., & Rees, G. (2010). Human parietal cortex structure predicts individual differences in perceptual rivalry. *Current Biology*, 20(18), 1626–1630.
- Kanai, R., Carmel, D., Bahrami, B., & Rees, G. (2011). Structural and functional fractionation of right superior parietal cortex in bistable perception. *Current Biology*, 21(3), R106–R107.
- Kang, M. S., Blake, R., & Woodman, G. F. (2011). Semantic analysis does not occur in the absence of awareness induced by interocular suppression. *Journal of Neuroscience*, 31(38), 13535–13545.
- Kanwisher, N., McDermott, J., & Chun, M. M. (1997). The fusiform face area: A module in human extrastriate cortex specialized for face perception. *Journal of Neuroscience*, 17(11), 4302–4311.
- Knapen, T., Brascamp, J., Pearson, J., van Ee, R., & Blake, R. (2011). The role of frontal and parietal brain areas in bistable perception. *Journal of Neuroscience*, 31(28), 10293–10301.
- Kovács, I., Papathomas, T. V., Yang, M., & Fehér, A. (1996). When the brain changes its mind: Interocular grouping during binocular rivalry. *Proceedings of the National Academy of Sciences USA*, 93(26), 15508–15511.
- Lamme, V. A., & Roelfsema, P. R. (2000). The distinct modes of vision offered by feedforward and recurrent processing. *Trends in Neurosciences*, 23(11), 571–579.
- Lansing, R. W. (1964). Electroencephalographic correlates of binocular rivalry in man. *Science*, 146(3649), 1325–1327.
- Lawwill, T., & Biersdorf, W. R. (1968). Binocular rivalry and visual evoked responses. *Investigative Ophthalmology*, 7(4), 378–385.
- Lee, S. H., Blake, R., & Heeger, D. J. (2005). Traveling waves of activity in primary visual cortex during binocular rivalry. *Nature Neuroscience*, 8(1), 22–23.
- Leopold, D. A., & Logothetis, N. K. (1999). Multistable phenomena: Changing views in perception. *Trends in Cognitive Sciences*, 3(7), 254–264.
- Lerner, Y., Hendler, T., & Malach, R. (2002). Object-completion effects in the human lateral occipital complex. *Cerebral Cortex*, 12(2), 163–177.
- Lin, Z., & He, S. (2009). Seeing the invisible: The scope and limits of unconscious processing in binocular rivalry. *Progress in Neurobiology*, 87(4), 195–211.
- Logothetis, N. K., Leopold, D. A., & Sheinberg, D. L. (1996). What is rivaling during binocular rivalry? *Nature*, 380(6575), 621–624.
- Logothetis, N. K., Pauls, J., Augath, M., Trinath, T., & Oeltermann, A. (2001). Neurophysiological investigation of the basis of the fMRI signal. *Nature*, 412(6843), 150–157.
- Lumer, E. D., Friston, K. J., & Rees, G. (1998). Neural correlates of perceptual rivalry in the human brain. *Science*, 280(5371), 1930–1934.

- Maier, A., Wilke, M., Aura, C., Zhu, C., Ye, F. Q., & Leopold, D. A. (2008). Divergence of fMRI and neural signals in V1 during perceptual suppression in the awake monkey. *Nature Neuroscience*, 11(10), 1193–1200.
- Miller, S. M., Liu, G. B., Ngo, T. T., Hooper, G., Riek, S., Carson, R. G. et al. (2000). Interhemispheric switching mediates perceptual rivalry. *Current Biology*, 10(7), 383–392.
- Milner, A. D., & Goodale, M. A. (1995). *The visual brain in action*. Oxford: Oxford University Press.
- Norman, K. A., Polyn, S. M., Detre, G. J., & Haxby, J. V. (2006). Beyond mind-reading: Multi-voxel pattern analysis of fMRI data. *Trends in Cognitive Sciences*, 10(9), 424–430.
- Orbach, J., Ehrlich, D., & Heath, H. A. (1963). Reversibility of the Necker cube: I. An examination of the concept of “satiation and orientation”. *Perceptual and Motor Skills*, 17(2), 439–458.
- Pasley, B. N., Mayes, L. C., & Schultz, R. T. (2004). Subcortical discrimination of unperceived objects during binocular rivalry. *Neuron*, 42(1), 163–172.
- Pearson, J., Tadin, D., & Blake, R. (2007). The effects of transcranial magnetic stimulation on visual rivalry. *Journal of Vision*, 7(7), 2. doi: 10.1167/7.7.2
- Pessoa, L. (2005). To what extent are emotional visual stimuli processed without attention and awareness? *Current Opinion in Neurobiology*, 15(2), 188–196.
- Pitts, M. A., & Britz, J. (2011). Insights from intermittent binocular rivalry and EEG. *Frontiers in Human Neuroscience*, 5, 107. doi: 10.3389/fnhum.2011.00107
- Pollen, D. A. (2003). Explicit neural representations, recursive neural networks and conscious visual perception. *Cerebral Cortex*, 13(8), 807–814.
- Polonsky, A., Blake, R., Braun, J., & Heeger, D. J. (2000). Neuronal activity in human primary visual cortex correlates with perception during binocular rivalry. *Nature Neuroscience*, 3(11), 1153–1159.
- Raemaekers, M., van der Schaaf, M. E., van Ee, R., & van Wezel, R. J. A. (2009). Widespread fMRI activity differences between perceptual states in visual rivalry are correlated with differences in observer biases. *Brain Research*, 1252, 161–171.
- Rahnev, D., Maniscalco, B., Graves, T., Huang, E., de Lange, F. P., & Lau, H. (2011). Attention induces conservative subjective biases in visual perception. *Nature Neuroscience*, 14(12), 1513–1515.
- Rees, G. (2007). Neural correlates of the contents of visual awareness in humans. *Philosophical Transactions of the Royal Society of London B: Biological Sciences*, 362(1481), 877–886.
- Sereno, M. I., Dale, A. M., Reppas, J. B., Kwong, K. K., Belliveau, J. W., Brady, T. J. et al. (1995). Borders of multiple visual areas in humans revealed by functional magnetic resonance imaging. *Science*, 268(5212), 889–893.
- Shimaoka, D., & Kaneko, K. (2011). Dynamical systems modeling of continuous flash suppression. *Vision Research*, 51(6), 521–528.
- Snodgrass, M. (2004). The dissociation paradigm and its discontents: How can unconscious perception or memory be inferred? *Consciousness and Cognition*, 13(1), 107–116.
- Srinivasan, R., Russell, D. P., Edelman, G. M., & Tononi, G. (1999). Increased synchronization of neuromagnetic responses during conscious perception. *Journal of Neuroscience*, 19(13), 5435–5448.
- Sterzer, P., Haynes, J.-D., & Rees, G. (2008). Fine-scale activity patterns in high-level visual areas encode the category of invisible objects. *Journal of Vision*, 8(15), 10. doi: 10.1167/8.15.10
- Sterzer, P., Jalkanen, L., & Rees, G. (2009a). Electromagnetic responses to invisible face stimuli during binocular suppression. *Neuroimage*, 46(3), 803–808.

- Sterzer, P., & Kleinschmidt, A. (2007). A neural basis for inference in perceptual ambiguity. *Proceedings of the National Academy of Sciences USA*, 104(1), 323–328.
- Sterzer, P., Kleinschmidt, A., & Rees, G. (2009b). The neural bases of multistable perception. *Trends in Cognitive Sciences*, 13(7), 310–318.
- Sterzer, P., & Rees, G. (2008). A neural basis for percept stabilization in binocular rivalry. *Journal of Cognitive Neuroscience*, 20(3), 389–399.
- Tong, F. (2003). Primary visual cortex and visual awareness. *Nature Reviews Neurosciences*, 4(3), 219–229.
- Tong, F., & Engel, S. A. (2001). Interocular rivalry revealed in the human cortical blind-spot representation. *Nature*, 411(6834), 195–199.
- Tong, F., Meng, M., & Blake, R. (2006). Neural bases of binocular rivalry. *Trends in Cognitive Sciences*, 10(11), 502–511.
- Tong, F., Nakayama, K., Vaughan, J. T., & Kanwisher, N. (1998). Binocular rivalry and visual awareness in human extrastriate cortex. *Neuron*, 21(4), 753–759.
- Tononi, G., Srinivasan, R., Russell, D. P., & Edelman, G. M. (1998). Investigating neural correlates of conscious perception by frequency-tagged neuromagnetic responses. *Proceedings of the National Academy of Sciences USA*, 95(6), 3198–3203.
- Tsuchiya, N., & Koch, C. (2005). Continuous flash suppression reduces negative afterimages. *Nature Neuroscience*, 8(8), 1096–1101.
- Tsuchiya, N., Koch, C., Gilroy, L. A., & Blake, R. (2006). Depth of interocular suppression associated with continuous flash suppression, flash suppression, and binocular rivalry. *Journal of Vision*, 6(10), 6. doi:10.1167/6.10.6
- Vuilleumier, P. (2005). How brains beware: Neural mechanisms of emotional attention. *Trends in Cognitive Sciences*, 9(12), 585–594.
- Wilke, M., Logothetis, N. K., & Leopold, D. A. (2006). Local field potential reflects perceptual suppression in monkey visual cortex. *Proceedings of the National Academy of Sciences USA*, 103(46), 17507–17512.
- Williams, M. A., Morris, A. P., McGlone, F., Abbott, D. F., & Mattingley, J. B. (2004). Amygdala responses to fearful and happy facial expressions under conditions of binocular suppression. *Journal of Neuroscience*, 24(12), 2898–2904.
- Wolfe, J. M. (1984). Reversing ocular dominance and suppression in a single flash. *Vision Research*, 24(5), 471–478.
- Wunderlich, K., Schneider, K. A., & Kastner, S. (2005). Neural correlates of binocular rivalry in the human lateral geniculate nucleus. *Nature Neuroscience*, 8(11), 1595–1602.
- Zaretskaya, N., Thielscher, A., Logothetis, N. K., & Bartels, A. (2010). Disrupting parietal function prolongs dominance durations in binocular rivalry. *Current Biology*, 20(23), 2106–2111.

Binocular rivalry, brain stimulation and bipolar disorder

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Mechanistic understanding of binocular rivalry (BR) has drawn upon psychophysical, electrophysiological and brain-imaging studies. The first brain *stimulation* approach occurred in the late 1990s and assessed a new mechanistic proposal, the interhemispheric switch (IHS) hypothesis. Both caloric vestibular stimulation (CVS) and transcranial magnetic stimulation (TMS) modulated rivalry predominance when applied *unilaterally*. We describe the IHS model, its genesis and the brain stimulation evidence on which it rests. We also review more recent CVS and TMS rivalry studies, and discuss the findings of slow BR in bipolar disorder (BD) and genetic contribution to individual variation in BR rate. Finally, we describe a recent *Drosophila* model that can shed light on genetic, molecular and neurophysiological aspects of both BR and BD.

Rivalry mechanisms: A tale of two levels

Several centuries ago, scholars sought to understand what happens in the brain when different, overlapping signals are received by the two eyes (see chapter by Wade & Ngo, this volume). Since then, binocular rivalry (BR) induced by dichoptic stimulation has been extensively researched and has been complemented by examination of dioptic (normal viewing) presentation of well-known forms of ambiguous-figure rivalry (AFR; e.g., the Necker cube) and other two-dimensional bistable perceptual stimuli (e.g., structure-from-motion [SFM] rotating sphere). As has been described in detail elsewhere (Leopold & Logothetis, 1999; Miller, Ngo, & van Swinderen,

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2012; Ngo, Liu, Tilley, Pettigrew, & Miller, 2008; see also chapter by Brascamp & Baker, this volume), evidence is accumulating for at least some degree of shared neural mechanism between BR and these other types of perceptual rivalry.

Since Hering and Helmholtz, there has been debate over whether BR is a low-level sensory competition phenomenon, or one based on high-level attentional competition (see chapter by Wade & Ngo, this volume). Early mechanistic theories of BR and AFR proposed that the perceptual alternations involved a reciprocal relationship between neuronal activity representing the dominant image and that representing the suppressed image (see also chapters by Sengpiel, Sterzer, and Wilson, this volume). On this account, perceptual dominance of one stimulus leads to adaptation of its neuronal representation until activity representing the other stimulus sufficiently recovers from adaption, thereby initiating a perceptual switch, and so on. Subsequent psychophysical evidence was relied upon for proposing that BR involves reciprocal inhibition between separate monocular channel neurons responsive to one, but not the other, eye (Blake, 1989). However, in contrast, electrophysiological studies in awake, behaving monkeys (Leopold & Logothetis, 1996; Logothetis & Schall, 1989; Sheinberg & Logothetis, 1997; reviewed in Logothetis, 1998; Logothetis, Leopold, & Sheinberg, 2003) showed that single-unit activity of monocular neurons bore little relationship to the monkeys' rivalrous perceptions (see also chapter by Sengpiel, this volume). Although 18% of tested V1 neurons did show perception-dependent activity, all but one of these neurons were binocular (i.e., responsive to input from either eye). As the investigators progressed through the visual processing hierarchy, they found greater percentages of perception-dependent units, until reaching the inferotemporal cortex and superior temporal sulcus where ~90% of recorded cells demonstrated activity that correlated with the monkeys' perceptual reports.

This electrophysiological data conflicted with subsequent human fMRI studies (see chapter by Sterzer, this volume) that showed activity in V1 (Lee & Blake, 2002; Polonsky, Blake, Braun, & Heeger, 2000; Tong & Engel, 2001; Wunderlich, Schneider, & Kastner, 2005) and LGN (Haynes, Deichmann, & Rees, 2005; Wunderlich et al., 2005) covaried with the dominance and suppression phases during BR. Middle ground was therefore found in the form of an 'amalgam' view of BR (Blake & Logothetis, 2002), in which the phenomenon was seen to result from a series of processes at multiple levels in the visual pathway. Most recently, there have been yet further contradictory mechanistic studies. Keliris, Logothetis and Tolia (2010) reported that during binocular flash suppression in awake primates, V1 perception-dependent spiking activity (again in 20% of units tested) occurred equally in binocular *and* monocular neurons, thus in contrast to the original report with BR by Leopold and Logothetis (1996). However, Keliris et al. (2010) also reported weaker V1 local field potential (LFP) modulations than

those seen in higher areas, and could not rule out the possibility that they were the result of modulatory top-down input (see chapter by Sengpiel, this volume). There is now also, remarkably, report of perception-dependent neural activity (both neuronal discharges and power modulation of high-frequency LFPs) in macaque lateral prefrontal cortex during binocular flash suppression (Panagiotaropoulos, Deco, Kapoor, & Logothetis, 2012).

As the above electrophysiological and brain-imaging evidence demonstrates, and as the psychophysical evidence reviewed by Brascamp and Baker (this volume) and Bressler, Denison and Silver (this volume) similarly demonstrates, mechanistic understanding of BR has exhibited a point-counterpoint history. This has been particularly so with respect to whether the phenomenon is mediated by low- or high-level mechanisms. Perhaps not surprisingly, given suggestions of common mechanistic processes underlying BR and AFR, the BR amalgam view has been mirrored by a 'hybrid' model of AFR (Long & Toppino, 2004). This hybrid model consists of a conceptual, multi-level framework (i.e., from low- to high-level: parallel feature-extraction channels, intermediate processing and representation, higher-order global operations) to account for the wealth of conflicting sensory (low-level) and cognitive (high-level) evidence in AFR studies.

Consistent with this pendulous history (Blake, 2001), the amalgam view of BR and corresponding hybrid view of AFR now acknowledge a role for processing at multiple stages in the visual hierarchy, and indeed even in non-visual areas concerning attention, behavior and decision-making. Whilst this consensus view brings perspective to low-level and high-level views of rivalry, there remains debate over the relevance of processing at each level (discussed in Ngo, Liu, Tilley, Pettigrew, & Miller, 2007). Moreover, too ready an acknowledgement of multi-level processing during rivalry could stifle proposals for more specific mechanistic clarification across and within levels.

The interhemispheric switch (IHS) model of rivalry

We previously proposed a specific high-level mechanistic model of BR and AFR (Miller et al., 2000) – the interhemispheric switch (IHS) model. This model is not inconsistent with the notion of multi-level processing, but has at its mechanistic core, a high-level process in which the attentional resources within each cerebral hemisphere act independently and in alternation. On this view, the perceptual switching that characterizes rivalry correlates with a process of alternating hemispheric activation, i.e., interhemispheric switching. The evidence garnered in support of the IHS model, and a range of issues raised therein, has been reviewed in detail elsewhere (Miller, 2001; Miller & Ngo, 2007; Miller et al., 2012; Ngo et

al., 2007, 2008; Pettigrew, 2001). Here, the genesis and key aspects of the model are discussed, and an updated commentary on its status is provided in light of recent developments in both rivalry research and comparative studies of inter-hemispheric switching.

The IHS hypothesis arose from the conjunction of separate lines of thinking by Pettigrew and Miller in the late 1990s (see Figure 1). Pettigrew, Collin and Ott (1999) had observed independent eye movement patterns in a small fish, the sandlance, and because this animal has completely crossed eye-hemisphere pathways, they reasoned that the alternating eye movements must be driven by an IHS process. Inspired by this observation, by Ramachandran's (1994) proposal regarding complementary (lateralized) cognitive styles of the cerebral hemispheres, and by a desire to examine neural mechanisms of the psychiatric condition, bipolar disorder (BD; manic depression), Pettigrew sought to identify an IHS process in humans that would help explain the extreme mood swings of BD. On this background, Miller proposed that BR could be exactly the sort of IHS process that Pettigrew was seeking to identify in humans. Miller's proposal was based on the convergence of three factors: (i) rivalry had been considered fundamentally attentional in nature (Helmholtz 1867/1925; see also Brascamp & Blake, 2012; Ling & Blake, 2012; Zhang, Jamison, Engel, He, & He, 2011; and chapters by Wade & Ngo and Bressler et al., this volume, and below), (ii) split-brain studies showed that the cerebral hemispheres are able to *independently* draw on attentional resources (Luck, Hillyard, Mangun, & Gazzaniga, 1989; see also Alvarez & Cavanagh, 2005; Alvarez, Gill, & Cavanagh, 2012), and (iii) hemispherectomy studies (removal of an entire cerebral hemisphere) showed that the remaining single hemisphere is able to sustain a coherent visual percept (Bogen et al., 1998; see also Bogen, 2000). Thus, Pettigrew and Miller proposed a rivalry model in which an IHS drives the perceptual alternations, with high-level regions in each hemisphere representing one, but not the other, rivaling percept.

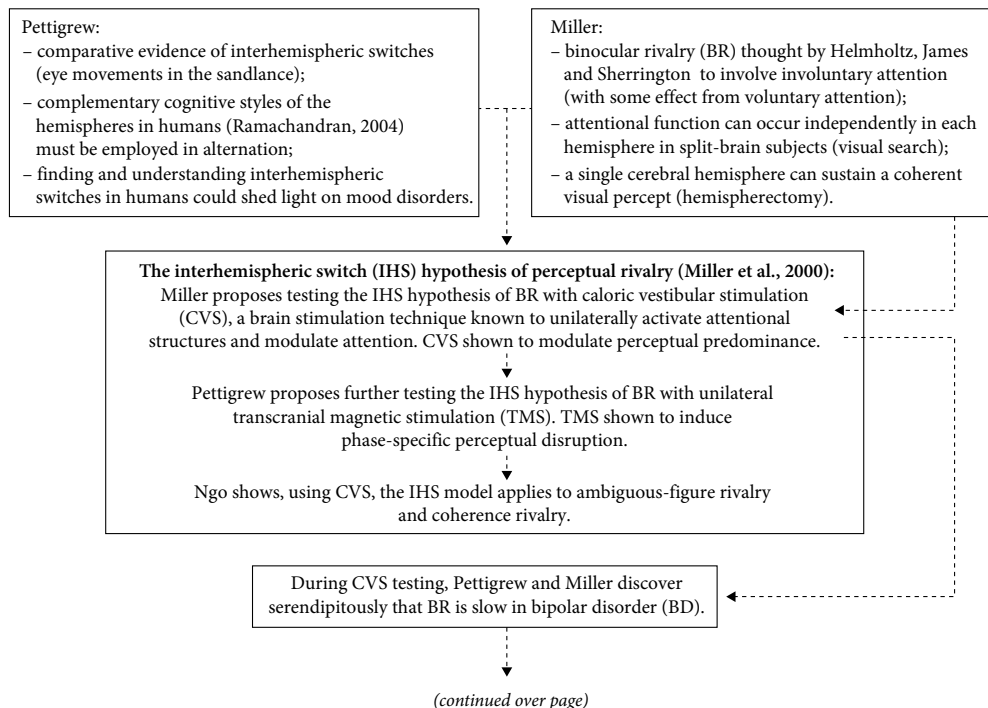
To test their model, Miller reasoned that if each cerebral hemisphere mediated perception of one, but not the other, image during rivalry, then preferentially activating one hemisphere should alter the relative time spent perceiving each image (predominance). He therefore hypothesized that the *unilateral* cortical activation properties of caloric vestibular stimulation (CVS), as had been used by Ramachandran (1994) in developing his cognitive style proposals, would alter perceptual predominance during rivalry if an IHS process indeed mediated the phenomenon. The strategy of examining the IHS model by unilateral brain stimulation was further bolstered by Pettigrew's hypothesis that transcranial magnetic stimulation (TMS) applied in this way should also alter predominance during BR. TMS was a relatively nascent technique in the late 1990s but is now in widespread use in the cognitive and clinical sciences. The technique is described in detail in

the chapter by Thomson and Fitzgerald (this volume). Below, we briefly review the CVS technique including the range of its neural and phenomenological effects, before describing results of the ensuing CVS and TMS studies of rivalry. Thereafter we turn to an unexpected finding encountered when Pettigrew and Miller commenced examination of the IHS model, one that enabled the linking of the notion of an IHS mechanism to the clinical condition, BD.

CVS technique overview

CVS is a commonly used technique for testing vestibular functioning and brain death. It involves slowly irrigating the ear with cold (or warm) water while the subject's head is reclined, to induce vertigo and nystagmus. Although CVS has primarily been used for clinical diagnostic purposes in the past century, in recent decades it has been applied to the examination of a wide range of cognitive and clinical phenomena such as attention, somatosensory representation, memory, mood, and pain. Several brain-imaging studies have shown that the technique consistently activates a network of structures known to be involved in mediating such phenomena, in addition to vestibular processing. CVS administration with cold water induces activation of cortical structures in the contralateral hemisphere, including anterior cingulate cortex, posterior insular and retroinsular cortices, temporoparietal junction, somatosensory area SII, inferior parietal lobule, parietal operculum and superior temporal gyrus (reviewed in Been, Ngo, Miller, & Fitzgerald, 2007; Lopez, Blanke, & Mast, 2012; Miller & Ngo, 2007; zu Eulenburg, Caspers, Roski, & Eickhoff, 2012). Figure 2a depicts the CVS technique and the key brain regions it activates.

In accordance with such activation, administration of CVS has the ability to modulate attentional disorders such as unilateral neglect following right-hemisphere lesions (Figure 2b), along with modulation of related conditions including anosognosia (denial of disease), somatoparaphrenia (bizarre beliefs), macrosomatognosia (misperception of body part size) and hemianesthesia (Bottini et al., 2005; Chokron, Dupierrix, Tabert, & Bartolomeo, 2007; Rode et al., 2012; Rossetti & Rode, 2002). CVS appears also able to modulate the manic phase of BD (Dodson, 2004; Levine et al., 2012; see also Pettigrew & Miller, 1998) (Figure 2c), as well as a variety of persistent pain disorders (André, Martinet, Paysant, Beis, & Le Chapelain, 2001; Kolev, 1990; Le Chapelain, Beis, Paysant, & André, 2001; McGeoch & Ramachandran, 2008; McGeoch, Williams, Lee, & Ramachandran, 2008; McGeoch et al., 2009). In healthy subjects CVS has been shown to affect a wide range of cognitive functions including spatial perception and localization (Karnath, 1994; Karnath, Fetter, & Dichigans, 1996; Karnath,

Figure 1. Genesis of the IHS model of rivalry and sticky switch model of BD, and recent genetic developments.

Pettigrew & Miller (1998) confirm BR is slow in BD and link IHS model of BR to slow BR in BD:

'Sticky switch' hypothesis of BD

Model incorporates existing data-based proposals of:

- complementary cognitive styles of the hemispheres
- hemispheric asymmetries of mood and mood disorders
- ultradian rhythms of alternating hemispheric activation

Model proposes:

- IHS driven by subcortical bistable oscillator (Pettigrew), subject to top-down influence;
- slow BR oscillators genetically (pleiotropically) coupled to slow ultradian rhythm oscillators (*Drosophila* precedent);
- ultradian rhythm IHS oscillators, by being slow in BD, are prone to being stuck in one or the other state by external synaptic input (cortical top-down input from environmental cues/stressors);
- thus mania = 'stuck' left hemisphere (relative activation) and depression = 'stuck' right hemisphere;
- CVS could restore hemispheric imbalances and thus potentially treat mania and depression;
- molecular defect in BD may be the number of cationic channels controlling I_h current;
- because several cationic channels can affect oscillator switch rate, this could explain multiple genetic candidates for BD;
- increased cellular and neuronal sensitivity in BD is the result of cortical compensation for reduced channel number, which further predisposes the subcortical switch to being stuck (by increased output from cortex to switch);
- slow BR could be a trait marker of BD for use in genetic studies of the disorder.

Slow BR in BD explored as a potential diagnostic aid in clinical psychiatry and endophenotype for BD. BR does not appear to be slow in schizophrenia or major depression (Miller et al., 2003).

Heritability of individual variation in BR rate examined in twin study with Martin and Wright. Substantial genetic contribution to BR rate demonstrated (Miller et al., 2010).

Drosophila attentional switching (Tang & Juusola, 2010) proposed as model to explore genetic and molecular determinants of switch rate (Miller, Ngo, & van Swinderen, 2012).

Multi-center study established to examine clinical diagnostic and endophenotype applications of slow BR in BD (Ngo et al., 2011).

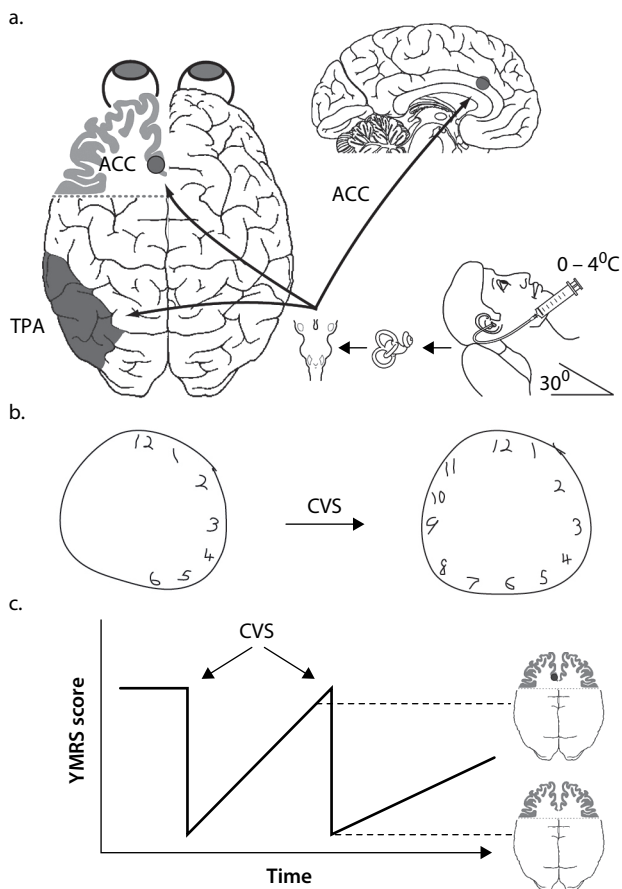


Figure 2. (a) The CVS technique. Irrigation of cold water with the head reclined activates, via the semicircular canals and vestibular pathways, contralateral cortical structures implicated in attentional and mood processing. These structures include the anterior cingulate cortex (ACC), insular cortex (not depicted) and various temporo-parietal areas (TPA). (b) CVS temporarily ameliorates left-sided attentional neglect following right-sided damage, as depicted by drawing of a complete clock face following the procedure. (c) Pettigrew and Miller's (1998) sticky switch model of BD predicted that right-hemisphere activation (via left-ear CVS) would alleviate the signs and symptoms of mania by restoring toward normal the greater relative left-hemisphere activation asymmetry associated with mania (Blumberg et al., 2000). This therapeutic effect was verified in a case study by Dodson (2004), as depicted by a dramatic reduction in the patient's Young Mania Rating Scale (YMRS) score following the procedure.

Himmelbach, & Perenin, 2003; Karnath, Sievering, & Fetter, 1994; Schmäl, Kunz, & Stoll, 2000), spatial and verbal memory (Bächtold et al., 2001), auditory space perception (Lewald & Karnath, 2000), visual imagery (Mast, Merfeld, & Kosslyn, 2006), tactile perception (Ferrè, Bottini, & Haggard, 2012; Ferrè, Bottini, Iannetti, & Haggard, 2013; Ferrè, Sedda, Gandola, & Bottini, 2011; Lopez, Schreyer, Preuss, & Mast, 2012), and positively biased beliefs (McKay et al., in press). Below we summarize a large series of studies we previously conducted in healthy controls, which demonstrated the ability of CVS to modulate perception during both BR and AFR. We then discuss more recent CVS studies and go on to review both earlier and recent TMS studies of rivalry.

Review of brain stimulation studies of rivalry

CVS and predominance modulation

In accordance with the predictions of the IHS model, unilateral CVS was found to modulate perceptual predominance during BR with drifting vertical and horizontal gratings, at least with respect to left-hemisphere activation (Miller et al., 2000; see Figure 3a). Hence, on an IHS interpretation, by activating attentional regions in the left hemisphere relative to the right, subjects spent more relative time perceiving the left hemisphere's image (though exactly which image that was could vary between individuals; see below). This result was difficult to interpret on models of rivalry that did not involve separate distribution of the two images, one to each hemisphere. However, an alternative explanation was that residual eye movements from the CVS-induced nystagmus would differentially affect perception of the horizontal and vertical gratings. Hence, we next repeated the experiment using orthogonal stationary oblique gratings to induce BR, thus excluding such eye movement interpretations. The same CVS-induced predominance shifts were demonstrated (Miller et al., 2000).

Ngo subsequently applied CVS to (i) Necker-cube rivalry (Miller et al., 2000), (ii) Rubin's vase-faces illusion (Ngo et al., 2008), and (iii) the grouped percepts during coherence rivalry (Ngo et al., 2007; see also below, Figure 3 in this chapter, and Figure 2 in chapter by Miller, this volume), again finding significant predominance modulation from left-hemisphere CVS in each case. Moreover, in all five experiments, the same *asymmetry* of CVS effects was observed (i.e., left-hemisphere but *not* right-hemisphere activation induced a significant predominance change). This asymmetry in the ability of CVS to modulate predominance during rivalry was interpreted (Miller et al., 2000) in terms of a previously demonstrated hemispheric asymmetry during BR (in which a right-lateralized fronto-parietal

region was active during perceptual transitions; Lumer, Friston, & Rees, 1998; see also chapter by Sterzer, this volume). Exactly why right-lateralized transition-related processing would mitigate CVS-induced predominance change is not clear, however hemispheric asymmetries relevant to rivalry dynamics have also recently been demonstrated with TMS applied to parietal regions (see below).

Thus, the ability of CVS to modulate predominance during perceptual rivalry contributes to evidence in support of (i) the IHS model, (ii) the relevance of attentional processing to perceptual rivalry, and (iii) structural overlap in the processing of apparently disparate functions such as vision, mood and pain (Miller & Ngo, 2007). However, in all of the above CVS rivalry experiments, it was clear the technique did not modulate rivalry in every subject tested (Miller et al., 2000; Ngo et al., 2007, 2008). Indeed, in two subsequent experiments, no significant group effects of predominance modulation were found following CVS (i.e., from either left- or right-hemisphere activation) (Ngo et al., 2007; Ngo, Blomberg, Liu, Pettigrew, & Miller, *submitted*).

The first of these experiments reported that CVS did not cause significant changes in predominance between the half-field percepts during multistable BR (Figure 3b). Multistable BR involves alternations between four different percepts: the two presented images (half-field rivalry) and two coherent images (coherence rivalry). Coherence rivalry is a phenomenon in which the brain synthesizes coherent aspects of each eye's image into coherent percepts with which to rival. First reported by Towne (1863) and then Díaz-Caneja (1928), this phenomenon attracted attention more recently through the work of Kovács, Papathomas, Yang and Fehér (1996), and was taken as evidence for rivaling stimulus representations rather than rivaling eyes during BR. In another study, stimulus representation rivalry was also supported by subjects reporting smooth and slow perceptual alternations during rivalry, despite the stimuli being rapidly swapped between the eyes (Logothetis, Leopold, & Sheinberg, 1996; so-called 'flicker-and-swap' rivalry). Ngo, Liu, Miller and Pettigrew (2000) showed that with Díaz-Caneja stimuli, coherent percepts occurred for around half the viewing time while half-field percepts (the same as those presented to each eye) occupied the remaining half (with some degree of individual variation in this temporal aspect). With this finding, and that of CVS modulating predominance of the coherent percepts, but not of the half-field percepts, Ngo and Miller (Ngo et al., 2007) developed a meta-rivalry model to explain interocular-grouping during rivalry (which may also extend to flicker-and-swap rivalry). This meta-rivalry model postulated that: (i) coherence rivalry occurs at a high level on an interhemispheric basis, (ii) half-field rivalry occurs at a low level on an intrahemispheric basis, and (iii) high-level stimulus rivalry and low-level eye rivalry themselves rival (i.e., meta-rivalry) for access to visual consciousness (see Figure 3b).

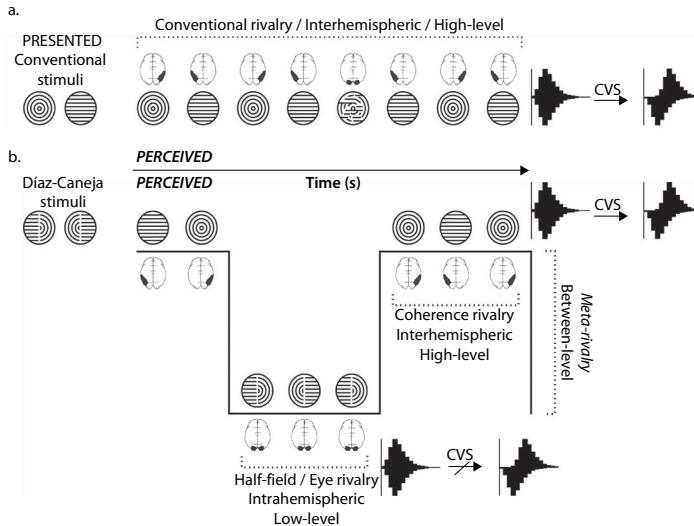


Figure 3. (a) The interhemispheric switch model of conventional BR and (b) the meta-rivalry model of interocular-grouping phenomena. (a) Unilateral activation induced by CVS modulates predominance during perceptual rivalry, thus supporting an IHS model of the phenomenon. CVS does not modulate rivalry predominance in all subjects however, or in all experiments, as depicted by the technique not inducing a significant change in group predominance with half-field/low-level rivalry (b), or with repeated CVS sessions to assess percept-to-hemisphere selection and retest reliability of predominance effects (see main text).

The second study in which CVS did not induce significant group predominance changes (Ngo et al., *submitted*) set out to investigate two aspects of the previous CVS data: (i) which hemisphere selects which percept during rivalry, and on what basis, and (ii) what the re-test reliability of CVS effects are, both generally and with respect to percept-to-hemisphere selection. To meet these objectives, Ngo employed a novel repeated-measures design involving multiple left-hemisphere CVS sessions within the same subjects, using three rivalry types: drifting horizontal/vertical BR, stationary oblique BR, and Necker-cube rivalry. Reproducibility of significant predominance change following CVS was found to be low both across the group and within individuals. Reproducibility was also low for the magnitude and direction of predominance changes. The substantial study-design differences in this experiment compared with the previous CVS rivalry studies may explain these negative findings, with possible habituation effects from repeated CVS. Further analyses of that data, based on such methodological considerations but limited by the consequent relatively low sample sizes, also revealed no significant group predominance change following CVS in any of the rivalry types (Ngo et al., *submitted*). Moreover, the negative findings made assessment of percept-to-hemisphere selection issues difficult, but scrutiny of group and individual data suggested that there was no apparent predilection for predominance to change in one or the other direction for any rivalry type. Interpreting the existing collection of CVS studies is discussed further below when the current status of the IHS model is considered.

Single-pulse TMS and perceptual disruption

Unlike CVS which induces relatively long-lasting unilateral hemisphere activation (approx. 10–15 min duration), and activates a wide network of inter-related cortical areas, single-pulse TMS (spTMS) induces short-term changes in brain activation in a more localized manner (though with possible secondary effects on connected neuronal populations). In the first application of the TMS technique to the study of rivalry (Miller et al., 2000), spTMS was delivered to temporo-parietal regions of the left hemisphere (given the CVS experiments' significant results with activation of this hemisphere), and caused disruption of underlying cortical activity. Therefore the key prediction for this experiment, on an IHS model, was that a TMS pulse timed to be delivered on a switch to one percept (the left hemisphere's percept, which could vary between individuals) would disrupt that percept, but that the same pulse (delivered at the same left hemisphere site) would have no effect when timed to occur on a switch to the *other* (the right hemisphere's) percept. Exactly this *phase-specific* pattern of spTMS effects was observed (Miller et al., 2000; see Figure 4).

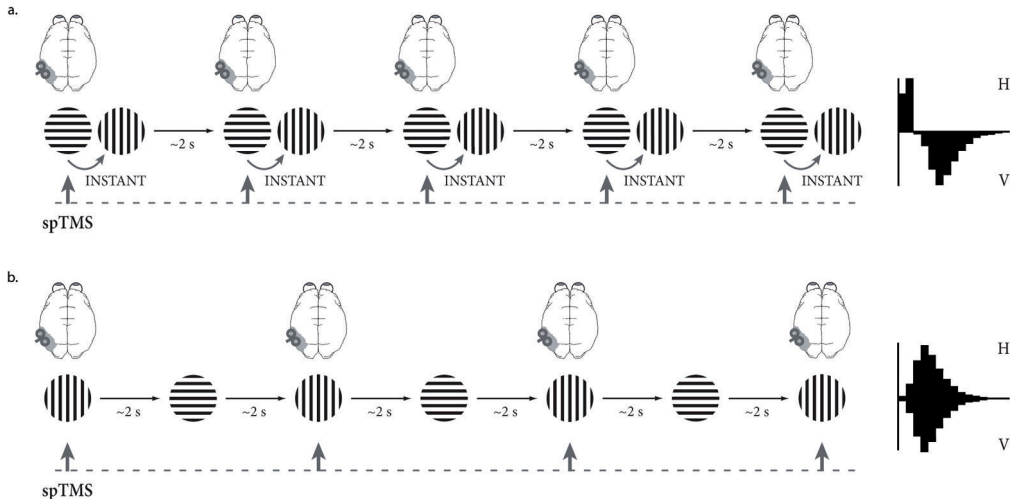


Figure 4. TMS evidence for the IHS model of rivalry. (a) spTMS delivered contingent on a subject's switch to the horizontal image immediately disrupted that percept, causing an instant switch to the other (vertical) rivaling percept. This phase-specific effect is shown in the frequency histogram with a substantial reduction in the perceptual interval duration for the horizontal image. (b) Response-contingent spTMS delivered when the same subject switched to the vertical percept had no corresponding effect, with regular rivalry alternations perceived. In some subjects the opposite pattern occurred (with disruption of the vertical but not horizontal percept; not depicted), and in 2 of 7 subjects, no perceptual disruption occurred. However, in 5 of 7 subjects, a phase-specific disruption effect (irrespective of direction) – the key prediction of an IHS model – was observed.

As might be expected, the predominance modulation observed in this original TMS experiment was far more dramatic than that seen in CVS experiments. The effect of CVS was visible in plotted frequency histograms of perceptual interval durations with (i) predominance induced where there was previously none, (ii) equalising of a previous predominance, or (iii) a previous predominance reversing its direction. However, the shape of the TMS frequency histograms on the other hand, reflected the immediate disruption of perceptual periods, i.e., causing very short percept durations for one of the rivaling images (see Figure 4). Moreover, as with the CVS experiments, the TMS data also revealed individual variation in response to stimulation. Two out of seven subjects did not exhibit the phase-specific perceptual disruption effects seen in the other five subjects. However, although the coil was always positioned broadly over temporo-parietal regions, there was no formal localization procedure employed, either stereotactically or with prior brain-imaging. Rather, the study's methods involved approximate positioning of the coil in temporo-parietal regions initially, followed by more detailed positioning based on trial and error (with the subject's verbal report of a disruption effect indicating the site for coil positioning for that subject's testing session). Whether non-responders would have showed an effect under more precise localization procedures is not clear. One aspect of this study that is clear however, is that the phase-specific effect could not be attributable to noise or motor artefacts, because for each subject, all aspects of the stimulation were held constant (cortical site, intensity, noise, motor artefact etc), with the only difference being the response-contingency triggering the TMS pulse.

The initial TMS rivalry study did not systematically investigate the effect of spTMS applied to *right*-sided temporo-parietal regions. Rather, as mentioned above, it concentrated on the left hemisphere due to the CVS experiments' significant results for this hemisphere. However, a few right-hemisphere pilot TMS sessions were conducted (data not reported in Miller et al., 2000), generally without phase-specific disruptions being observed. This mirrored the asymmetry seen in CVS experiments as described above. These CVS and TMS experimental asymmetries indicated that simple predictions of the IHS model – i.e., of equal and opposite effects from left- and right-hemisphere stimulation or disruption – were not observed, and hence that the relative hemispheric contributions to rivalry may be complex. Indeed, hemispheric asymmetries would a decade later be a feature of a series of studies on the effects on rivalry of repetitive TMS (rTMS), as discussed in the next section.

In a follow-up spTMS study, Funk and Pettigrew (2003) sought to examine whether the IHS model of BR and AFR also applied to another phenomenon that involved periodic appearance and disappearance phases – motion-induced blindness (MIB; Bonnef, Cooperman, & Sagi, 2001). As well as setting out to address

that issue, they sought to examine whether perceptual disruption effects could in fact be elicited with *right-hemisphere* TMS. Using a figure-of-eight coil delivering single pulses applied to the intraparietal sulcus (IPS) and superior parietal lobe (SPL), they employed two pulse-triggering conditions in the study. In one condition, as with the earlier study (Miller et al., 2000), the subject's report of the start of a perceptual phase triggered the pulse. This showed that MIB, like BR, exhibits phase-specific perceptual disruption when TMS is applied over the left hemisphere, thus suggesting that MIB may also be an IHS phenomenon. However, the converse effect from right-hemisphere stimulation was again difficult to elicit. This led to testing a second condition in which the TMS pulse was timed to occur 300 ms prior to an *expected* transition, with that expectation calculated according to baseline viewing (the period of MIB being relatively regular within individuals, as it is with BR). Although this timing strategy in effect yielded a TMS pulse that preceded, coincided with or followed a perceptual transition, the manipulation appeared to improve the ability of right-hemisphere parietal spTMS to induce phase-specific perceptual disruption (Funk & Pettigrew, 2003).

The third (and only other) spTMS study of rivalry conducted to date is that by Pearson, Tadin and Blake (2007). These investigators used a figure-of-eight coil over V1 and V2 centrally (thus stimulating both occipital cortices), with pulses triggered automatically every 3.2 seconds. When subjects viewed conventional BR and with analyses removing any effects time-locked to a pulse, the overall effect was a small increase in switch rate (observed in 5 out of 6 subjects), thought to possibly be an effect of arousal due to the TMS. More interestingly however, when analyses did examine time-locked effects, there was shown to be a disproportionately large number of perceptual switches that occurred following a TMS pulse (observed in all subjects). However, two important features of this effect were not reported: (i) whether the switch-inducing effect varied in a phase-specific manner as had occurred in previous studies (Funk & Pettigrew, 2003; Miller et al., 2000), and (ii) exactly what proportion of pulses were followed by a perceptual switch (discussed further below). Another main finding of Pearson et al.'s (2007) study was that there was a correlation between the time of onset of time-locked perceptual disruption effects and a subject's rivalry rate. Further, a control condition in which stimulus contrast was varied to alter a subject's rivalry rate showed that the TMS-induced modulation delay was linked to an individual's endogenous switch rate because the delay was independent of the contrast manipulations. Other controls employed in this study accounted for eye movements, auditory/tactile artefacts and transients that could potentially explain the data, though none of these factors were found to be relevant.

A further finding of the Pearson et al. (2007) study was that they repeated their protocol with flicker-and-swap rivalry. Under these stimulus conditions, as

described above, subjects reported perceiving smooth slow perceptual alternations rather than rapidly swapping images, indicating a likely high-level selection and stimulus representation process (Logothetis et al., 1996). When occipital TMS was applied during this rivalry type, the time-locked effects that the investigators had seen during conventional rivalry were not observed. This led Pearson et al. (2007) to argue that conventional rivalry and stimulus rivalry occur at discrete neural levels (i.e., low and high levels, respectively). This finding was partly in keeping with the proposal by Ngo et al. (2007) that the coherent percepts during Díaz-Caneja stimuli viewing (another type of stimulus representation rivalry) and half-field percepts with the same stimuli, occurred at discrete neural levels (see above and also chapter by Bressler et al., this volume). Indeed, Ngo et al. (2007) specifically argued that flicker-and-swap rivalry, as used by Pearson et al. (2007), might similarly engage the sort of meta-rivalry process proposed to mediate the perceptions with Díaz-Caneja stimuli and other interocular-grouping stimuli. However, Ngo et al. (2007) also maintained that conventional rivalry, in the absence of interocular-grouping or flicker-and-swap conditions, occurs via a fundamentally high-level IHS process. Given the IHS model does engage the notion of multi-level processing via feedback from high- to low-level regions (attentional selection mechanisms biasing pools of competing neurons; Miller, 2001), we consider it not entirely surprising that TMS applied to such low-level pools could also modulate perception, increasing the probability of inducing a switch by affecting input to, or the effect of feedback from, the higher levels. Another possibility is that conventional rivalry itself engages a meta-rivalry process, though further TMS data would be needed to explore that proposal. A summary of existing single-pulse TMS studies of rivalry is presented in Table 1.

Repetitive TMS and rate modulation

If interpretation of CVS and single-pulse TMS studies of rivalry is hampered by conflicting data (which by now should not be surprising given similar conflict in electrophysiological, brain-imaging and psychophysical data), the results of applying rTMS to rivalry have been even further conflicting. We provide a summary in Table 1 of rTMS rivalry studies, the methodologies employed including stimulation parameters and sites targeted, and the findings of each study. As noted in the chapter by Thomson and Fitzgerald (this volume), rTMS differs from spTMS in that repeated stimulation can progressively alter the activity of neuronal populations during the course of stimulation and for some time after its cessation. The technique has localized effects on the targeted brain regions and associated neuronal populations (like spTMS), with the perceptual outcome being partly dependent on the stimulation protocol that is employed (see below).

As shown in Table 1, studies have focussed on rTMS of the SPL and found that depending on various methodological aspects, rivalry switch rate can be increased or decreased following rTMS, including with BR, an ambiguous SFM rotating sphere and a bistable spinning wheel illusion (SWI; which induces alternating directions of motion perception). Using the SWI, Iramina and colleagues (Ge, Ueno, & Iramina, 2007a, 2007b, 2008) focussed on the SPL based on findings from previous brain-imaging studies of rivalry (Lumer et al., 1998; Sterzer, Russ, Preibisch, & Kleinschmidt, 2002). This work was the first of a series of experiments by this group, which are discussed in more detail below.

Using a bistable SFM rotating sphere, Kanai, Bahrami and Rees (2010) examined the effect of rTMS on switch rate by targeting the posterior SPL. rTMS was applied in between periods of rivalry recording to left SPL and right SPL (with the vertex as control) in separate sessions using a continuous theta-burst stimulation protocol (i.e., 3 pulses at 50 Hz, every 200 ms for 40 s). Rivalry rate was found to be significantly slower following rTMS of either left or right SPL. Using structural brain-imaging and diffusion tensor imaging (DTI), this study also examined rivalry rate in relation to measures of cortical thickness, local grey matter density and local white matter integrity. Cortical thickness of bilateral SPL and bilateral post-central gyrus (but not any other brain area, including prefrontal regions) was found to be negatively correlated with percept duration, i.e., the thinner the cortex, the slower the switch rate. In relation to grey matter density and white matter integrity, bilateral SPL similarly showed this association with alternation rate. These brain-imaging findings suggested SPL structure could account for the wide inter-individual variation observed in rivalry rate. The authors also note the overlap of their identified relevant regions and those subserving attention and attention-switching functions, and consider the possibility that feedback from SPL to lower regions is the mechanism of influence (i.e., the larger the SPL, the stronger the feedback signal to switch and hence the faster the switch rate). The authors base their conclusions on an inhibition-based interpretation of their protocol.

In a follow-up study of rTMS on rivalry rate, Carmel, Walsh, Lavie and Rees (2010) used drifting BR stimuli to examine the effect of 1Hz pulses targeted at SPL. In contrast to the previous study (Kanai et al., 2010) however, they found that following rTMS of right SPL (cf. left SPL and no-TMS conditions), there was an *increase* in the rate of perceptual switches. The authors consider their stimulation protocol to be inhibitory and that the right SPL maintains a perceptual state (hence disrupting it leads to faster switch rate). The authors also provide an attention-based interpretation of their findings involving feedback from the right SPL to lower visual regions (i.e., impairing this maintenance function leads to a weaker top-down signal, making it easier for the suppressed image to overcome suppression).

Table 1. Summary of TMS studies of visual rivalry

Study	N	Stimulus-type	TMS type	Region	Key methodological points	Effects
Miller et al. (2000)	7	Stationary BR	Inhibitory spTMS; 0.66–1 T.	Left TPC.	Online; spTMS time-locked to reported reversal, triggered by button press indicating switch; No-TMS (control).	– Phase-specific spTMS disruption in 5/7 observers.
Funk & Pettigrew (2003)	13	MIB	Inhibitory spTMS; 50–70% of RMT.	Bilateral IPS/SPL.	Online; in one condition, triggered according to report; in another, triggered based on response pattern from baseline recording; 4 trials/region.	– Phase-specific left spTMS disruption; Right spTMS <300 msec prior to an expected transition improved phase-specific disruptive effect for this hemisphere.
Pearson et al. (2007)	6 5	Stationary BR Eye-swap BR	Inhibitory spTMS; 51–83% of maximum 1.8 kV.	Midline V1/V2 (central & peripheral phosphenes).	Online; spTMS computer-triggered at predetermined interval; Every 3.2 s; No-TMS (control); 3 trials/region.	– Midline V1/V2 spTMS increased switch rate in BR by 300 ms (10%) in 5/6 observers; this time-locked effect was not observed in eye-swap BR. – Subjects with slower switch rate experienced more delayed TMS effects – More perceptual switches following TMS pulse; but did not examine (i) if this was phase-specific or (ii) proportion of pulses followed by perceptual switch. – Positive correlation between onset of perceptual disruption effect & switch rate for stationary BR only.
Ge et al. (2007b) ¹	8	SWI	Inhibitory rTMS; 90% of RMT.	Right SPL, posterior TL.	Offline; Computer-triggered rTMS before stimulus viewing; 60-pulse & 240-pulse; 60 s; 1 Hz; No-TMS (control); 1 trial/region.	– Right SPL 60-pulse rTMS increased switch rate. – Right SPL 240-pulse rTMS decreased switch rate.

¹ These findings included 7 previous subjects' data reported in Ge et al. (2007a). The decrease in switch rate finding was subsequently shown in 4 more subjects (Ge et al., 2008).

Study	N	Stimulus-type	TMS type	Region	Key methodological points	Effects
Nojima et al. (2010a) ²	11	SWI	Inhibitory & excitatory rTMS ³ ; 90% of RMT.	Right SPL, posterior TL.	Offline; Computer-triggered rTMS before stimulus viewing; All rTMS types delivered consecutively over each brain region; 0.25 Hz 60-pulse & 0.25/0.5/1 Hz 120-pulse; No-TMS (control).	– Right SPL 0.25 & 1 Hz⁴ 60-pulse rTMS increased switch rate. – Right SPL 1 Hz 240-pulse rTMS decreased switch rate⁴. – No right SPL 0.25/0.5/1 Hz 120-pulse rTMS effects.
Nojima et al. (2011a) ⁵	11	SWI	Inhibitory & excitatory rTMS; 90% of RMT.	Right SPL, posterior TL.	Offline; Computer-triggered rTMS before stimulus viewing; Biphasic; 0.25 Hz 60/120-pulse, 0.5 Hz 60/120-pulse, 1 Hz 60/120/240-pulse. 90% of RMT; > 120-pulse is inhibitory based on reduced MEP amplitude; No-TMS (control).	– Right SPL 0.25/0.5/1 Hz 60-pulse rTMS increased switch rate. – Right SPL 1 Hz 240-pulse rTMS decreased switch rate. – No right SPL 0.25/0.5/1 Hz 120-pulse rTMS effects.
de Graaf et al. (2011)	10	SFM	Inhibitory; rTMS; 110% of RMT.	Right posterior PC, dorsolateral PFC, OP, hMT/V5.	Offline; Passive viewing & voluntary control conditions; Computer-triggered rTMS in between stimulus viewing; Biphasic; 300-pulse; 5 mins; 1 Hz 300-pulse; 2 trials/region.	– Right dorsolateral PFC rTMS reduced dominance duration during SFM voluntary control condition, with PC rTMS showing only trend effects. No OP or hMT/V5 rTMS effect on SFM voluntary control condition. – No PC, PFC, OP or hMT/V5 rTMS effect on passive viewing.
Carmel et al. (2010)	6	Drifting BR	Inhibitory ⁶ rTMS; 90% of RMT.	Bilateral anterior SPL	Offline; Computer-triggered rTMS before stimulus viewing; 30 mins; 1 Hz; No-TMS (control); 1 trial/region.	– Right SPL rTMS increased switch rate. – No effect on switch rate by left SPL rTMS.

² Paper also published in Japanese (Nojima et al., 2010c).

³ It was reported that the number of pulses rather than frequency accounted for the results, following a previous similar study which employed slight variations in the rTMS protocols (Nojima et al., 2010b).

⁴ Analyses included the previous data from Ge et al. (2007b, 2008).

⁵ This study has also been presented elsewhere (Nojima et al., 2011b).

⁶ This TMS protocol is considered by Zaretskaya et al. (2010) to have an excitatory effect.

Study	N	Stimulus-type	TMS type	Region	Key methodological points	Effects
Zaretskaya et al. (2010)	15	House/face BR	Inhibitory rTMS ⁷ ; 120% of RMT.	Bilateral posterior PC, SPL, anterior IPS.	Online; Order of stimulation randomised within & across sessions in each subject; rTMS computer-triggered; Biphasic; 9–15 trains; 2 Hz; Vertex (control); 3 trials/region; 1–2 sessions.	– Individual variation in baseline lateralized activation (left/right SPL & IPS) during rivalry transitions. – Right anterior IPS rTMS significantly decreased switch rate cf. left anterior IPS rTMS decreasing switch rate according to individual transition-related lateralized activation. – Greater baseline lateralization associated with greater lateralization of IPS rTMS effect on switch rate.
Kanai et al. (2010)	10	SFM	Inhibitory continuous theta-burst rTMS; 45% of stimulator output.	Bilateral posterior SPL.	Offline; Computer-triggered rTMS in between stimulus viewing; 40 s; 50 Hz 3-pulse; 200 ms intervals; Vertex (control); 1 trial/region.	– Right & left SPL rTMS decreased switch rate.
Kanai et al. (2011)	8	SFM	Inhibitory continuous theta-burst rTMS; 40% of stimulator output.	Right anterior SPL.	Offline; Computer-triggered rTMS in between stimulus viewing; 3-pulse; 40 s; 50 Hz at 200 ms intervals; Vertex (control); 1 trial/region.	– Right anterior SPL rTMS increased switch rate.

⁷ Evidence from Arai et al. (2005) suggests an excitatory effect of this type of rTMS protocol may also be likely as biphasic rTMS tends to activate both inhibitory and excitatory neurons (cf. monophasic rTMS).

spTMS: single-pulse transcranial magnetic stimulation; rTMS: repetitive transcranial magnetic stimulation.

MIB: motion-induced blindness; SWI: spinning wheel illusion; SFM: structure-from-motion bistable motion illusion; BR: conventional binocular rivalry.

All rivalry stimuli passively viewed unless otherwise stated.

RMT: resting motor threshold.

TPC: temporo-parietal cortex; PC: parietal cortex; IPS: intraparietal sulcus; PFC: prefrontal cortex; OP: occipital pole; hMT/V5: human middle temporal/V5 complex; V1/V2: early visual cortex.

Another study of rTMS effects on rivalry employed fMRI to first identify brain regions that were associated with the perceptual alternations (Zaretskaya, Thielscher, Logothetis, & Bartels, 2010). By comparing rivalry to replay activation scans, left and right SPL along with left and right anterior IPS were identified, with nine subjects showing right-lateralized activity during BR while six other subjects showed left-lateralized activity in these regions. In all subjects, 2Hz continuous rTMS was subsequently applied to these four parietal areas during BR viewing (with the vertex as control). TMS-induced inhibition of right IPS was found to significantly decrease rivalry rate, whereas no significant effect of left-sided TMS was found overall. However, when the TMS data were examined according to individual subject's lateralized activation identified with fMRI, left-sided rTMS of IPS was also found to decrease rivalry rate. The investigators concluded that IPS, mainly in the right hemisphere, has a destabilizing function on perceptual continuity in BR, in accordance with its role in perceptual selection, including with respect to attention. They also note that their TMS data were consistent with Kanai et al.'s (2010) findings, despite the use of different rivalry types and stimulation protocols (i.e., online cf. offline rTMS). Other methodological differences (cf. Carmel et al., 2010; Kanai et al., 2010) that were highlighted included pulse frequency, duration of TMS, effect on cortical activity (i.e., facilitatory rather than disruptive; Carmel et al., 2010), small sample size (Carmel et al., 2010), and the lack of a vertex control condition (Carmel et al., 2010; i.e., not controlling for arousal with the no-TMS condition).

To resolve the conflicting findings concerning rTMS effects on switch rate between two previous studies mentioned above (Carmel et al., 2010; Kanai et al., 2010), Kanai, Carmel, Bahrami and Rees (2011) employed a more precise structural imaging approach to first identify sub-regions within right SPL for subsequent testing with TMS. Using a SFM rotating sphere, they found that grey matter density in right anterior SPL was positively correlated with switch rate, in contrast to their previous finding of the opposite association in posterior SPL (Kanai et al. 2010). They also showed that rTMS applied to anterior SPL (with the vertex as control) resulted in decreasing percept duration (i.e., faster switch rate), which was consistent with the findings of Carmel et al. (2010), but in contrast to those of Kanai et al. (2010) who targeted posterior SPL. These authors argued that the previous discrepant results were unlikely to be due to different neural bases for different forms of perceptual bistability or to dissimilar stimulation protocols. Rather, they considered the conflicting results as reflecting a fractionation of parietal cortex function, such that different regions within parietal cortex play opposing roles in the control of bistability. They also note that their findings are in contrast to Zaretskaya et al.'s (2010), who found that *online* rTMS applied to a region of SPL close to an area they targeted with *offline* rTMS, instead decreased

the rate of perceptual alternations, which could therefore be due to stimulation protocol differences between the studies.

The issue of protocol differences when comparing results from TMS studies is complex (e.g., de Graaf & Sack, 2011; Sandrini, Umiltà, & Rusconi, 2011). As indicated in Table 1, it is not always clear whether a TMS protocol is excitatory or inhibitory, and as outlined in the chapter by Thomson and Fitzgerald (this volume), individuals vary in their response to TMS. Comparisons are further complicated by the fact that reference to, and interpretation on the basis of, differences in one methodological element may only be relevant if all other methodological elements are held constant in the studies compared, which is often not the case. These issues make interpretation of conflicting TMS studies difficult and indicate that further studies will be required to examine cortical contributions to rivalry and its modulation (see also chapter by Sterzer, this volume). Studies such as those by Kanai et al. (2011), in which rTMS protocol elements were held constant and only cortical targets were varied, and by Miller et al. (2000), in which cortical site was held constant and only response-contingency was varied, are particularly informative in light of the methodological and protocol interpretation complexities associated with perceptual TMS research.

Another rTMS protocol issue that has been raised comes from studies using the SWI. Nojima et al. (2010a, 2010c, 2011a) examined the effect of differential rTMS protocols on SWI switch rate. These investigators applied rTMS trains varying in stimulation frequency and pulse number to the right SPL and right posterior temporal lobe. Pooling data reported in their previous studies (Ge et al., 2007b, 2008), they found that 1 Hz 240-pulse rTMS to the right SPL (cf. right posterior temporal lobe TMS and no-TMS conditions) significantly decreased switch rate. In contrast, rTMS to the right SPL using 60-pulse protocols significantly increased switch rate, whereas no effects were observed with 120-pulse protocols. The investigators interpreted these differential pulse-based results on the basis of previously reported biphasic rTMS effects (i.e., activation of both facilitatory and inhibitory neurons), suggesting that the rTMS protocol which decreased switch rate indicated inhibition of brain activity, and vice versa. However, the very high degree of voluntary control that we observe to be exercised over the SWI suggests these findings require confirmation with types of rivalry that are less amenable to voluntary control. Indeed, direct exploration of the effect of TMS on voluntary control during rivalry is informative and was examined by de Graaf, de Jong, Goebel, van Ee and Sack (2011). These investigators assessed the role of frontal cortical areas (classically implicated in attentional processing) using a SFM rotating sphere. They found that right-hemisphere rTMS applied to dorsolateral prefrontal cortex, the posterior parietal cortex, occipital pole and hMT/V5 had no significant effect on switch rate during passive viewing, but when subjects were

asked to voluntarily speed up switch rate, rTMS to right dorsolateral prefrontal cortex significantly impaired this control. These findings led to the proposal that a specialized mechanism exists for voluntary control during bistable perception (cf. spontaneous alternations during passive viewing; see also chapter by Sterzer, this volume).

Status of the IHS model

The TMS data just described are illuminating with respect to the CVS data discussed earlier and the IHS model of rivalry. Although the initial series of CVS experiments provided support for the IHS model, all with an identical asymmetry of modulation effects, more recent CVS experiments did not find significant predominance changes. While perhaps due to design issues, and while the consistent asymmetry observed in the first series of experiments would be remarkable to have occurred by chance, it could be argued that support for the IHS model in light of the recent CVS negative findings is questionable. However, we point out that the history of BR and AFR research, particularly with respect to mechanisms, has been one of evidence-based claim and counter-claim, exhibited most dramatically in the last decade by the electrophysiological and brain-imaging findings as discussed above (Blake & Logothetis, 2002; Keliris et al., 2010; Sterzer, Kleinschmidt, & Rees, 2009; Tong, Meng, & Blake, 2006). Similar conflicting data were evident in the recent series of rTMS studies of parietal cortex regions. It is thus hardly likely to expect a single experimental success or failure to conclusively resolve issues of perceptual rivalry mechanisms.

Moreover, the spTMS data showing a phase-specific perceptual disruption pattern cannot be explained on anything but an IHS model (which is perhaps why alternative explanations for this effect have not been forthcoming). In addition, the spTMS and rTMS data have shown, along with earlier brain-imaging findings, that the asymmetries observed in the early series of CVS experiments are very likely veridical, given the reports of asymmetries in the ability of left versus right-hemisphere TMS to modulate rivalry. In our view, mechanistic understanding of rivalry will benefit from further detailed and targeted TMS studies, particularly using single-pulse, online, phase-specific protocols with pulses applied at various processing regions, including high and low levels, unilaterally and even bilaterally (i.e., two coils). Additional brain-stimulation techniques may also be employed in the future, such as intracranial stimulation during surgery in humans (Mukamel & Fried, 2012) and microstimulation in primates (see chapter by Sengpiel, this volume). Stimulation at multiple sites and combined stimulation/recording protocols may prove to be particularly informative.

There has to date been only one independent attempt to falsify the IHS model of rivalry, by examining BR in subjects with a split brain (O'Shea & Corballis, 2001, 2003, 2005a, 2005b). These experiments showed that each disconnected hemisphere can experience its own rivalry (interestingly, at different rates), thus challenging the IHS model. However, this approach was not grounds for abandoning the IHS model, for several reasons that have been outlined in detail elsewhere (Miller, 2001; Ngo et al., 2007; Pettigrew, 2001). One such reason entailed Pettigrew and Miller's specific *prediction* that rivalry would survive callosotomy (Miller et al., 2000) because the IHS process was considered to be driven by a subcortical oscillator and not by the corpus callosum. This notion of a subcortical oscillator was proposed by Pettigrew and elaborated upon in a subsequent paper (Pettigrew, 2001; see Figure 1).

Miller's elaboration of the IHS model on the other hand, focussed on attentional mechanisms. This included how a subcortical oscillator and/or top-down activity might act, as mentioned above, via attentional processes that bias competition between populations of neurons, or response synchronization therein (Miller, 2001). He thus proposed that interhemispheric switching involves a process of *alternating unihemispheric attentional selection*. On this account, two further proposals included (i) an additional attention-based explanation for the asymmetry of CVS modulation effects, and (ii) the callosum not being entirely irrelevant to interhemispheric switching during rivalry. In relation to the latter, though inconsistent with the data from split-brain BR experiments, this is consistent with a report of slow AFR rate in subjects with callosal agenesis (Fagard et al., 2008). However, while studies have shown that aspects of bistable perception with the motion quartet and binocular rivalry are linked, respectively, to microstructural properties of specific callosal regions connecting human MT/V5 (Genç, Bergmann, Singer, & Kohler, 2011) and V1 (Genç, Bergmann, Tong, Blake, Singer, & Kohler, 2011), such findings rely on the use of stimuli that dynamically integrate across the two visual hemifields. Callosal microstructural properties (other than agenesis) have not as yet been assessed with respect to small, central rivalry stimuli that do not engage dynamic cross-hemifield integration. Examining correlations of rivalry rate using small, central stimuli with structural and DTI measures of callosal regions connecting cortical attentional regions would be an informative line of future research for assessing the IHS model, the callosum's role therein, and factors determining individual variation in rivalry rate (as has occurred for SPL; see above).

Also raised in Miller's elaboration of the IHS model was the distinction between mechanisms of attentional selection and mechanisms of visual consciousness during rivalry, and between mechanisms of attentional selection and mechanisms of feature representation (or between the 'sites' and 'sources'

of attentional selection; Miller, 2001). By refining the notion of 'alternating hemispheric activation' to include the possibility of 'alternating unihemispheric attentional selection', and considering the distinction between neural mechanisms of attentional selection and those of visual consciousness, Miller (2001) noted that brain-imaging or electrophysiological data showing neural activity that is synchronous across the hemispheres would not necessarily argue against an IHS model. Rather, the key observation of interhemispheric switching during rivalry would be the presence of hemispherically asynchronous activity (even if in other cortical regions, hemispherically synchronous activity was observed). There have been suggestions of just such asynchronous activity in a number of brain-imaging studies with centrally located stimuli (Brouwer, Tong, Schwarzbach, & van Ee, 2005; Freeman, Sterzer, & Driver, 2012; Hsu, Yeh, Tien, & Lin, 2008; Kamphuisen, Bauer, & van Ee, 2008), though without explicit reference to the IHS model. Alternating hemispheric activation has also been shown in a brain-imaging study using an AFR stimulus that was horizontally elongated across the two hemifields (Slotnick & Yantis, 2005), however this finding may be purely due to the hemifield aspect rather than alternating unihemispheric attentional selection.

Most recently, direct electrophysiological evidence of an IHS mechanism underlying perceptual rivalry has been demonstrated in *Drosophila* (Tang & Juusola, 2010). This involved counterphase (left-right) alternations in unilateral optic lobe spiking and LFP activity, in accordance with the fly's rivalry-like left-right switching behavior during dichoptic presentation of orthogonally moving stimuli (see Figure 6). We return to this *Drosophila* model of rivalry in the last section.

On the issue of the status of the IHS model of rivalry, we have noted two recurring comments in the literature and in discussion with colleagues and other investigators. The first is that the IHS model appears unable to be tested. We argue quite the opposite, holding that instead the model is one of the most readily testable in the literature (e.g., see Miller, 2001; Ngo et al., 2007). Electrophysiology, brain-imaging and brain stimulation methods can all be applied to its examination, though some care needs to be taken in the procedures used and conclusions made, given the multitude of conceptual and methodological complexities detailed in this chapter and previous papers. The second common comment we encounter is that the model is unlikely. This is despite the fact that in recent years, comparative evidence for IHS phenomena has been steadily growing.

In our view, biological IHS precedents make claims of the unlikelihood of the IHS model of rivalry less defensible. Indeed, the existing and emerging human and animal IHS literature raises an important conceptual and methodological issue: is interhemispheric switching a generally under-investigated neurophysiological principle in organisms with brain structures that are paired across the midline?

The list of biological IHS phenomena now includes: (i) slowly alternating unihemispheric activity in humans (Bemelmans, Heijdanus, Jansen, & Rietveld, 1984; Shannahoff-Khalsa, Gillin, Yates, Schlosser, & Zawadzki, 2001; Werntz, Bickford, Bloom, & Shannahoff-Khalsa, 1983); (ii) alternations between relative left and right nasal patency (the nasal cycle) in humans and other species (Eccles, 2000; Kikuta, Kashiwadani, & Mori, 2008; Sobel, Khan, Saltman, Sullivan, & Gabrieli, 1999); (iii) alternating unihemispheric EEG activity during REM sleep in humans (Imbach et al., 2012); (iv) alternating unihemispheric slow-wave sleep in birds and aquatic mammals (Fuchs, Maury, Moore, & Bingman, 2009; Low, Shank, Sejnowski, & Margoliash, 2008; Lyamin, Manger, Ridgway, Mukhametov, & Siegel, 2008; Rattenborg, Lima, & Amlaner, 1999); (v) independent alternating eye movements in the sandlance and chameleon (Pettigrew et al., 1999); (vi) birdsong production (Long & Fee, 2008; Wang, Herbst, Keller, & Hahnloser, 2008); and (vii) alternations between left and right suprachiasmatic nucleus electrophysiological activity and *Per* mRNA expression in rodents (de la Iglesia, Meyer, Carpino, & Schwartz, 2000; Ohta Yamazaki, & McMahon, 2005; Schaap, Albus, Eilers, Détári, & Meijer, 2001; Yan, Foley, Bobula, Kriegsfeld, & Silver, 2005). To this list can now be added, direct electrophysiological evidence for an IHS mechanism underlying perceptual rivalry in *Drosophila* (Tang & Juusola, 2010; Miller et al., 2012). Thus we continue to argue for a multi-pronged attempt to examine the IHS model of human rivalry, employing brain-imaging, electrophysiological and brain stimulation methods, in the hope of arriving at its verification or falsification.

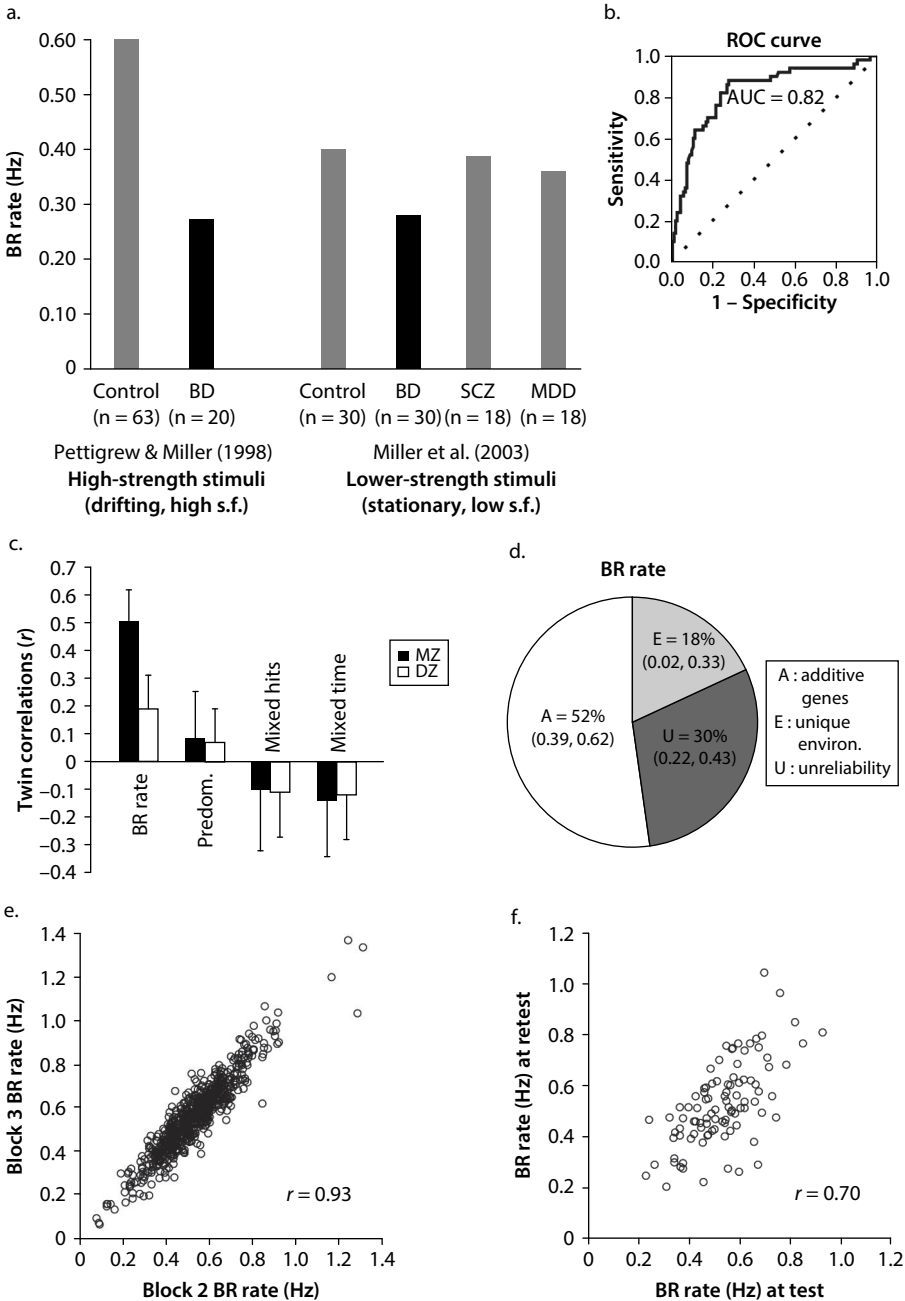
Clinical, genetic and molecular aspects of rivalry

On the first day of testing the IHS hypothesis with CVS, Pettigrew and Miller serendipitously observed that the rate of BR was notably slower in a subject with BD. They pursued this observation and confirmed in two studies (Miller et al., 2003; Pettigrew & Miller, 1998) that BD was indeed associated with slow BR rate (Figure 5a). The slow BR finding was evident in BD subjects who were well at the time of testing, suggesting that it may represent a trait (as opposed to state) marker of the disorder. It also did not appear to reflect the type of medication being taken by the subject and in some cases was evident in un-medicated subjects. Slow BR rate was also not found in groups of subjects with schizophrenia or major depression, disorders which can often be difficult to distinguish from BD. On this basis, and given BD is known to be strongly heritable, Pettigrew and Miller proposed that slow BR rate may serve as a useful 'endophenotype' for BD (discussed further below). Consistent with their empirical findings, and

again supporting the notion of common neural mechanisms of BR and AFR, it was reported in the early 20th Century (Ewen, 1931; Hunt & Guilford, 1933), that Necker-cube rivalry was slower in BD ('manic depression') compared with controls and subjects with schizophrenia ('dementia Praecox'). Since Pettigrew and Miller's reports, there have been three independent replication studies of the basic finding of significantly slower rivalry rate in BD relative to controls, two using BR (Nagamine, Yoshino, Miyazaki, Takahashi, & Nomura, 2009; Vierck et al., 2013) and one using a bistable SFM rotating sphere (Krug, Brunskill, Scarna, Goodwin, & Parker, 2008).

The finding of slow BR in BD was utilized by Pettigrew and Miller (1998) to propose a detailed pathophysiological model of BD (the 'sticky switch' model), that also incorporated the IHS model of rivalry. This BD model involved a series of conceptual postulates that are detailed in Figure 1. Through a mixture therefore, of observation, hypothesis, experimentation, serendipity and conceptual development, Pettigrew and Miller were indeed able to link the notion of interhemispheric switching to the extreme mood *alternations* seen in BD. Their model entailed the notion of anterior hemispheric activation asymmetries underlying mania (greater relative left activation) and depression (greater relative right activation). The model also drew upon brain-imaging, hemisphere-inactivation, lesion, electrophysiological and rTMS studies (e.g., see citations in Pettigrew & Miller, 1998), with the latter showing that right-hemisphere application was required to treat mania (Grisaru, Chudakov, Yaroslavsky, & Belmaker, 1998) while left-hemisphere application was required to treat depression (Pascual-Leone, Rubio, Pallardó, & Catalá, 1996). The model also explicitly predicted hemisphere-specific mood-modulating effects from CVS, which have since been confirmed for mania, albeit in two case studies to date (Dodson, 2004; Levine et al., 2012).

Quite apart from aiding Pettigrew and Miller in their development of a BD pathophysiological model, the empirical finding of slow BR in BD has sparked renewed interest in the issue of individual variation in rivalry rate. It has long been known that rivalry rate exhibits wide individual variation but is relatively stable within individuals (e.g., Aafjes, Hueting, & Visser, 1966; Borsellino, de Marco, Allazetta, Rinesi, & Bartolini, 1972; Enoksson, 1963; Ewen, 1931; George, 1936; McDougall, 1906) (see also chapter by Wade & Ngo, this volume). The AFR studies mentioned above show that in the first half of the 20th Century, individual variation in perceptual rivalry was investigated from a clinical psychiatric perspective (Ewen, 1931; Hunt & Guilford, 1933). However, there was relatively little interest in this line of research again until decades later. Similarly, until the 1960s there was interest in examining individual variation in rivalry parameters (e.g., Bagby, 1957; Crain, 1961; Frederiksen & Guilford, 1934), but this approach waned thereafter (though with some interest in AFR with respect to psychiatric



conditions; e.g., Gorenstein, Mammato, & Sandy, 1989; Meldman, 1965). Most recently, and as described in detail above, the issue of individual variation in rivalry rate has been utilized in brain-imaging and rTMS studies. Thus, cortical thickness in SPL and other measures were shown to correlate with rivalry rate, while rTMS to this region modulated rivalry rate (Kanai et al., 2010). These authors also noted that cortical thinning of SPL had been shown in BD (Lyyo et al., 2006), consistent both with their findings and with the finding of slow BR in BD.

Again renewing interest in individual variation of BR rate, and to pursue investigation of the trait as a potential endophenotype for BD, a large twin study was embarked upon by Pettigrew and Miller in collaboration with genetic epidemiology researchers, Nick Martin and Margie Wright (Miller et al., 2010; Figure 5c, d, e, f). That approach sought to examine the heritability of individual variation in rivalry rate and found that additive genetic factors accounted for more than 50% of the variance in rivalry rate (with monozygotic twins, who have identical genotypes, showing significantly higher concordance of BR rates than dizygotic twins, who share only half of their genetic make-up). The remainder of the variance was accounted for by unique environmental factors (18%) and measurement unreliability (30%). This twin study involved a sample size of 722 individuals and is the largest published population dataset of any rivalry type. It conclusively showed the previously-reported wide individual variation in BR rate, and further that an individual's rate is very highly reliable within testing sessions ($r = 0.93$; $N = 722$) and highly reliable between tests, 2 years apart ($r = 0.70$; $N = 97$). This study was followed by a smaller twin study (Shannon, Patrick, Jiang, Bernat, & He, 2011) which confirmed the heritability finding for BR rate and reported a similar finding for AFR (with the Necker cube).

Figure 5. (a) Slow BR rate in BD. The bars show the central tendency of BR rate for each group (medians in Pettigrew and Miller, 1998; means in Miller et al., 2003). These studies suggest that high-strength BR stimuli distinguish BD subjects from non-BD subjects better than lower-strength stimuli (s.f. = spatial frequency). (b) An ROC (receiver operating characteristic) curve of high- and lower-strength stimuli, generated from subjects' data in Figure 5a with BD as 'positive' and controls, schizophrenia (SCZ) and major depressive disorder (MDD) as 'negative'. The area under the curve (AUC) of 0.82 indicates that from random selection of a pair of subjects in Figure 5a, 82% of individuals would be correctly identified as a BD subject or a non-BD subject on the basis of their BR rate. A large-scale heritability study of BR (Miller et al., 2010) demonstrated the following: (c) monozygotic (MZ) vs dizygotic (DZ) twin correlations for BR rate were significant but not for other BR measures; (d) genetic modeling analyses indicated a substantial genetic contribution to individual variation in BR rate; (e) wide individual variation and very high within-session reliability of BR rate; and (f) high between-session (retest) reliability of BR rate.

Demonstration of substantial genetic contribution to individual variation in BR rate adds support to the notion of using slow BR as an endophenotype for BD. Endophenotypes are biomarkers that are 'intermediate' between genotype and phenotype (reviewed in Gottesman & Gould, 2003; Gould & Gottesman, 2006; Hasler, Drevets, Gould, Gottesman, & Manji, 2006). They are useful in studies of complex genetic disorders, such as BD, because they can accurately mark an affected genotype even though the individual may not have yet manifested (or indeed, may never manifest) the clinical disorder. By improving the accuracy of classifying affected (at-risk) and unaffected (not at-risk) genotypes in this way, endophenotypes can increase the power of genome-wide association studies which aim to identify disease-causing genes (Kendler & Neale, 2010). Toward this end, we and our genetic epidemiology and clinical psychiatry colleagues have recently established a multi-center study to collect BR data and DNA samples from several different subject groups (i.e., BD Type I, BD Type II, schizophrenia, major depressive disorder, relatives of bipolar probands, and healthy controls; Ngo, Mitchell, Martin, & Miller, 2011). By collecting BR data from large numbers of clinical psychiatric subjects, this multi-center study will also enable assessment of the potential diagnostic utility of slow BR rate, such as in distinguishing psychosis due to BD from that due to schizophrenia, and depression due to BD from that due to major depressive disorder (in both cases, with treatment implications; Ngo et al., 2011; see Figure 5b).

For a trait to be an endophenotype, it must meet key criteria (Gottesman & Gould, 2003; Kendler & Neale, 2010): (i) high association with the condition (high sensitivity), (ii) high heritability, (iii) high reliability, (iv) be unaffected by clinical state (and medication), (v) co-segregate with illness in families, and (vi) be observed in first-degree relatives of probands more commonly than in the general population. Our studies have shown that the BR rate trait appears to satisfy the first three criteria (Miller et al., 2003, 2010; Pettigrew & Miller, 1998). Our data, and work by others (Nagamine et al., 2009), also suggested that state and medication did not account for slow BR (see also Ngo et al., 2011) though these factors required further assessment.

In a recently published study, further independent evidence has been demonstrated for slow BR rate as an endophenotype for BD. In a large sample of 96 BD subjects, Vierck et al. (2013) recorded BR rate, a range of clinical variables and several cognitive functioning measures. The BD subject group consisted of 71 participants with BD-I, 22 with BD-II and 3 with BD-not otherwise specified (the latter two groups being collapsed into a bipolar spectrum disorder group). Compared to a small group of healthy controls ($N = 24$), the BD-I and bipolar spectrum disorder groups both had significantly slower BR rates, whereas there was no difference in BR rate between the two BD subgroups. Furthermore, it

was found that medication, depressive mood state, lifetime comorbid psychiatric diagnosis, and diminished cognitive functioning were not associated with slow BR rate in the BD subjects, and hence could not explain the trait. Ultimately however, testing BR rate in large numbers (i.e., hundreds to thousands) of clinical subjects, control subjects and family members is required to confirm the endophenotype criteria listed above (Ngo et al., 2011).

In addition to potential genetic and clinical psychiatric diagnostic utility, the findings of slow BR in BD and of genetic contribution to individual variation in BR rate, suggest new mechanistic approaches to investigating rivalry and its modulation. Thus, examining molecular aspects of BR will not only help to understand pharmacological modulation of the phenomenon, but also provide further mechanistic clues. It has been reported for example, that both noradrenergic and serotonergic systems are relevant to rivalry (Carter et al., 2005; Einhäuser, Stout, Koch, & Carter, 2008; Nagamine, Yoshino, Miyazaki, Takahashi, & Nomura, 2008; see also Bressler et al., this volume). Indeed since then, the candidate gene approach has been applied to rivalry, in both visual and auditory domains, showing that serotonergic genes are relevant to the former and dopaminergic genes to the latter (Kondo et al., 2012). While these findings may not themselves reveal key mechanisms of rivalry, they provide pieces of the mechanistic puzzle that may ultimately be revealing. For instance, candidate genes shown to encode for particular neurotransmitter receptor systems may shed light on the role of particular subcortical, sensory and higher-level processing regions during rivalry.

Finally, one particularly promising approach to elucidating genetic and molecular aspects of both rivalry and BD is the *Drosophila* rivalry model mentioned above. *Drosophila melanogaster* has proven an immensely powerful tool for dissecting the genetic, molecular and neurophysiological aspects of development, memory, learning, circadian rhythms and attention, and can even shed light on neuropsychiatry (Bellen, Tong, & Tsuda, 2010; Miller et al., 2012; O’Kane, 2011; van Alphen & van Swinderen, 2013; van Swinderen, 2011). The existence of perceptual switching behavior in response to incongruent dichoptic visual stimulation in *Drosophila* (Figure 6), indeed switching behavior that exhibits individual variation in rate (Tang & Juusola, 2010), offers novel and exciting research strategies that we have recently outlined in detail (Miller et al., 2012). Thus fly rivalry can be compared to human rivalry, with a host of human rivalry characteristics examined for in the *Drosophila* model (e.g., temporal dynamics, stimulus factors, relationships with other cognitive functions such as memory and attention; see chapters by Brascamp & Baker and Bressler et al., this volume). The *Drosophila* model can also be used to explore neurophysiological aspects of rivalry, given its amenability to direct electrophysiological recording, pharmacological manipulation and emerging

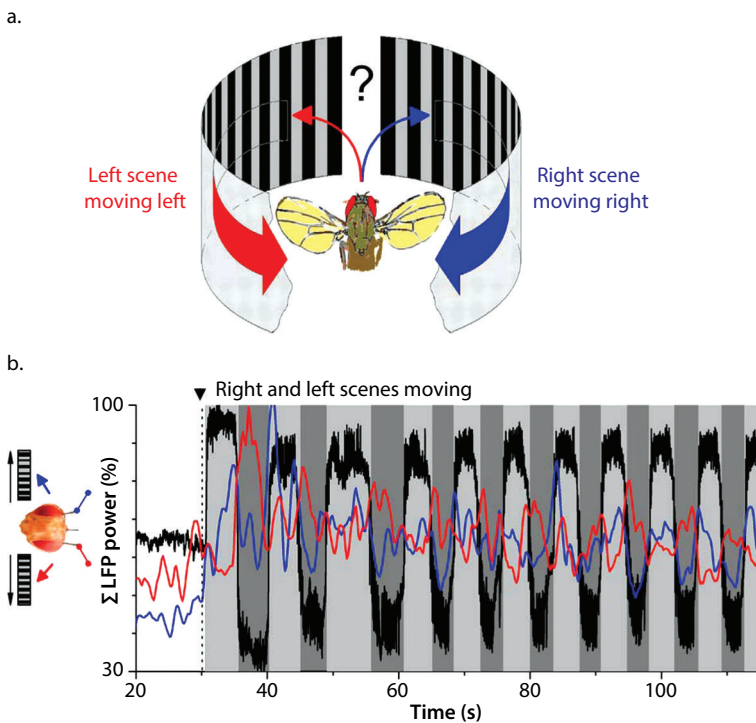


Figure 6. Rivalry in *Drosophila* and its IHS electrophysiological basis. (a) A fly presented with dichoptic visual stimulation in a tethered flight setup displays rivalry-like orienting behavioral switches between the left and right competing stimuli, which are measured using a torque meter (not shown). Bilateral electrophysiological recordings from the fly's optic lobes (b) revealed unilateral LFP activity preceded the switch towards the same side (while LFP activity on the opposite side was inhibited), and that this unilateral LFP activity exhibited left-right (interhemispheric) alternations in accordance with the fly's switching behavior (reprinted from *PLoS One*, Tang & Juusola, 2010, 5, 12, e14455).

methods such as photostimulation (optogenetics). Indeed, the model enables mechanistic aspects of rivalry to be probed at molecular, cellular and systems levels. Moreover, known genetic mutants such as the short/long circadian and behavioral courtship rhythm *per* variants, can be examined, with short/long rivalry intervals hypothesized, to examine the notion of period-coupled oscillators, as proposed by Pettigrew and Miller (1998; see Figure 1) to underlie the link between slow BR in BD and the alternating mood states of BD. Other known *Drosophila* mutant strains can also be screened for rivalry rate anomalies, with results potentially shedding light on both genetic aspects of rivalry and of BD. Utilization of *Drosophila* to examine attention-like rivalry and visual competition has commenced (Paulk, Millard, & van Swinderen, 2013; van Swinderen, 2012) with frequency-tagging

methods previously used in attention and rivalry studies (e.g., Kamphuisen et al., 2008; Srinivasan, Russell, Edelman, & Tononi, 1999; Vialatte, Maurice, Dauwels, & Cichocki, 2010), and is continuing with a range of other neurophysiological and genetic methods (A. Paulk & B. van Swinderen, personal communication). Rivalry experiments have also recently been extended to mice (Zhang et al., 2012), thus providing further scope for probing the phenomenon from genetic through to systems levels.

Concluding remarks

In this chapter we have discussed the point-counterpoint nature of mechanistic rivalry research, and the high-, low- and multi-level processing engaged by the phenomenon. We discussed the genesis and status of one proposal in particular, the IHS model. On this background we reviewed brain stimulation approaches to studying rivalry, including CVS and TMS, noting that these methods too have yielded conflicting results, but that they also offer the potential for further mechanistic clarification. We have argued that the IHS model has yet to be conclusively verified or falsified and that it is one which is readily amenable to examination with electrophysiological, brain-imaging and brain stimulation approaches. Finally, we have outlined the links between the IHS model and the finding of slow BR in BD, and have described current and future research aimed at elucidating genetic and molecular aspects of both rivalry and BD. The renewed fascination with rivalry mechanisms looks set to grow and spread further to clinical, genetic and new comparative contexts.

References

- Aafjes, M., Hueting, J. E., & Visser, P. (1966). Individual and interindividual differences in binocular retinal rivalry in man. *Psychophysiology*, 3(1), 18–22.
- Alvarez, G. A., & Cavanagh, P. (2005). Independent resources for attentional tracking in the left and right visual hemifields. *Psychological Science*, 16(8), 637–643.
- Alvarez, G. A., Gill, J., & Cavanagh, P. (2012). Anatomical constraints on attention: Hemifield independence is a signature of multifocal spatial selection. *Journal of Vision*, 12(5), 9. doi: 10.1167/12.5.9
- André, J.-M., Martinet, N., Paysant, J., Beis, J.-M., & Le Chapelain, L. (2001). Temporary phantom limbs evoked by vestibular caloric stimulation in amputees. *Neuropsychiatry, Neuropsychology, and Behavioural Neurology*, 14(3), 190–196.
- Arai, N., Okabe, S., Furubayashi, T., Terao, Y., Yuasa, K., & Ugawa, Y. (2005). Comparison between short train, monophasic and biphasic repetitive transcranial magnetic stimulation (rTMS) of the human motor cortex. *Clinical Neurophysiology*, 116(3), 605–613.

- Bächtold, D., Baumann, T., Sándor, P.S., Kritos, M., Regard, M., & Brugger, P. (2001). Spatial- and verbal-memory improvement by cold-water caloric stimulation in healthy subjects. *Experimental Brain Research*, 136(1), 128–132.
- Bagby, J.W. (1957). A cross-cultural study of perceptual predominance in binocular rivalry. *Journal of Abnormal Psychology*, 54(3), 331–334.
- Been, G., Ngo, T. T., Miller, S. M., & Fitzgerald, P. B. (2007). The use tDCS and CVS as methods of non-invasive brain stimulation. *Brain Research Reviews*, 56(2), 346–361.
- Bellen, H. J., Tong, C., & Tsuda, H. (2010). 100 years of *Drosophila* research and its impact on vertebrate neuroscience: A history lesson for the future. *Nature Reviews Neuroscience*, 11(7), 514–522.
- Bemelmans, K. J., Heijdanus, P. J. H., Jansen, T. C., & Rietveld, W. J. (1984). Periodicities in the basic rest-activity cycle range during the waking phase. *IRCS Medical Science: Psychology and Psychiatry*, 12(5–6), 444–445.
- Blake, R. (1989). A neural theory of binocular rivalry. *Psychological Review*, 96(1), 145–167.
- Blake, R. (2001). A primer on binocular rivalry, including current controversies. *Brain and Mind*, 2(1), 5–38.
- Blake, R., & Logothetis, N. K. (2002). Visual competition. *Nature Reviews Neuroscience*, 3(1), 13–21.
- Blumberg, H. P., Stern, E., Martinez, D., Ricketts, S., de Asis, J., White, T. et al. (2000). Increased anterior cingulate and caudate activity in bipolar mania. *Biological Psychiatry*, 48(11), 1045–10452.
- Bogen, J. E., Berker, E., van Lancker, D. L., Sudia, S., Lipstad, B., Sadun, A. et al. (1998). Left hemiserebrectomy: Vision, olfaction and mentation 45 years later. *Proceedings of the 28th Annual Meeting of the Society for Neuroscience*, 24, 173.
- Bogen, J. E. (2000). Split-brain basics: Relevance for the concept of one's other mind. *Journal of American Academy of Psychoanalysis*, 28(2), 341–369.
- Bonneh, Y. S., Cooperman, A., & Sagi, D. (2001). Motion-induced blindness in normal observers. *Nature*, 411(6839), 798–801.
- Borsellino, A., De Marco, A., Allazetta, A., Rinesi, S., & Bartolini, B. (1972). Reversal time distribution in the perception of visual ambiguous stimuli. *Kybernetik*, 10(3), 139–144.
- Bottini, G., Paulesu, E., Gandola, M., Loffredo, S., Scarpa, P., Sterzi, R. et al. (2005). Left caloric vestibular stimulation ameliorates right hemianesthesia. *Neurology*, 65(8), 1278–1283.
- Brascamp J. W., & Blake, R. (2012). Inattention abolishes binocular rivalry: Perceptual evidence. *Psychological Science*, 23(10), 1159–1167.
- Brouwer, G. J., Tong, F., Schwarzbach, J., & van Ee, R. (2005). Voluntary control over perceptual changes during bistable structure-from-motion, revealed by fMRI. *Society for Neuroscience*, 31, 390.17.
- Carmel, D., Walsh, V., Lavie, N., & Rees, G. (2010). Right parietal TMS shortens dominance durations in binocular rivalry. *Current Biology*, 20(18), R799–R800.
- Carter, O. L., Pettigrew, J. D., Hasler, F., Wallis, G. M., Liu, G. B., Hell, D. et al. (2005). Modulating the rate and rhythmicity of perceptual rivalry alternations with the mixed 5-HT_{2A} and 5-HT_{1A} agonist psilocybin. *Neuropsychopharmacology*, 30(6), 1154–1162.
- Chokron, S., Dupierri, E., Tabert, M., & Bartolomeo, P. (2007). Experimental remission of unilateral spatial neglect. *Neuropsychologia*, 45(14), 3127–3148.
- Crain, K. (1961). Binocular rivalry: Its relation to intelligence, and general theory of its nature and physiological correlates. *Journal of General Psychology*, 64(2), 259–283.

- de Graaf, T. A., de Jong, M. C., Goebel, R., van Ee, R., & Sack, A. T. (2011). On the functional relevance of frontal cortex for passive and voluntarily controlled bistable vision. *Cerebral Cortex*, 21(10), 2322–2331.
- de Graaf T. A., & Sack, A. T. (2011). Null results in TMS: From absence of evidence to evidence of absence. *Neuroscience & Biobehavioral Reviews*, 35(3), 871–877.
- de la Iglesia, H. O., Meyer, J., Carpino, A. Jr., & Schwartz, W. J. (2000). Antiphase oscillation of the left and right suprachiasmatic nuclei. *Science*, 290(5492), 799–801.
- Díaz-Caneja, E. (1928). Sur l'alternance binoculaire. *Annales D'Oculistique*, 165, 721–731.
- Dodson, M. J. (2004). Vestibular stimulation in mania: A case report. *Journal of Neurology, Neurosurgery & Psychiatry*, 75(1), 168–169.
- Eccles, R. (2000). Nasal airflow in health and disease. *Acta Otolaryngologica*, 120(5), 580–595.
- Einhäuser, W., Stout, J., Koch, C., & Carter, O. (2008). Pupil dilation reflects perceptual selection and predicts subsequent stability in perceptual rivalry. *Proceedings of the National Academy of Sciences USA*, 105(5), 1704–1709.
- Enoksson, P. (1963) Binocular rivalry and monocular dominance studied with optokinetic nystagmus. *Acta Ophthalmologica*, 41(5), 544–563.
- Ewen, J. H. (1931). The psychological estimation of the effects of certain drugs upon the syntonetic and schizophrenic psychoses: With a brief enquiry into a physiological basis of temperament. *Journal of Mental Science*, 77(319), 742–766.
- Fagard, J., Sacco, S., Yvenou, C., Domellöf, E., Kieffer, V., Tordjman S. et al. (2008). The role of the corpus callosum in the perception of reversible figures in children. *Vision Research*, 48(23–24), 2451–2455.
- Ferrè, E. R., Bottini, G., & Haggard, P. (2012). Vestibular modulation of somatosensory perception. *European Journal of Neuroscience*, 34(8), 1337–1344.
- Ferrè, E. R., Bottini, G., Iannetti, G. D., & Haggard, P. (2013). The balance of feelings: Vestibular modulation of bodily sensations. *Cortex*, 49(3), 748–758.
- Ferrè, E. R., Sedda, A., Gandola, M., & Bottini, G. (2011). How the vestibular system modulates tactile perception in normal subjects: A behavioural and physiological study. *Experimental Brain Research*, 208(1), 29–38.
- Frederiksen, N. O., & Guilford, J. P. (1934). Personality traits and fluctuations of the outline cube. *American Journal Psychology*, 46(3), 470–474.
- Freeman, E. D., Sterzer, P., & Driver, J. (2012). fMRI correlates of subjective reversals in ambiguous structure-from-motion. *Journal of Vision*, 12(6), 35. doi: 10.1167/12.6.35
- Fuchs, T., Maury, D., Moore, F. R., & Bingham, V. P. (2009). Daytime micro-naps in a nocturnal migrant: An EEG analysis. *Biology Letters*, 5(1), 77–80.
- Funk, A. P., & Pettigrew, J. D. (2003). Does interhemispheric competition mediate motion-induced blindness? A transcranial magnetic stimulation study. *Perception*, 32(11), 1325–1338.
- Ge, S., Ueno, S., & Iramina, K. (2007a). Repetitive transcranial magnetic stimulation effect on perceptual reversals of ambiguous figures. *Proceedings of 2007 IEEE/ICME International Conference on Complex Medical Imaging*, 1400–1403.
- Ge, S., Ueno, S., & Iramina, K. (2007b). The rTMS effect on perceptual reversal of ambiguous figures. *Proceedings of 29th Annual International Conference of the IEEE on Engineering in Medicine and Biology Society*, 4743–4746.
- Ge, S., Ueno, S., & Iramina, K. (2008). Effects of repetitive transcranial-magnetic stimulation on perceptual reversal. *Journal of the Magnetism Society of Japan*, 32(4), 458–461.

- Genç, E., Bergmann, J., Singer, W., & Kohler, A. (2011). Interhemispheric connections shape subjective experience of bistable motion. *Current Biology*, 21(17), 1494–1499.
- Genç, E., Bergmann, J., Tong, F., Blake, R., Singer, W., & Kohler, A. (2011). Callosal connections of primary visual cortex predict the spatial spreading of binocular rivalry across the visual hemifields. *Frontiers in Human Neuroscience*, 5, 161. doi: 10.3389/fnhum.2011.00161
- George, R. W. (1936). The significance of the fluctuations experienced in observing ambiguous figures and in binocular rivalry. *Journal of General Psychology*, 15(1), 39–61.
- Gorenstein, E. E., Mammato, C. A., & Sandy, J. M. (1989). Performance of inattentive-overactive children on selected measures of prefrontal-type function. *Journal of Clinical Psychology*, 45(4), 619–632.
- Gottesman, I. I., & Gould, T. D. (2003). The endophenotype concept in psychiatry: etymology and strategic intentions. *American Journal of Psychiatry*, 160(4), 636–645.
- Gould, T. D., & Gottesman, I. I. (2006). Psychiatric endophenotypes and the development of valid animal models. *Genes, Brain and Behavior*, 5(2), 113–119.
- Grisaru, N., Chudakov, B., Yaroslavsky, Y., & Belmaker, R. H. (1998). Transcranial magnetic stimulation in mania: A controlled study. *American Journal of Psychiatry*, 155(11), 1608–1610.
- Hasler, G., Drevets, W. C., Gould, T. D., Gottesman, I. I., & Manji, H. K. (2006). Toward constructing an endophenotype strategy for bipolar disorders. *Biological Psychiatry*, 60(2), 93–105.
- Haynes, J. D., Deichmann, R., & Rees, G. (2005). Eye-specific effects of binocular rivalry in the human lateral geniculate nucleus. *Nature*, 438(7067), 496–499.
- Helmholtz, H. (1867). *Handbuch der physiologischen Optik*, Leipzig: Voss. J. P. C. Southall, 1925 (Trans. 3rd ed., A. Gullstrand, J. von Kries, & W. Nagel, Eds., 1910; Hamburg: Verlag von Leopold Voss), *Helmholtz's treatise on physiological optics*, Vol 3. New York: Optical Society of America.
- Hsu, L.-C., Yeh, S.-L., Tien, Y.-M. & Lin, C.-Y. (2008, June 19–22). *Oscillation of conscious experience and brain activity in motion-induced blindness and the Necker cube*. Paper presented at the 12th Annual Meeting of the Association for the Scientific Study of Consciousness, Taipei, Taiwan.
- Hunt, J., & Guilford, J. P. (1933). Fluctuation of an ambiguous figure in dementia praecox and in manic-depressive patients. *Journal of Abnormal and Social Psychology*, 27(4), 443–452.
- Imbach, L. L., Werth, E., Kallweit, U., Sarthein, J., Scammell, T. E., & Baumann, C. R. (2012). Inter-hemispheric oscillations in human sleep. *PLoS One*, 7(11), e48660. doi: 10.1371/journal.pone.0048660
- Kamphuisen, A., Bauer, M., & van Ee, R. (2008). No evidence for widespread synchronized networks in binocular rivalry: MEG frequency tagging entrains primarily early visual cortex. *Journal of Vision*, 8(5), 4. doi: 10.1167/8.5.4
- Karnath, H.-O. (1994). Subjective body orientation in neglect and the interactive contribution of neck muscle proprioception and vestibular stimulation. *Brain*, 117(5), 1001–1012.
- Karnath, H.-O., Fetter, M., & Dichigans, J. (1996). Ocular exploration of space as a function of neck proprioceptive and vestibular input – observations in normal subjects and patients with spatial neglect after parietal lesions. *Experimental Brain Research*, 109(2), 333–342.
- Karnath, H.-O., Himmelbach, M., & Perenin, M.-T. (2003). Neglect-like behavior in healthy subjects. Dissociation of space exploration and goal-directed pointing after vestibular stimulation. *Experimental Brain Research*, 153(2), 231–238.

- Karnath, H.-O., Sievering, D., & Fetter, M. (1994). The interactive contribution of neck muscle proprioception and vestibular stimulation to subjective "straight head" orientation in man. *Experimental Brain Research*, 101(1), 140–146.
- Kanai, R., Bahrami, B., & Rees, G. (2010). Human parietal cortex structure predicts individual differences in perceptual rivalry. *Current Biology*, 20(18), 1626–1630.
- Kanai, R., Carmel, D., Bahrami, B., & Rees, G. (2011). Structural and functional fractionation of right superior parietal cortex in bistable perception. *Current Biology*, 21(3), R106–R107.
- Keliris, G. A., Logothetis, N. K., & Tolias, A. S. (2010). The role of the primary visual cortex in perceptual suppression of salient visual stimuli. *Journal of Neuroscience*, 30(37), 12353–12365.
- Kendler, K. S., & Neale, M. C. (2010). Endophenotype: A conceptual analysis. *Molecular Psychiatry*, 15(8), 789–797.
- Kikuta, S., Kashiwadani, H., & Mori, K. (2008). Compensatory rapid switching of binasal inputs in the olfactory cortex. *Journal of Neuroscience*, 28(46), 11989–11997.
- Kolev, O. (1990). How caloric vestibular irritation influences migraine attacks. *Cephalalgia*, 10(4), 167–169.
- Kondo, H., Kitagawa, N., Kitamura, M., Koizumi, A., Nomura, M., & Kashino, M. (2012). Separability and commonality of auditory and visual bistable perception. *Cerebral Cortex*, 22(8), 1915–1922.
- Kovács, I., Papathomas, T. V., Yang, M., & Fehér, A. (1996). When the brain changes its mind: Interocular grouping during binocular rivalry. *Proceedings of the National Academy of Sciences USA*, 93(26), 15508–15511.
- Krug, K., Brunskill, E., Scarna, A., Goodwin, G. M., & Parker, A. J. (2008). Perceptual switch rates with ambiguous structure-from-motion figures in bipolar disorder. *Proceedings of the Royal Society of London B: Biological Sciences*, 275(1645), 1839–1848.
- Le Chapelain, L., Beis, J.-M., Paysant, J., & André, J.-M. (2001). Vestibular caloric stimulation evokes phantom limb illusions in patients with paraplegia. *Spinal Cord*, 39(2), 85–87.
- Lee, S.-H., & Blake, R. (2002). V1 activity is reduced during binocular rivalry. *Journal of Vision*, 2(9), 4. doi: 10.1167/2.9.4
- Leopold, D. A., & Logothetis, N. K. (1996). Activity changes in early visual cortex reflect monkeys' percepts during binocular rivalry. *Nature*, 379(6565), 549–553.
- Leopold, D. A., & Logothetis, N. K. (1999). Multistable phenomena: Changing views in perception. *Trends in Cognitive Sciences*, 3(7), 254–264.
- Levine, J., Toder, D., Geller, V., Kraus, M., Gauchman, T., Puterman, M. et al. (2012). Beneficial effects of caloric vestibular stimulation on denial of illness and manic delusions in schizoaffective disorder: A case report. *Brain Stimulation*, 5(3), 267–273.
- Lewald, J., & Karnath, H.-O. (2000). Vestibular influence on human auditory space perception. *Journal of Neurophysiology*, 84(2), 1107–1111.
- Ling, S., & Blake, R. (2012). Normalization regulates competition for visual awareness. *Neuron*, 75(3), 531–540.
- Logothetis, N. K. (1998). Single units and conscious vision. *Philosophical Transactions of the Royal Society of London B: Biological Sciences*, 353(1377), 1801–1818.
- Logothetis, N. K., Leopold, D. A., & Sheinberg, D. L. (1996). What is rivalling during binocular rivalry? *Nature*, 380(6575), 621–624.
- Logothetis, N. K., Leopold, D. A., & Sheinberg, D. L. (2003). Neural mechanisms of perceptual organization. In N. Osaka (Ed.), *Neural basis of consciousness* (pp. 87–103). Advances in Consciousness Research (Vol. 49). Philadelphia, PA: John Benjamins Publishing Company.

- Logothetis, N. K., & Schall, J. D. (1989). Neuronal correlates of subjective visual perception. *Science*, 245(4919), 761–763.
- Long, G. M., & Toppino, T. C. (2004). Enduring interest in perceptual ambiguity: Alternating views of reversible figures. *Psychological Bulletin*, 130(5), 748–768.
- Long, M. A., & Fee, M. S. (2008). Using temperature to analyse temporal dynamics in the songbird motor pathway. *Nature*, 456(7219), 189–194.
- Lopez, C., Blanke, O., & Mast, F. W. (2012). The human vestibular cortex revealed by coordinate-based activation likelihood estimation meta-analysis. *Neuroscience*, 212, 159–179.
- Lopez, C., Schreyer, H.-M., Preuss, N., & Mast, F. W. (2012). Vestibular stimulation modifies the body schema. *Neuropsychologia*, 50(8), 1830–1837.
- Low, P. S., Shank, S. S., Sejnowski, T. J., & Margoliash, D. (2008). Mammalian-like features of sleep structure in zebra finches. *Proceedings of the National Academy of Sciences USA*, 105(26), 9081–9086.
- Lyamin O. I., Manger, P. R., Ridgway, S. H., Mukhametov, L. M., & Siegel, J. M. (2008). Cetacean sleep: An unusual form of mammalian sleep. *Neuroscience & Biobehavioral Reviews*, 32(8), 1451–1484.
- Luck, S. J., Hillyard, S. A., Mangun, G. R., & Gazzaniga, M. S. (1989). Independent hemispheric attentional systems mediate visual search in split-brain patients. *Nature*, 342(6249), 543–545.
- Lumer, E. D., Friston, K. J., & Rees, G. (1998). Neural correlates of perceptual rivalry in the human brain. *Science*, 280(5371), 1930–1934.
- Lyoo, I. K., Sung, Y. H., Dager, S. R., Friedman, S. D., Lee, J. Y., Kim, S. J. et al. (2006). Regional cerebral cortical thinning in bipolar disorder. *Bipolar Disorders*, 8(1), 65–74.
- Mast, F. W., Merfeld, D. M., & Kosslyn, S. M. (2006). Visual mental imagery during caloric vestibular stimulation. *Neuropsychologia*, 44(1), 101–109.
- McDougall, W. (1906). III. – Physiological factors of the attention-process (IV.). *Mind*, 15(59), 329–359.
- McGeoch, P. D., & Ramachandran, V. S. (2008). Vestibular stimulation can relieve central pain of spinal origin. *Spinal Cord*, 46(11), 756–757.
- McGeoch, P. D., Williams, L. E., Lee, R. R., & Ramachandran, V. S. (2008). Behavioural evidence for vestibular stimulation as a treatment for central post-stroke pain. *Journal of Neurology, Neurosurgery & Psychiatry*, 79(11), 1298–1301.
- McGeoch, P. D., Williams, L. E., Song, T., Lee, R. R., Huang, M., & Ramachandran, V. S. (2009). Post-stroke tactile allodynia and its modulation by vestibular stimulation: A MEG case study. *Acta Neurologica Scandinavica*, 119(6), 404–409.
- McKay, R., Tamagni, C., Palla, A., Krummenacher, P., Hegemann, S. C. A., Straumann, D. et al. (in press). Vestibular stimulation attenuates unrealistic optimism. *Cortex*. doi: 10.1016/j.cortex.2013.04.005
- Meldman, M. J. (1965). The quantitative analysis of anxiety and depression. *Psychosomatics*, 6(1), 8–15.
- Miller, S. M. (2001). Binocular rivalry and the cerebral hemispheres: With a note on the correlates and constitution of visual consciousness. *Brain and Mind*, 2(1), 119–149.
- Miller, S. M., Gynther, B. D., Heslop, K. R., Liu, G. B., Mitchell, P. B., Ngo, T. T. et al. (2003). Slow binocular rivalry in bipolar disorder. *Psychological Medicine*, 33(4), 683–692.
- Miller, S. M., Hansell, N. K., Ngo, T. T., Liu, G. B., Pettigrew, J. D., Martin, N. G. et al. (2010). Genetic contribution to individual variation in binocular rivalry rate. *Proceedings of the National Academy of Sciences USA*, 107(6), 2664–2668.

- Miller, S. M., Liu, G. B., Ngo, T. T., Hooper, G., Riek, S., Carson, R. G. et al. (2000). Interhemispheric switching mediates perceptual rivalry. *Current Biology*, 10(7), 383–392.
- Miller, S. M., & Ngo, T. T. (2007). Studies of caloric vestibular stimulation: Implications for the cognitive neurosciences, the clinical neurosciences and neurophilosophy. *Acta Neuropsychiatrica*, 19(3), 183–203.
- Miller, S. M., Ngo, T. T., & van Swinderen, B. (2012). Attentional switching in humans and flies: Rivalry in large and miniature brains. *Frontiers in Human Neuroscience*, 5, 188. doi: 10.3389/fnhum.2011.00188
- Mukamel, R., & Fried, I. (2012). Human intracranial recordings and cognitive neuroscience. *Annual Review of Psychology*, 63, 511–537.
- Nagamine, M., Yoshino, A., Miyazaki, M., Takahashi, Y., & Nomura, S. (2008). Effects of selective 5-HT_{1A} agonist tandospirone on the rate and rhythmicity of binocular rivalry. *Psychopharmacology*, 198(2), 279–286.
- Nagamine, M., Yoshino, A., Miyazaki, M., Takahashi, Y., & Nomura, S. (2009). Difference in binocular rivalry rate between patients with bipolar I and bipolar II disorders. *Bipolar Disorders*, 11(5), 539–546.
- Ngo, T. T., Blomberg, S. P., Liu, G. B., Pettigrew, J. D., & Miller, S. M. (submitted). Retesting the interhemispheric switch model of perceptual rivalry.
- Ngo, T. T., Liu, G. B., Tilley, A. J., Pettigrew, J. D., & Miller, S. M. (2008). The changing face of perceptual rivalry. *Brain Research Bulletin*, 75(5), 610–618.
- Ngo, T. T., Liu, G. B., Tilley, A. J., Pettigrew, J. D., & Miller, S. M. (2007). Caloric vestibular stimulation reveals discrete neural mechanisms for coherence rivalry and eye rivalry: A meta-rivalry model. *Vision Research*, 47(21), 2685–2699.
- Ngo, T. T., Miller, S. M., Liu, G. B., & Pettigrew, J. D. (2000). Binocular rivalry and perceptual coherence. *Current Biology*, 10(4), R134–R136.
- Ngo, T. T., Mitchell, P. B., Martin, N. G., & Miller, S. M. (2011). Psychiatric and genetic studies of binocular rivalry: An endophenotype for bipolar disorder? *Acta Neuropsychiatrica*, 23(1), 37–42.
- Nojima, K., Ge, S., Katayama, Y., & Iramina, K. (2010a). Time change of perceptual reversal of ambiguous figures by rTMS. *Proceedings of 32nd Annual International Conference of the IEEE Engineering in Medicine and Biology Society*, 6579–6582.
- Nojima, K., Ge, S., Katayama, Y., & Iramina, K. (2011a). Number of pulses of rTMS affects the inter-reversal time of perceptual reversal. In N. A. A. Osman, W. A. B. W. Abas, A. K. A. Wahab, & H.-N. Ting (Eds.), *IFMBE Proceedings BIOMED 2011, 5th Kuala Lumpur International Conference on Biomedical Engineering 2011* (Vol. 35, pp. 336–339), Springer.
- Nojima, K., Ge, S., Katayama, Y., & Iramina, K. (2011b). Relationship between pulse number of rTMS and inter reversal time of perceptual reversal. *Proceedings of 33rd Annual International Conference of the IEEE Engineering in Medicine and Biology Society*, 8106–8109.
- Nojima, K., Ge, S., Katayama, Y., Ueno, S., & Iramina, K. (2010b). Effect of the stimulus frequency and pulse number of repetitive transcranial magnetic stimulation on the inter-reversal time of perceptual reversal on the right superior parietal lobule. *Journal of Applied Physics*, 107(9), 09B320-1–09B320-3.
- Nojima, K., Katayama, Y., Ueno, S., & Iramina, K. (2010c). Effect of repetitive transcranial magnetic stimulation on perceptual reversals of ambiguous figures. *Journal of the Magnetism Society of Japan*, 34(4), 548–551.
- Ohta, H., Yamazaki, S., & McMahon, D. G. (2005). Constant light desynchronizes mammalian clock neurons. *Nature Neuroscience*, 8(3), 267–269.

- O'Kane, C. J. (2011). *Drosophila* as a model organism for the study of neuropsychiatric disorders. In J. J. Hagan (Ed.), *Molecular and functional models in neuropsychiatry* (pp. 37–60). Berlin, Heidelberg: Springer-Verlag.
- O'Shea, R. P., & Corballis, P. M. (2001). Binocular rivalry between complex stimuli in split-brain observers. *Brain and Mind*, 2(1), 151–160.
- O'Shea, R. P., & Corballis, P. M. (2003). Binocular rivalry in split-brain observers. *Journal of Vision*, 3(10), 3. doi:10.1167/3.10.3
- O'Shea, R. P., & Corballis, P. M. (2005a). Visual grouping on binocular rivalry in a split-brain observer. *Vision Research*, 45(2), 247–261.
- O'Shea, R. P., & Corballis, P. M. (2005b). Binocular rivalry in the divided brain. In D. Alais & R. Blake (Eds.), *Binocular rivalry* (pp. 301–315). Cambridge, MA: MIT Press.
- Panagiotaropoulos, T. I., Deco, G., Kapoor, V., & Logothetis, N. K. (2012). Neuronal discharges and gamma oscillations explicitly reflect visual consciousness in the lateral prefrontal cortex. *Neuron*, 74(5), 924–935.
- Pascual-Leone, A., Rubio, B., Pallardó, F., & Catalá, M. D. (1996). Rapid-rate transcranial magnetic stimulation of left dorsolateral prefrontal cortex in drug-resistant depression. *Lancet*, 348(9022), 233–237.
- Paulk, A., Millard, S. S., & van Swinderen, B. (2013). Vision in *Drosophila*: Seeing the world through a model's eyes. *Annual Review of Entomology*, 58, 313–332.
- Pearson, J., Tadin, D., & Blake, R. (2007). The effects of transcranial magnetic stimulation on visual rivalry. *Journal of Vision*, 7(7), 2. doi:10.1167/7.7.2
- Pettigrew, J. D. (2001). Searching for the switch: Neural bases for perceptual rivalry alternations. *Brain and Mind*, 2(1), 85–118.
- Pettigrew, J. D., Collin, S. P., & Ott, M. (1999). Convergence of highly-specialised behaviour, eye movements and visual optics in the sandlance (Teleostei) and the chameleon (Reptilia). *Current Biology*, 9(8), 421–424.
- Pettigrew, J. D., & Miller, S. M. (1998). A 'sticky' interhemispheric switch in bipolar disorder? *Proceedings of the Royal Society of London B: Biological Sciences*, 265(1411), 2141–2148.
- Polonsky, A., Blake, R., Braun, J., & Heeger, D. J. (2000). Neuronal activity in human primary visual cortex correlates with perception during binocular rivalry. *Nature Neuroscience*, 3(11), 1153–1159.
- Ramachandran, V. S. (1994). Phantom limbs, neglect syndromes and Freudian psychology. *International Review of Neurobiology*, 37, 291–333.
- Rattenborg, N. C., Lima, S. L., & Amlaner, C. J. (1999). Half-awake to the risk of predation. *Nature*, 397(6718), 397–398.
- Rode, G., Vallar, G., Revol, P., Tilikete, C., Jacquin-Courtois, S., Rossetti, Y. et al. (2012). Facial macrosomatognosia and pain in a case of Wallenberg's syndrome: Selective effects of vestibular and transcutaneous stimulations. *Neuropsychologia*, 50(2), 245–253.
- Rossetti, Y., & Rode, G. (2002). Reducing spatial neglect by visual and other sensory manipulations: Noncognitive (physiological) routes to the rehabilitation of a cognitive disorder. In H.-O. Karnath, D. Milner, & G. Vallar (Eds.), *The cognitive and neural bases of spatial neglect* (pp. 375–396). Oxford: Oxford University Press.
- Sandrini, M., Umiltà, C., & Rusconi, E. (2011). The use of transcranial magnetic stimulation in cognitive neuroscience: A new synthesis of methodological issues. *Neuroscience & Biobehavioral Reviews*, 35(3), 516–536.

- Schaap, J., Albus, H., Eilers, P. H. C., D  t  ri, L., & Meijer, J. H. (2001). Phase differences in electrical discharge rhythms between neuronal populations of the left and right suprachiasmatic nuclei. *Neuroscience*, 108(3), 359–363.
- Schm  l, F., Kunz, R., & Stoll, W. (2000). The localization of an imaginary target under the influence of caloric vestibular stimulation in healthy adults. *European Archives of Otorhinolaryngology*, 257(9), 473–479.
- Shannahoff-Khalsa, D. S., Gillin, J. C., Yates, F. E., Schlosser, A., & Zawadzki, E. M. (2001). Ultradian rhythms of alternating cerebral hemispheric EEG dominance are coupled to rapid eye movement and non-rapid eye movement stage 4 sleep in humans. *Sleep Medicine*, 2(4), 333–346.
- Shannon, R. W., Patrick, C. J., Jiang, Y., Bernat, E., & He, S. (2011). Genes contribute to the switching dynamics of bistable perception. *Journal of Vision*, 11(3), 8. doi:10.1167/11.3.8
- Sheinberg, D. L., & Logothetis, N. K. (1997). The role of temporal cortical areas in perceptual organization. *Proceedings of the National Academy of Sciences USA*, 94(7), 3408–3413.
- Slotnick, S. D., & Yantis, S. (2005). Common neural substrates for the control and effects of visual attention and perceptual bistability. *Cognitive Brain Research*, 24(1), 97–108.
- Sobel, N., Khan, R. M., Saltman, A., Sullivan, E. V., & Gabrieli, J. D. E. (1999). The world smells different to each nostril. *Nature*, 402(6757), 35.
- Sterzer, P., Kleinschmidt, A., & Rees, G. (2009). The neural bases of multistable perception. *Trends in Cognitive Sciences*, 13(7), 310–318.
- Sterzer, P., Russ, M. O., Preibisch, C., & Kleinschmidt, A. (2002). Neural correlates of spontaneous direction reversals in ambiguous apparent visual-motion. *Neuroimage*, 15(4), 908–916.
- Srinivasan, R., Russell, D. P., Edelman, G. M., & Tononi, G. (1999). Increased synchronization of neuromagnetic responses during conscious perception. *Journal of Neuroscience*, 19(13), 5435–5448.
- Tang, S., & Juusola, M. (2010). Intrinsic activity in the fly brain gates visual information during behavioral choices. *PLoS One*, 5(12), e14455. doi:10.1371/journal.pone.0014455
- Tong, F., & Engel, S. (2001). Interocular rivalry revealed in the human cortical blind-spot representation. *Nature*, 411(3834), 195–199.
- Tong, F., Meng, M., & Blake, R. (2006). Neural bases of binocular rivalry. *Trends in Cognitive Sciences*, 10(11), 502–511.
- Towne, J. (1863). The stereoscope, and stereoscopic results – Section III. *Guy’s Hospital Reports*, 9, 103–126.
- van Alphen, B., & van Swinderen, B. (2013). *Drosophila* strategies to study psychiatric disorders. *Brain Research Bulletin*, 92, 1–11.
- van Swinderen, B. (2011). Attention in *Drosophila*. *International Review of Neurobiology*, 99, 51–85.
- van Swinderen, B. (2012). Competing visual flicker reveals attention-like rivalry in the fly brain. *Frontiers in Integrative Neuroscience*, 6, 96. doi:10.3389/fnint.2012.00096
- Vialatte, F.-B., Maurice, M., Dauwels, J., and Cichocki, A. (2010). Steady-state visually evoked potentials: Focus on essential paradigms and future perspectives. *Progress in Neurobiology*, 90(4), 418–438.
- Vierck, E., Porter, R. J., Luty, S. E., Moor, S., Crowe, M. T., Carter, J. D. et al. (2013). Further evidence for slow binocular rivalry rate as a trait marker for bipolar disorder. *Australian and New Zealand Journal of Psychiatry*, 47(4), 371–379.

- Wang, C. Z. H., Herbst, J. A., Keller, G. B., & Hahnloser, R. H. R. (2008). Rapid interhemispheric switching during vocal production in a songbird. *PLoS Biology*, 6(10), e250. doi: 10.1371/journal.pbio.0060250
- Werntz, D., Bickford, R. G., Bloom F. E., & Shannahoff-Khalsa, D. S. (1983). Alternating cerebral hemispheric activation and the lateralization of autonomic nervous function. *Human Neurobiology*, 2(1), 39–43.
- Wunderlich, K., Schneider, K. A., & Kastner, S. (2005). Neural correlates of binocular rivalry in the human lateral geniculate nucleus. *Nature Neuroscience*, 8(11), 1595–1602.
- Yan, L., Foley, N. C., Bobula, J. M., Kriegsfeld, L. J., & Silver, R. (2005). Two antiphase oscillations occur in each suprachiasmatic nucleus of behaviorally split hamsters. *Journal of Neuroscience*, 25(39), 9017–9026.
- Zaretskaya, N., Thielscher, A., Logothetis, N. K., & Bartels, A. (2010). Disrupting parietal function prolongs dominance durations in binocular rivalry. *Current Biology*, 20(23), 2106–2111.
- Zhang, P., Jamison, K., Engel, S., He, B., & He, S. (2011). Binocular rivalry requires visual attention. *Neuron*, 71(2), 362–369.
- Zhang Q.-f., Wen, Y., Zhang, D., She, L., Wu, J.-y., Dan, Y. et al. (2012). Priming with real motion biases visual cortical response to bistable apparent motion. *Proceedings of the National Academy of Sciences USA*, 109(50), 20691–20696.
- zu Eulenburg, P., Caspers, S., Roski, C., & Eickhoff, S. B. (2012). Meta-analytical definition and functional connectivity of the human vestibular cortex. *Neuroimage*, 60(1), 162–169.

High-level modulations of binocular rivalry

Effects of stimulus configuration, spatial and temporal context, and observer state

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The selection and maintenance of a specific percept during binocular rivalry have often been considered to be relatively automatic and influenced primarily by low-level stimulus attributes such as contrast and luminance. However, numerous studies have identified other, higher-level, factors that substantially influence perceptual selection, dominance, and suppression in binocular rivalry. These factors include the configuration of stimulus elements, the spatial and temporal context in which the rivaling stimuli are presented, and manipulations of attentional and pharmacological state. The studies summarized in this chapter broaden traditional conceptions of binocular rivalry as a competition between populations of stimulus-selective neurons and demonstrate that multiple factors can operate over extended spatial and temporal scales to modulate the competitive processes underlying perceptual selection.

Introduction

Much of the early research on factors that influence perception of stimuli in binocular rivalry focused on manipulations of fundamental physical attributes of the rivaling stimuli such as luminance, contrast, and spatial frequency (Blake, 1989; Levelt, 1965; see chapter by Brascamp & Baker, this volume). Such research has generated important insights into the mechanisms of binocular rivalry and has had a lasting influence on theoretical conceptions of rivalry as resulting from low-level, stimulus driven competition. For example, models of rivalry often consist of competitive pools of model neurons, without consideration of contextual or modulatory influences (Blake, 1989; Lehky, 1988; Moreno-Bote, Rinzel, & Rubin, 2007). Even models that incorporate multiple stages of stimulus processing (Dayan, 1998; Freeman, 2005; Gigante, Mattia, Braun, & Del Giudice, 2009;

Wilson, 2003) often do not account for influences on rivalry beyond the physical properties of the rivaling stimuli. While there is little doubt that low-level competitive processes capture many critical features of binocular rivalry, it has also become clear that binocular rivalry is substantially influenced by multiple factors beyond the features of the rivaling stimuli themselves. Characterization of these higher-order factors and their effects on perception of rivaling stimuli facilitates the study of binocular rivalry within the larger context of visual processing and perception. In turn, this opens new possibilities for binocular rivalry to be used as an experimental tool for addressing questions related to mid- and high-level vision and systems-level modulation of neural circuit dynamics. In this chapter, we review psychophysical studies of the roles of three classes of higher-order factors in determining perceptual experience during rivalry: stimulus configuration, visual context, and observer state.

In the first section, we discuss the effects of *stimulus configuration*: the influence of the arrangement and grouping properties of rivaling stimulus elements on the dynamics of rivalry. Effects of stimulus configuration are tied to the global organization of features in the visual display, as opposed to the specific visual features of rivaling stimuli. In the second section, we move from the rivaling stimuli themselves to the *visual context* in which rivaling stimuli are presented. We discuss both spatial context, which includes non-rivaling visual stimuli that surround a rivaling stimulus pair, and temporal context, which encompasses stimuli presented before the onset of rivalry. Visual context incorporates the state of the visual world in which rivaling stimuli are embedded, and effects of visual context on binocular rivalry reveal how perceptual selection is influenced by unambiguous visual information that is integrated over extended regions of space and periods of time. In the third section, we turn from the state of the external world to the state of the viewer observing the rivaling stimuli. By *observer state*, we mean cognitive and intrinsic subject factors that are unrelated to the visual display but nevertheless modulate rivalry. In this section, we discuss attention to rivaling stimulus features, volitional efforts to control the contents of perception during rivalry, and pharmacological manipulations and/or genetic factors that influence the neurochemical state of the observer's brain. As we review the effects of higher-order factors on perception of rivaling stimuli, we discuss their implications for understanding perceptual selection, maintenance of a dominant percept, and perceptual alternation in binocular rivalry.

Effects of stimulus configuration

Higher-level configural and semantic factors can significantly influence perception in binocular rivalry. Specifically, stimuli with meaningful content or a coherent configuration tend to have greater predominance (i.e., the proportion of viewing time that a given percept is dominant). For example, an upright face predominates over an inverted face (Engel, 1956; Hastorf & Myro, 1959), and natural images predominate over scrambled versions of the same images (Baker & Graf, 2009). In addition, emotional stimuli have greater predominance compared to neutral stimuli (Anderson, Siegel, & Barrett, 2011; Sheth & Pham, 2008; Yoon, Hong, Joormann, & Kang, 2009).

Gestalt grouping can also increase the amount of time that grouped elements are simultaneously dominant. For example, if portions of two rivaling images are swapped between the two eyes, resulting in a patchy mixture of both images in each eye, interocular grouping can occur, resulting in rivalry between the two original images (Kovács, Papathomas, Yang, & Fehér, 1996; Lee & Blake, 2004). Interocular grouping can also occur for simple geometric shapes (Alais, O'Shea, Mesana-Alais, & Wilson, 2000; Díaz-Caneja, 1928; Ngo, Miller, Liu, & Pettigrew, 2000; Ooi & He, 2003). Other studies have shown that collinearity (Alais, Lorenceau, Arrighi, & Cass, 2006; Fukuda & Blake, 1992; Stuit, Paffen, van der Smagt, & Verstraten, 2011; Whittle, Bloor, & Pocock, 1968), color similarity (Kim & Blake, 2007; Kovács et al., 1996; Kulikowski, 1992; Ooi & He, 2003; Papathomas, Kovács, & Conway, 2005; Silver & Logothetis, 2004), configural complexity (Alais & Melcher, 2007), luminance uniformity (Silver & Logothetis, 2004), and orientation similarity (Papathomas et al., 2005; Stuit et al., 2011; Wade, 1973) of stimulus elements spread either across space or between the two eyes increase the amount of time that the grouped elements are simultaneously dominant. However, not all types of grouping enhance simultaneous dominance to the same degree: the effects of grouping of common color are stronger than those of grouping of common orientation, spatial frequency, or motion (Kulikowski, 1992; Papathomas et al., 2005; van Lier & de Weert, 2003; Wong & Freeman, 1999), and the effects of grouping of collinear orientations are greater than those of grouping of parallel orientations (Alais & Blake, 1999; Alais & Parker, 2006; Stuit et al., 2011; Whittle et al., 1968). Meanwhile, increasing the directional similarity of motion elements actually decreases the amount of simultaneous dominance, compared to stimuli with more incoherent motion (Silver & Logothetis, 2004).

Grouping could increase the amount of time that grouped elements are simultaneously dominant by (i) prolonging the average dominance duration of the grouped elements, and/or (ii) enhancing the likelihood that the individual

elements simultaneously become selected for dominance. Although grouping can significantly alter the mean dominance duration of the grouped elements (Bonneh, Sagi, & Karni, 2001; Ooi & He, 2003; Silver & Logothetis, 2004; Stuit et al., 2011; Yu & Blake, 1992), there is also evidence that grouping has stronger effects on selection than maintenance. For instance, increasing the collinearity of two spatially separated gratings increases the probability that they simultaneously attain dominance but has no effect on the mean dominance duration of either individual grating (Alais & Blake, 1999; Alais et al., 2006). Similar findings have been obtained for luminance and color uniformity (Silver & Logothetis, 2004) and for the extent to which a stimulus can be perceived as a coherent surface (Ooi & He, 2003). Moreover, changing the Gestalt grouping properties of multistable rivalry stimuli mainly influences likelihood of selection and has only minimal impact on dominance durations (de Weert, Snoeren, & Koning, 2005).

The effects of grouping on binocular rivalry are in some cases critically dependent on local eye-based processes. For instance, even though interocular grouping can promote rivalry between images that are partially presented to each eye (Kovács et al., 1996), abruptly swapping a pair of local image patches between the eyes causes an immediate switch in the patch that is perceived (Lee & Blake, 2004). In these cases, global form binds multiple local patches across the eyes, but rivalry between local patches may still occur at the level of monocular representations. Other studies show that even considerable differences between global forms in the two eyes do not result in rivalry if there are no local interocular conflicts between contours in the stimuli (Bradley, 1982; Carlson & He, 2004; de Weert & Wade, 1988). Finally, the importance of local eye-based mechanisms is further supported by results that show that grouping is stronger within an eye compared to when stimulus elements are spread between the eyes (Fukuda & Blake, 1992; Kovács et al., 1996; Lee & Blake, 2004; Ooi & He, 2003; Papathomas et al., 2005; Stuit et al., 2011; Wade, 1973; Whittle et al., 1968).

In summary, grouping can increase predominance of a rivaling stimulus and can also cause grouped elements to fluctuate in and out of dominance simultaneously. Enhancing configural information mainly increases the likelihood that stimulus elements that are spread across space and between the eyes will simultaneously become selected for dominance, and to a lesser degree prolongs dominance durations of the grouped stimulus features. Finally, the effects of grouping on binocular rivalry interact with local eye-based processes.

Effects of visual context

The previous section considered the importance of configural content in binocular rivalry. The contextual environment in which the rivaling images are experienced can also result in visual as well as non-visual influences on rivalry dynamics. Non-visual context from olfactory (Zhou, Jiang, He, & Chen, 2010), auditory (Conrad, Bartels, Kleiner, & Noppeney, 2010), and somatosensory (Lunghi, Binda, & Morrone, 2010) stimuli, and even from self-generated movements (Maruya, Yang, & Blake, 2007), can promote predominance of a congruous visual stimulus. For example, the scent of a rose enhances predominance of an image of a rose (Zhou et al., 2010). These interesting observations emphasize the complexity of rivalry dynamics and their interactions with non-visual systems in the brain.

Spatial context

Visual context that surrounds a pair of rivaling stimuli but is not itself rivaling can also profoundly influence predominance. Presentation of a surrounding visual stimulus to just one eye increases predominance of the surrounded rivaling stimulus (Fukuda & Blake, 1992), but binocular presentation of a surround enhances predominance of the rivaling stimulus that is most dissimilar to the surround. For example, if the binocular surround has the same orientation or color as one of a pair of rivaling stimuli but not the other, the predominance of the dissimilar stimulus is increased (Carter, Campbell, Liu, & Wallis, 2004; Fukuda & Blake, 1992; Ichihara & Goryo, 1978; Mapperson & Lovegrove, 1991). Similar effects have been reported for moving stimuli: surrounding motion enhances the predominance of the rivaling stimulus moving in the opposite direction (Blake, Yu, Lokey, & Norman, 1998; Paffen, Tadin, te Pas, Blake, & Verstraten, 2006; Paffen, van der Smagt, te Pas, & Verstraten, 2005). These findings likely result from surround suppression of visual cortical neuronal responses. For example, the responses of individual neurons to an optimally oriented stimulus are often reduced by simultaneous presentation of a stimulus outside the neuron's receptive field, and this suppression is maximal when the two stimuli share the same orientation (Blakemore & Tobin, 1972; Knierim & van Essen, 1992).

In addition to surround suppression, a boundary contour mechanism can also contribute to contextual effects in binocular rivalry (Ooi, 2005; Ooi & He, 2006; Su, He, & Ooi, 2009, 2011; van Bogaert, Ooi, & He, 2008; Xu, He, & Ooi, 2010). When one of a pair of rivaling stimuli is continuous with the surrounding binocular contextual background and the other contains a physical boundary between the stimulus and the surround, an ecologically valid perceptual interpretation is

that the stimulus with the boundary is an occluder that is closer in depth than the surrounding background. In this case, the predominance of the “occluder” is greater than that of the stimulus that is continuous with the “background” surround. As the border between a rivaling stimulus and the surrounding “background” becomes more distinct, the predominance of the “occluding” stimulus increases (Ooi, 2005; Ooi & He, 2006; Xu et al., 2010).

Most of the results we have described so far can be explained by relatively low-level interactions between rivaling stimuli and their contextual surrounds. However, there is also strong evidence that global context influences rivalry dynamics. For example, if a rivaling drifting grating is surrounded by other non-rivaling drifting gratings that result in perception of global motion of all the gratings, the predominance of the grating that is congruent with the global motion is increased (Alais & Blake, 1998; Sobel & Blake, 2002). Similarly, a rivaling perspective-defined stimulus that is congruent with the surrounding depth-defined plane predominates over a stimulus that is incongruent with the surrounding plane (Graf & Adams, 2008). These contextual effects of global structure enhance predominance of the congruent rivaling stimulus, in contrast to the studies in which surrounding context enhances the incongruent rivaling stimulus in a manner consistent with center-surround receptive field organization of visual cortical neurons. These results provide evidence that top-down feedback from global form representations is distinct from the kind of contextual modulation that is likely to take place within more local cortical circuits. The effects of global form may also differ from those provided by contextual semantic congruity: when natural scenes contain embedded rivaling objects that are either congruous or incongruous with the rest of the scene, incongruous objects have longer mean dominance durations than congruous objects (Mudrik, Deouell, & Lamy, 2011).

In summary, non-rivaling visual context has substantial effects on the predominance of rivaling stimuli. A rivaling stimulus will exhibit enhanced predominance if (i) a surrounding stimulus is presented only to the same eye, (ii) it has features such as color, orientation, and motion direction that are dissimilar to a binocularly presented surrounding context, or (iii) it is congruent with the global form provided by the context. These results provide evidence that perception during binocular rivalry is not only a low-level local automatic process but is also substantially affected by non-rivaling stimuli and higher-order global structure.

Temporal context

The previous section described how spatial context surrounding binocular rivalry stimuli influences perceptual selection. In this section, we turn to temporal context – visual stimulation occurring at the same location as the rivalry stimuli in space, but preceding them in time. Effects of temporal context on perceptual selection reflect the ways that perception of the current state of the visual world is shaped by past events.

Most rivalry research on the effects of temporal context has focused on two basic phenomena: adaptation and perceptual stabilization. In studies of adaptation, an adapting stimulus typically shares a feature with one of a pair of rivalry stimuli. When the adapter is presented prior to the onset of the rivalry stimuli, the rivaling stimulus that shares features with the adapter is less likely to predominate (Blake & Overton, 1979; Wade & de Weert, 1986). These effects can be explained via well-known feature-specific adaptation properties of neuronal responses.

Perceptual stabilization refers to the finding that repeated, brief presentations of rivalry stimuli tend to cause the same percept to dominate for many successive presentations, resulting in a significant slowing of perceptual alternations compared to continuous rivalry viewing (Leopold, Wilke, Maier, & Logothetis, 2002). Thus, perceptual selection for a briefly presented rivalry display is affected by the observer's recent perceptual selection history. These priming-like effects must be mediated by some form of perceptual memory, and the study of perceptual stabilization and its mechanisms is an active area of research (Brascamp, Kanai, Walsh, & van Ee, 2010; Brascamp, Knapen, Kanai, Noest, van Ee, & van den Berg, 2008; Brascamp, Pearson, Blake, & van den Berg, 2009; Kang & Shevell, 2011; Noest, van Ee, Nijs, & van Wezel, 2007; Pastukhov & Braun, 2008; Pearson & Clifford, 2004).

Adaptation and perceptual stabilization are basic and important ways that temporal context can affect binocular rivalry (Pearson & Clifford, 2005). However, rather than review this literature in detail here (see Pearson & Brascamp, 2008, and chapter by Brascamp & Baker, this volume, for recent reviews of perceptual memory effects in rivalry), we will focus on the effects of expectations – specifically, those generated by patterns occurring in a visual stimulus over time – on perceptual selection during rivalry and other ambiguous displays.

An observer's prior knowledge about the likely contents of a visual scene influences the perceptual interpretation of that scene (Gregory, 1997; Helmholtz, 1867; Kersten, Mamassian, & Yuille, 2004). Such prior knowledge need not be conscious. Rather, the brain may store representations of frequently encountered patterns in the visual environment that then affect the perceptual interpretation of incoming sensory signals through implicit mechanisms. In a dynamic visual environment,

an important source of prior information about the likely contents of the current visual scene is the recent visual past. For example, a landscape is not expected to change suddenly into a cityscape; a ball flying through the air is expected to continue its trajectory. In this section, we discuss evidence that the brain generates and uses predictions (i.e., expectations about the likely future state of the world) when selecting a single perceptual interpretation of a visual scene from competing alternatives. We focus on studies in which learned stimulus expectations or predictable patterns of visual stimulation, which we call “predictive context”, influence perceptual selection during rivalry and other ambiguous displays. We include discussion of studies using ambiguous displays other than binocular rivalry in this section, because rivalry studies investigating predictive context have only just begun to be conducted. However, we believe that this will be a fruitful area for future binocular rivalry research.

Prior experience with unambiguous visual stimuli influences perceptual selection in several types of ambiguous displays. For example, Haijiang and colleagues (Haijiang, Saunders, Stone, & Backus, 2006) presented subjects with Necker cubes (Figure 1a) rotating unambiguously in a clockwise or counterclockwise direction (which was defined by stereoscopic and other depth cues), and they paired the rotation direction with secondary stimulus cues, including the position of the cube on the screen and its direction of translation across the screen. Over the course of many trials, this pairing began to bias perceptual selection for ambiguous rotating cubes that were interleaved with the disambiguated training trials. Observers were increasingly likely to see ambiguous cubes as rotating in the direction that was paired with the secondary cue, and this effect persisted for at least one day after the termination of the unambiguous pairing. Haijiang et al. called this learned associative effect on perceptual selection “cue recruitment”. Similarly, Sterzer and colleagues (Sterzer, Frith, & Petrovic, 2008) showed that stereoscopically viewing unambiguous rotating dot cylinders (Figure 1b) through red-green anaglyph glasses worn in a certain configuration (e.g., red lens on the left) subsequently biased perception of ambiguous cylinders viewed through the glasses in the direction of the previous association. The effect disappeared when the glasses were removed.

However, not all cues can influence perception of ambiguous rotation in this way. Subsequent studies showed that the retinal location of the rotating stimulus associatively influences perceptual selection (Harrison & Backus, 2010), whereas spatial location (which is distinct from retinal location if the direction of gaze is different for training and test) (Harrison & Backus, 2010), background patterns (Jain, Fuller, & Backus, 2010), and sounds (Haijiang et al., 2006; Jain et al., 2010) do not. This suggests specificity in the domains of associative learning that are able

to influence perceptual selection. One possibility is that only cues that are encoded by the same neurons that represent, and perhaps participate in the perceptual resolution of, ambiguous stimuli can exert associative influence over perceptual selection of those stimuli. Further work will be required to more completely characterize cue recruitment, including its dependence on type of cue and ambiguous stimulus. Such work promises to help us understand the types of learning that can influence perceptual selection. More broadly, associations learned over the course of development may be of widespread importance for interpreting visual scenes as an adult. For example, humans tend to perceive visual displays as lit from above, and this prior tends to become stronger over the course of development (Brewster, 1826; Thomas, Nardini, & Mareschal, 2010).

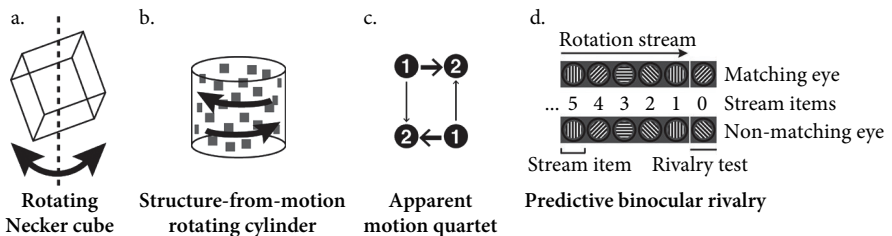


Figure 1. Examples of ambiguous visual displays used in studies of predictive effects on perceptual selection. (a) Rotating Necker cube. A wire frame cube can be perceived as rotating either clockwise or counterclockwise about a vertical axis. Depth cues can be added to make the direction of rotation unambiguous. (b) Structure-from-motion rotating cylinder. Coherent random dots move as though they form the front and back surfaces of a rotating cylinder. The cylinder can be seen either as rotating clockwise (leftward-moving dots in front) or counterclockwise (leftward-moving dots in back). The addition of stereoscopic depth cues can disambiguate the direction of rotation. (c) Apparent motion quartet. If presentation of two dots on opposite corners of an imaginary rectangle (position 1) is followed by two dots on the other corners (position 2), an apparent motion percept results, in which the dots are seen as moving from position 1 to position 2. The direction of motion is ambiguous but can be biased by the aspect ratio of the rectangle. In the example shown, perception of horizontal motion between positions 1 and 2 is more likely, since the distance between the dots on this path is shorter than the distance on the path of vertical motion. (d) Predictive binocular rivalry. A sequence of gratings rotating in steps of 45° is presented identically to the two eyes (the rotation stream), generating an expectation about the next image in the series. Immediately following the rotation stream, a rivalry display is presented in which the grating presented to one eye (the matching eye) matches the preceding rotation direction (i.e., is the expected next image), and the grating presented to the other eye (the non-matching eye) has an orthogonal, unexpected orientation.

Cue recruitment demonstrates the influence of prior learning on perceptual selection, but in this paradigm, contextual information from secondary cues is presented simultaneously with the ambiguous stimulus at the time of perceptual selection. We now turn to predictive context, in which prior information precedes the ambiguous stimulus in time. Predictive context that generates an expectation about the forthcoming visual display can bias perceptual selection in favor of the expected (predicted) percept, as shown in two recent studies. In the first study, Maloney and colleagues (Maloney, Dal Martello, Sahm, & Spillmann, 2005) employed motion quartets (Figure 1c) in which a pair of dots was presented for 250 ms at two diagonally opposite corners of an invisible rectangle in one frame, followed by a 250 ms blank interval and then presentation of dots for 250 ms at the alternate opposite corners in a second frame. For rectangles with an aspect ratio close to 1 (squares), the dot motion is ambiguous, and the dots can be experienced as moving either clockwise or counterclockwise from the first to the second frame. To study effects of predictive context on these stimuli, Maloney et al. (2005) measured perception of sequences of two-frame motion quartets and found that the likelihood of perceiving a clockwise or counterclockwise rotation on a given trial was influenced by the pattern of perceptual reports on preceding trials. They documented first a priming effect, in which repeating sequences (e.g., a few clockwise responses in a row) resulted in increased probability of perceptual reports of the same rotation direction in subsequent trials. Interestingly, an analogous effect was also observed for alternating sequences (e.g., clockwise–counterclockwise–clockwise), with subjects tending to report the next rotation direction that was expected from an alternating sequence (in this example, counterclockwise). Note that this is opposite to what would be expected from simple priming of motion direction and instead reflects an expectation generated from a longer temporal pattern that integrates over multiple directions of perceived motion. This finding indicates that the predictive context of structured temporal patterns can influence subsequent perceptual selection.

More recently, we have documented effects of predictive context on perceptual selection during binocular rivalry (Denison, Piazza, & Silver, 2011). In our experiments, observers viewed a sequence of gratings presented identically (and therefore with unambiguous orientations) to the two eyes, followed by a pair of rivaling orthogonal gratings. To generate an expectation that could influence subsequent perceptual selection during rivalry, we used a pre-rivalry sequence of gratings that appeared to rotate either clockwise or counterclockwise (Figure 1d). This apparent rotation biased perceptual selection of the subsequently presented rivaling gratings such that, at the onset of rivalry, observers were more likely to perceive the grating that was consistent with the preceding rotation (Denison et al., 2011). Observers were also faster to report predicted grating orientations compared to non-predicted orientations.

In other experiments, we characterized some of the temporal properties of the prediction effect. In particular, we measured the time period over which the visual system integrated predictive information prior to rivalry. We varied the length of the pre-rivalry rotation stream, from very short streams with only 2 rotation items (the minimal number required to specify a rotation direction) to long streams with 15 rotation items (containing multiple cycles of complete rotation). We found clear and equivalent effects of predictive context for all of these pre-rivalry stream lengths – that is, whenever a rotation direction was specified by at least two rotation items, we observed the maximum prediction effect on initial perceptual selection of the rivaling stimuli (Denison et al., 2011). This effect was not diminished even when gratings that were inconsistent with the rotation direction were inserted into the stream prior to the final two rotation items. This suggests that only recent stimulus history (two rotation items, or 800 ms of stimulation) contributed to the predictive bias in our experiments. An interesting avenue for future research will be a more complete characterization of the build-up and decay of the effects of different types of predictive context on perceptual selection.

This is the first study to demonstrate predictive context effects on perceptual selection during binocular rivalry, and the use of the rivalry paradigm is important for at least two reasons. First, it allows the study of predictive context and perceptual awareness to be connected to the extensive physiological literature on binocular rivalry (see chapters by Sengpiel and Sterzer, this volume), enabling effects of predictive context to be interpreted in light of existing knowledge about the neural mechanisms of rivalry. Second, there is both psychophysical and fMRI evidence that rivalry between orthogonal gratings can be resolved at a relatively early stage of visual processing (Blake, Westendorf, & Overton, 1980), as early as V1 (Polonsky, Blake, Braun, & Heeger, 2000; Tong & Engel, 2001) and the lateral geniculate nucleus (LGN) (Haynes, Deichmann, & Rees, 2005; Wunderlich, Schneider, & Kastner, 2005). It should be noted that the existence of rivalry-related modulations in the earliest visual areas is less clear in electrophysiological studies, with evidence for only a weak relationship in V1 between neuronal spiking and rivalry alternations (Leopold & Logothetis, 1996) or suppression (Keliris, Logothetis, & Tolia, 2010) and no relationship in the LGN (Lehky & Maunsell, 1996), but clear evidence for a relationship between rivalry suppression and the lower frequency bands of the local field potentials in V1 (Wilke, Logothetis, & Leopold, 2006) and the LGN (Wilke, Mueller, & Leopold, 2009). Thus, effects of predictive context on binocular rivalry between gratings likely point to an early locus for predictive neural signals in the visual processing hierarchy, but further work is required to more completely understand the nature of these signals and their role in perceptual selection. Future studies that measure brain activity related to predictive context will help to answer these questions and potentially inform our understanding of rivalry in general.

Studies of predictive context in a variety of ambiguous visual displays, including binocular rivalry, have begun to characterize the influence of the brain's own predictions on the contents of conscious perception. In these studies, predictive information biases perception to be more consistent with the predicted percept. These findings relate to computational models of predictive coding that have been proposed to describe cortical function (Friston, 2005; Friston & Kiebel, 2009; Mumford, 1992; Rao & Ballard, 1999). In these models, the cerebral cortex is considered to be hierarchical, with relatively higher-level brain areas generating ongoing predictions of activity in lower-level areas, where the lowest areas are those closest to the signals from the sensory periphery. By predicting upcoming brain activity in sensory brain areas, predictive coding provides a mechanism for the prediction of incoming sensory input. Findings of predictive effects in perceptual selection help to formulate specific hypotheses regarding the neural representation of prior information and the dynamics of predictive signals in the brain, which can then be used to test and refine dynamic models of sensory processing such as predictive coding. Future research could combine psychophysical tasks that provide sensitive measures of perception (like binocular rivalry) with quantitative manipulations of predictive information as well as physiological measures of neural activity. Such investigations will elucidate the ways in which the brain draws on the past to generate our experience of the present.

Effects of observer state

Volition and attention

The previous sections discussed how higher-order visual factors, including stimulus configuration and visual context, can influence perception during binocular rivalry. In this section, we move beyond the influences of external input to describe how factors internal to the observer can play important roles in determining the contents of perception in binocular rivalry. To begin, the volitional and attentional states of the subject can significantly alter rivalry dynamics (for recent reviews, see Dieter & Tadin, 2011; Paffen & Alais, 2011).

In “volitional control” studies, subjects are instructed to attempt to willfully change the rate of alternation between rivaling percepts or to enhance the dominance of a specific percept while suppressing other percepts. The rate of perceptual alternation is particularly susceptible to voluntary control, with up to a three-fold difference following subjects' attempts either to increase or to decrease the alternation rate (George, 1936; Klink, van Ee, Nijs, Brouwer, Noest, & van Wezel, 2008; Lack, 1978; Meng & Tong, 2004; Meredith & Meredith, 1962; van Ee, van

Dam, & Brouwer, 2005). To a lesser extent, subjects can enhance the predominance of a specific rivaling percept through voluntary effort (Breese, 1899; Collyer & Bevan, 1970; de Vries & Washburn, 1909; Helmholtz, 1867; Klink et al., 2008; Lack, 1978; McDougall, 1903; Meng & Tong, 2004; van Dam & van Ee, 2006; van Ee, van Boxtel, Parker, & Alais, 2009; van Ee et al., 2005; Washburn & Gillette, 1933), although these volitional effects are not as strong as those for other types of bistable percepts such as the Necker cube (George, 1936; Klink et al., 2008; Meng & Tong, 2004; van Ee et al., 2005; Washburn & Gillette, 1933). The effects of volition on binocular rivalry are much more pronounced following practice. Tibetan monks who extensively practice a type of meditation that requires sustained selective attention are able to maintain the dominance of a selected percept indefinitely (Carter, Presti, Callistemon, Ungerer, Liu, & Pettigrew, 2005). In addition, following several days of practice, previously untrained subjects can produce a ten-fold difference in the rate of alternation in binocular rivalry (Lack, 1969, 1973, 1978).

Unlike volitional control experiments, in which subjects willfully bias their perception, attentional cueing studies manipulate attention to a particular stimulus without additional instructions to attempt to control perception in rivalry. Attention can be directed to one of a pair of rivaling stimuli either by using a physical cue that captures involuntary attention ("exogenous cueing") or by instructing subjects to perform a task on one of the stimuli ("endogenous cueing"). Exogenous cueing of one stimulus prior to the onset of rivalry increases the likelihood that the cued stimulus will initially become dominant, and the time course of this effect is similar to that of exogenous visual attention (Chong & Blake, 2006; Hancock & Andrews, 2007; Mitchell, Stoner, & Reynolds, 2004; Ooi & He, 1999). Although early studies (Blake, 1988; Neisser & Becklen, 1975) reported conflicting effects of endogenous attention on rivalry, subsequent studies employing demanding voluntary attention tasks have shown that allocation of endogenous attention to a stimulus increases the likelihood that the attended stimulus will be dominant, both at the onset of rivalry (Chong & Blake, 2006) and during sustained viewing (Chong, Tadin, & Blake, 2005; Hancock & Andrews, 2007). Finally, drawing attention away from rivaling stimuli decreases the rate of perceptual alternation (Alais, van Boxtel, Parker, & van Ee, 2010; Paffen & Alais, 2011; Paffen, Alais, & Verstraten, 2006; Paffen & Van der Stigchel, 2010). In addition, measurements of neural responses to two conflicting monocular stimuli suggest that fully withdrawing attention from the stimuli eliminates alternations and results in binocular combination, indicating that some amount of attention to the rivaling stimuli is required for alternations to occur (Zhang, Jamison, Engel, He, & He, 2011).

It is possible that the effects of volitional control and/or attentional cueing on perception during binocular rivalry result from eye movements that change the location of the rivaling images on the retinae. Helmholtz (1867) claimed that he

could maintain dominance of a rivaling stimulus by selectively attending to it or by moving his eyes, and Breese (1899) reported that his ability to volitionally enhance predominance of a rivaling stimulus was reduced if he did not move his eyes. Other early studies found that volitional control of rivalry is reduced (George, 1936; McDougall, 1903) or abolished (Fry, 1936) if the oculomotor muscles are paralyzed. However, Lack (1978) reported no significant decrement in volitional control of rivalry alternation rate following paralysis of the oculomotor muscles or by measuring rivalry between afterimages following adaptation (which are stabilized on the retinae even during eye movements). Furthermore, although there is a correlation between saccades and the timing of perceptual alternations in binocular rivalry, the pattern of this correlation does not differ for passive viewing and volitional control conditions (van Dam & van Ee, 2006). Therefore, although eye movements can modulate rivalry alternations, they cannot fully account for the effects of volitional control on perception.

Another possible confound is that the effects of volitional or attentional state may be due to changes in response bias instead of phenomenological experience (Blake, 1988; Fox, 1991). For example, subjects may simply alter their responses to better match the perceived expectations of the experimenter. Some studies have attempted to control for this by objectively measuring observers' ability to perform a visual discrimination on a selected stimulus, instead of relying on subjective report of perceptual alternations. For instance, instructing subjects to increase predominance of one of a pair of rivaling stimuli significantly enhances subsequent target detection performance within that stimulus (Collyer & Bevan, 1970; Lack, 1978). More recently, Chong et al. (2005) developed a unique experimental paradigm in which subjects reported small changes in a designated rivaling stimulus only when it was dominant. Dominance durations of the attended stimulus were defined as the periods of time for which subjects correctly reported stimulus changes, and these dominance durations were 50% greater than those based on subjective reports of perceptual alternations during passive viewing. However, it is possible that stimulus changes could have been detected even when the attended stimulus was not completely dominant (Chong et al., 2005). Therefore, potential contributions of response bias to volitional and attentional effects in rivalry have not yet been completely ruled out. One interesting direction for future research on response bias in binocular rivalry would be to design an objective task that can only be performed when all components of a given rivaling stimulus are fully dominant.

There is striking variety in volitional and attentional effects on rivalry dynamics, including increases in the probability of selection for dominance (van Ee et al., 2005), increases in mean dominance duration of the stimulus that has been selected (either by attention or volition) (Chong et al., 2005; de Vries & Washburn,

1909; Lack, 1978; van Ee et al., 2009), and decreases in the mean dominance duration of the non-selected stimulus (de Vries & Washburn, 1909; Hancock & Andrews, 2007; Lack, 1978; Meng & Tong, 2004; van Ee et al., 2009). In addition, the magnitude of these effects ranges from small (Meng & Tong, 2004; van Ee et al., 2005) to large (Chong et al., 2005; Klink et al., 2008; McDougall, 1903; van Ee et al., 2009). Finally, these effects are greater for complex compared to simple stimuli (Meng & Tong, 2004; van Ee et al., 2005), for smaller compared to larger stimuli (van Ee et al., 2005), and perhaps for tasks that require active discrimination of some aspect of the visual stimulus, compared to tasks that involve only volitional control (Chong et al., 2005; Helmholtz, 1867).

We recently conducted an experiment to further investigate how volitional control influences selection and maintenance processes in binocular rivalry and how Gestalt grouping interacts with these processes. Multistable horseshoe-shaped stimuli (Figure 2) can generate four distinct percepts: left- and right-oriented horseshoes (corresponding to the monocular stimuli) and concentric circles and horizontal lines (which require interocular Gestalt grouping) (Díaz-Caneja, 1928; Ngo et al., 2000; Figure 3). In most rivalry studies, there are only two possible perceptual interpretations of the stimuli. However, the existence of four perceptual interpretations of Díaz-Caneja stimuli means that dominance of one percept does not necessarily immediately follow the dominance of another specific percept, thereby allowing independent measures of dominance duration and the probability of perceptual selection for each percept.

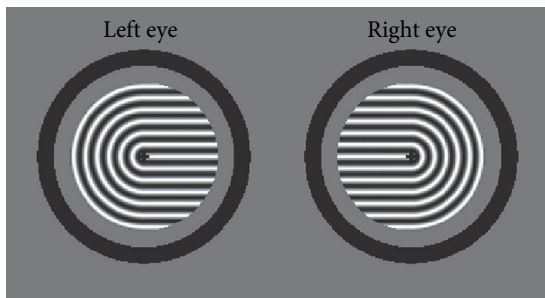


Figure 2. Díaz-Caneja stimuli. The stimulus presented to each eye is a horseshoe pattern oriented either leftward or rightward. Possible perceptual interpretations include one of the horseshoe patterns themselves (corresponding to one of the monocular stimuli) as well as percepts that arise from interocular grouping. In this example, perception of horizontal lines occurs when the right half of the left eye's stimulus and the left half of the right eye's stimulus become dominant at the same time. Alternatively, perception of concentric circles occurs when the left half of the left eye's stimulus and the right half of the right eye's stimulus become simultaneously dominant.

When multiple stimulus elements are engaged in rivalry, configural grouping among elements generally leads to greater predominance if the elements are in the same eye (eye-based grouping) than if they are in different eyes (interocular grouping) (Fukuda & Blake, 1992; Kovács et al., 1996; Lee & Blake, 2004; Ooi & He, 2003; Papathomas et al., 2005; Stuit et al., 2011; Wade, 1973; Whittle et al., 1968). However, we found that for passive viewing of Díaz-Caneja stimuli (without explicit volitional instructions), Gestalt grouping caused interocularly-grouped percepts to predominate just as much as (lines) or even more than (circles) eye-based percepts. The high predominance of concentric circles (Figure 3) was mainly due to the fact that this percept had a probability of selection that was twice that of the other percepts, consistent with previous reports that enhancing the configural content of a rivaling stimulus affects probability of selection more than mean dominance duration (Alais et al., 2006; Apthorp, Wenderoth, & Alais, 2009; de Weert et al., 2005; Ooi & He, 2003; Silver & Logothetis, 2004; Whittle et al., 1968).

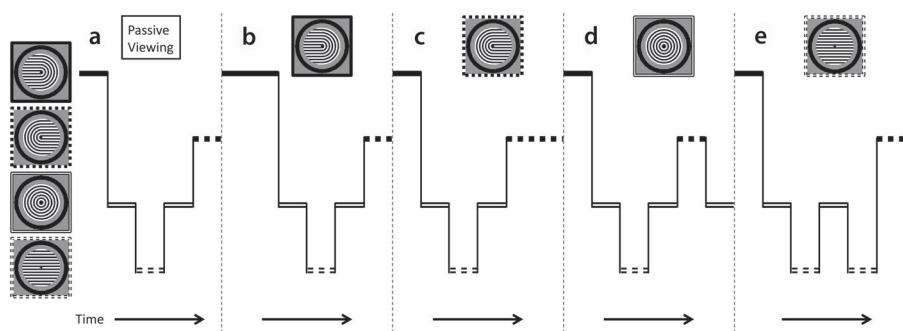


Figure 3. Schematic representation of results from volitional control experiment.

(a) In the passive viewing condition, concentric circles are more likely to be selected for dominance than the other percepts (represented in this schematic by a greater number of horizontal line segments for the circles compared to the other percepts). However, all four percepts have approximately equal mean dominance durations. Note that the length of each horizontal line segment schematically represents the mean dominance duration of each percept; in the actual data, individual dominance durations are highly variable. (b/c) Volitional enhancement of one of the eye-based percepts generally increases mean dominance duration of the selected percept (represented by longer horizontal line segments for the leftward- and rightward-oriented horseshoes in these conditions compared to the passive viewing condition). (d/e) Volitional enhancement of one of the interocularly-grouped percepts generally increases the probability of perceptual selection (represented by a greater number of horizontal line segments for the circles and lines percepts in these conditions compared to the passive viewing condition).

In separate blocks of trials, subjects either passively viewed the stimuli or attempted to volitionally enhance one of the four possible percepts. This resulted in an increase in predominance of the selected percept in all cases, although the pattern of effects differed for eye-based and interocularly-grouped percepts. For eye-based percepts, mean dominance duration increased by up to 50%, with no change in the probability of selection (Figure 3b and c). In addition, the magnitude of this volitional effect is greater than that typically reported for rivalry displays with only two perceptual interpretations (Meng & Tong, 2004; van Ee et al., 2005). Interestingly, increasing the contrast of a currently dominant stimulus also prolongs its mean dominance duration (Chong et al., 2005; Mueller & Blake, 1989), and therefore volitionally enhancing predominance of an eye-based percept may be similar to increasing low-level stimulus strength during a period of dominance.

In contrast, volitional enhancement of interocularly-grouped percepts occurred via an increase of up to 50% in the probability of selection, with no change in mean dominance duration (Figure 3d and e). This result is similar to the effects of strengthening the configural properties of a stimulus (Alais & Blake, 1999; Alais et al., 2006; de Weert et al., 2005; Ooi & He, 2003; Silver & Logothetis, 2004; Whittle et al., 1968), resulting in increased likelihood that grouped elements will be simultaneously selected for dominance. A recent study using Díaz-Caneja stimuli found distinct effects of caloric vestibular stimulation (CVS) on eye-based and interocularly-grouped percepts (Ngo, Liu, Tilley, Pettigrew, & Miller, 2007). These results and ours show that high-level manipulations such as exertion of volitional control and CVS can differentially affect interocular competition and interocular grouping. In addition, our finding of different mechanisms underlying the effects of volitional control (perceptual maintenance versus selection), depending on the type of percept, establishes a foundation for further study of the interactions between volitional control and visual perception and their corresponding neural substrates.

Pharmacology and genetics

Sustained attention and volitional cognitive control affect the observer's state and the contents of perception through explicit experimental instructions. In addition, the observer's state is affected by levels of activity in specific neurotransmitter systems that can be experimentally manipulated with pharmacological interventions. Signaling by particular neurotransmitters can also be investigated by exploiting naturally occurring variations in genes that code for proteins involved in synaptic transmission, such as neurotransmitter receptors and enzymes that synthesize neurotransmitters. In this section, we focus on the use of pharmacological

interventions and genetic studies to elucidate the neurochemical substrates of binocular rivalry.

Pharmacology can be a powerful approach for studying complex phenomena such as visual awareness, as it involves perturbations that are well-defined at the biochemical level yet are compatible with simultaneous psychophysical (e.g., Mednick, Cai, Kanady, & Drummond, 2008; Rokem, Landau, Garg, Prinzmetal, & Silver, 2010) and physiological (e.g., Furey, Pietrini, & Haxby, 2000; Silver, Shenhav, & D'Esposito, 2008) measurements obtained while subjects are performing cognitive and perceptual tasks. In addition, for many pharmacological agents used in research with human subjects, much is known regarding the specific neurotransmitter systems and particular types of receptors, transporters, or enzymes that are affected. In many cases, the same drugs have been used in human studies as well as in experiments with non-human animal models, allowing a direct biochemical link between investigations of human subjects and those employing more invasive experimental methods (Cools & Robbins, 2004; Hasselmo & Sarter, 2011).

Administration of a number of pharmacological agents has been shown to affect the rate of perceptual alternation in binocular rivalry, with some drugs increasing (caffeine: George, 1936) and others decreasing (sodium amytal: George, 1936; ethanol: Bárány & Halldén, 1947; Donnelly & Miller, 1995; ayahuasca: Frecska, White, & Luna, 2004; psilocybin: Carter, Pettigrew, Hasler, Wallis, Liu, Hell, & Vollenweider, 2005; tandospirone: Nagamine, Yoshino, Miyazaki, Takahashi, & Nomura, 2008) the frequency of perceptual switching.

Certain agents may have more specific effects on rivalry alternations, as illustrated by an intriguing anecdotal observation reported by Carter and Pettigrew (2003). In their study, a single subject exhibited a distribution of mean dominance durations that was distinct from the typical pattern that is often described by a gamma function (Fox & Herrmann, 1967; Levelt, 1967). Specifically, most of this subject's dominance durations were restricted to approximately one, two, three, or four seconds, with few instances of dominance durations with intervening values. This subject subsequently reported having self-administered the hallucinogen LSD (lysergic acid diethylamide) about ten hours before testing. Although confirmation of this finding awaits replication in a double-blind, placebo-controlled design, the anecdotal evidence presented by Carter and Pettigrew suggests that a biochemical action of LSD may have imparted or revealed a rhythmicity in binocular rivalry alternations. This could provide insight into mechanisms that control perceptual switching, as a given dominance duration is typically largely independent of the duration of the dominance period immediately preceding or following it (Fox & Herrmann, 1967; van Ee, 2009).

Another promising experimental approach involves genotyping subjects (i.e., determining which DNA nucleotide sequence variant each subject has for the

genes of interest) and correlating these genotypes with behavioral (Goldberg & Weinberger, 2004; Parasuraman, Greenwood, Kumar, & Fossella, 2005) and/or physiological (Fan, Fossella, Sommer, Wu, & Posner, 2003) responses, and with pharmacological effects on behavior (Rokem, Landau, Prinzmetal, Wallace, Silver, & D'Esposito, 2012; van Holstein, Aarts, van der Schaaf, Geurts, Verkes, Franke, van Schouwenburg, & Cools, 2011) and/or brain activity (Cohen, Krohn-Grimberghe, Elger, & Weber, 2007). In a recent example of this genetic approach to the study of perceptual selection, behavioral data were collected for several visual and auditory bistable perception tasks and correlated with genotypes for catechol-O-methyltransferase (COMT; an enzyme that metabolizes dopamine and other catecholamines) and the 2A subtype of the serotonin receptor (Kondo, Kitagawa, Kitamura, Koizumi, Nomura, & Kashino, 2012). A double dissociation of genetic and sensory modality effects on perceptual alternation rate was found, with COMT genotype predicting the rate of auditory bistable perceptual alternation and serotonin receptor genotype predicting the rate of visual perceptual alternation. Given recent twin studies that demonstrate the importance of heritable factors in accounting for individual variation in binocular rivalry rate (Miller et al., 2010), the combination of genetic, behavioral, pharmacological, and physiological methods in the study of binocular rivalry promises to shed light on its neurophysiological and neurochemical mechanisms.

Although most of the pharmacological studies of binocular rivalry to date have simply measured the effects of particular drugs on perceptual alternation rate, more specific insights could be obtained by measuring the effects of pharmacological interventions on distinct aspects of binocular rivalry and on the modulation of rivalry by stimulus and extra-stimulus factors. As we have described in this chapter, psychophysical studies of binocular rivalry have revealed differential effects of configural, contextual, volitional, and other high-level factors on probability of perceptual selection, maintenance, and suppression during rivalry. This rich repertoire of modulatory influences on binocular rivalry could be investigated in pharmacological studies in order to better understand the properties and neural substrates of visual perceptual selection.

Conclusions

Although binocular rivalry is typically considered to be a relatively automatic process governed mainly by competitive interactions between the rivaling stimuli, perception during rivalry can be dramatically altered by factors beyond low-level stimulus properties. In this chapter, we have discussed three classes of higher-order effects on rivalry: stimulus configuration, stimulus context, and observer

state. First, strengthening the configuration of stimulus features through grouping can increase the likelihood that they become simultaneously dominant. Second, non-rivaling visual context surrounding a rivalrous stimulus (in space or time) can influence the predominance of a rivaling percept. Third, factors internal to the observer (such as the observer's attentional or pharmacological state) can modulate rivalry dynamics. Taken together, these psychophysical results suggest that multiple locations in the visual system contribute to visual competition and that higher-level brain processes can influence low-level perceptual dynamics. The findings discussed in this chapter also emphasize the need for more complete models of binocular rivalry that incorporate the influence of higher-order factors, as well as further neurophysiological studies that identify the neural structures and processes that underlie modulations of rivalry by these factors. Characterizing the effects of higher-order factors on binocular rivalry broadens our understanding of competitive processes in perception and opens new possibilities for binocular rivalry to be used as a tool for studying mid- and high-level vision.

References

- Alais, D., & Blake, R. (1998). Interactions between global motion and local binocular rivalry. *Vision Research*, 38(5), 637–644.
- Alais, D., & Blake, R. (1999). Grouping visual features during binocular rivalry. *Vision Research*, 39(26), 4341–4353.
- Alais, D., Lorenceau, J., Arrighi, R., & Cass, J. (2006). Contour interactions between pairs of Gabors engaged in binocular rivalry reveal a map of the association field. *Vision Research*, 46(8–9), 1473–1487.
- Alais, D., & Melcher, D. (2007). Strength and coherence of binocular rivalry depends on shared stimulus complexity. *Vision Research*, 47(2), 269–279.
- Alais, D., O'Shea, R. P., Mesana-Alais, C., & Wilson, I. G. (2000). On binocular alternation. *Perception*, 29(12), 1437–1445.
- Alais, D., & Parker, A. (2006). Independent binocular rivalry processes for motion and form. *Neuron*, 52(5), 911–920.
- Alais, D., van Boxtel, J. J., Parker, A., & van Ee, R. (2010). Attending to auditory signals slows visual alternations in binocular rivalry. *Vision Research*, 50(10), 929–935.
- Anderson, E., Siegel, E. H., & Barrett, L. F. (2011). What you feel influences what you see: The role of affective feelings in resolving binocular rivalry. *Journal of Experimental Social Psychology*, 47(4), 856–860.
- Apthorp, D., Wenderoth, P., & Alais, D. (2009). Motion streaks in fast motion rivalry cause orientation-selective suppression. *Journal of Vision*, 9(5), 10. doi:10.1167/9.5.10
- Baker, D. H., & Graf, E. W. (2009). Natural images dominate in binocular rivalry. *Proceedings of the National Academy of Sciences USA*, 106(13), 5436–5441.
- Bárány, E. H., & Halldén, U. (1947). The influence of some central nervous depressants on the reciprocal inhibition between the two retinae as manifested in retinal rivalry. *Acta Physiologica Scandinavica*, 13(4), 296–316.

- Blake, R. (1988). Dichoptic reading: The role of meaning in binocular rivalry. *Perception & Psychophysics*, 44(2), 133–141.
- Blake, R. (1989). A neural theory of binocular rivalry. *Psychological Review*, 96(1), 145–167.
- Blake, R., & Overton, R. (1979). The site of binocular rivalry suppression. *Perception*, 8(2), 143–152.
- Blake, R., Westendorf, D. H., & Overton, R. (1980). What is suppressed during binocular rivalry? *Perception*, 9(2), 223–231.
- Blake, R., Yu, K., Lokey, M., & Norman, H. (1998). Binocular rivalry and motion perception. *Journal of Cognitive Neuroscience*, 10(1), 46–60.
- Blakemore, C., & Tobin, E. A. (1972). Lateral inhibition between orientation detectors in the cat's visual cortex. *Experimental Brain Research*, 15(4), 439–440.
- Bonneh, Y., Sagi, D., & Karni, A. (2001). A transition between eye and object rivalry determined by stimulus coherence. *Vision Research*, 41(8), 981–989.
- Bradley, D. R. (1982). Binocular rivalry of real vs. subjective contours. *Perception & Psychophysics*, 32(1), 85–87.
- Brascamp, J. W., Kanai, R., Walsh, V., & van Ee, R. (2010). Human middle temporal cortex, perceptual bias, and perceptual memory for ambiguous three-dimensional motion. *Journal of Neuroscience*, 30(2), 760–766.
- Brascamp, J. W., Knapen, T. H. J., Kanai, R., Noest, A. J., van Ee, R., & van den Berg, A. V. (2008). Multi-timescale perceptual history resolves visual ambiguity. *PLoS ONE*, 3(1), e1497. doi:10.1371/journal.pone.0001497
- Brascamp, J. W., Pearson, J., Blake, R., & van den Berg, A. V. (2009). Intermittent ambiguous stimuli: Implicit memory causes periodic perceptual alternations. *Journal of Vision*, 9(3), 3. doi:10.1167/9.3.3
- Breese, B. B. (1899). On inhibition. *Psychological Monographs*, 3(1), 1–65.
- Brewster, D. (1826). On the optical illusion of the conversion of cameos into intaglios, and of intaglios into cameos, with an account of other analogous phenomena. *Edinburgh Journal of Science*, 4(7), 99–108.
- Carlson, T. A., & He, S. (2004). Competing global representations fail to initiate binocular rivalry. *Neuron*, 43(6), 907–914.
- Carter, O. L., Campbell, T. G., Liu, G. B., & Wallis, G. (2004). Contradictory influence of context on predominance during binocular rivalry. *Clinical & Experimental Optometry*, 87(3), 153–162.
- Carter, O. L., & Pettigrew, J. D. (2003). A common oscillator for perceptual rivalries? *Perception*, 32(3), 295–305.
- Carter, O. L., Pettigrew, J. D., Hasler, F., Wallis, G. M., Liu, G. B., Hell, D. et al. (2005). Modulating the rate and rhythmicity of perceptual rivalry alternations with the mixed 5-HT_{2A} and 5-HT_{1A} agonist psilocybin. *Neuropsychopharmacology*, 30(6), 1154–1162.
- Carter, O. L., Presti, D. E., Callistemon, C., Ungerer, Y., Liu, G. B., & Pettigrew, J. D. (2005). Meditation alters perceptual rivalry in Tibetan Buddhist monks. *Current Biology*, 15(11), R412–R413.
- Chong, S. C., & Blake, R. (2006). Exogenous attention and endogenous attention influence initial dominance in binocular rivalry. *Vision Research*, 46(11), 1794–1803.
- Chong, S. C., Tadin, D., & Blake, R. (2005). Endogenous attention prolongs dominance durations in binocular rivalry. *Journal of Vision*, 5(11), 6. doi:10.1167/5.11.6
- Cohen, M. X., Krohn-Grimberghe, A., Elger, C. E., & Weber, B. (2007). Dopamine gene predicts the brain's response to dopaminergic drug. *European Journal of Neuroscience*, 26(12), 3652–3660.

- Collyer, S. C., & Bevan, W. (1970). Objective measurement of dominance control in binocular rivalry. *Perception & Psychophysics*, 8(6), 437–439.
- Conrad, V., Bartels, A., Kleiner, M., & Noppeney, U. (2010). Audiovisual interactions in binocular rivalry. *Journal of Vision*, 10(10), 27. doi:10.1167/10.10.27
- Cools, R., & Robbins, T. W. (2004). Chemistry of the adaptive mind. *Philosophical Transactions of the Royal Society of London A: Mathematical, Physical and Engineering Sciences*, 362(1825), 2871–2888.
- Dayan, P. (1998). A hierarchical model of binocular rivalry. *Neural Computation*, 10(5), 1119–1135.
- de Vries, A., & Washburn, M. F. (1909). A study of retinal rivalry in the after-image. *American Journal of Psychology*, 20(1), 131–135.
- de Weert, C. M. M., Snoeren, P. R., & Koning, A. (2005). Interactions between binocular rivalry and Gestalt formation. *Vision Research*, 45(19), 2571–2579.
- de Weert, C. M. M., & Wade, N. J. (1988). Compound binocular rivalry. *Vision Research*, 28(9), 1031–1040.
- Denison, R. N., Piazza, E. A., & Silver, M. A. (2011). Predictive context influences perceptual selection during binocular rivalry. *Frontiers in Human Neuroscience*, 5, 166. doi:10.3389/fnhum.2011.00166
- Díaz-Caneja, E. (1928). Sur l'alternance binoculaire. *Annales D'Oculistique*, 165, 721–731.
- Dieter, K. C., & Tadin, D. (2011). Understanding attentional modulation of binocular rivalry: A framework based on biased competition. *Frontiers in Human Neuroscience*, 5, 155. doi:10.3389/fnhum.2011.00155
- Donnelly, M., & Miller, R. J. (1995). Ingested ethanol and binocular rivalry. *Investigative Ophthalmology & Visual Science*, 36(8), 1548–1554.
- Engel, E. (1956). The role of content in binocular resolution. *American Journal of Psychology*, 69(1), 87–91.
- Fan, J., Fossella, J., Sommer, T., Wu, Y., & Posner, M. I. (2003). Mapping the genetic variation of executive attention onto brain activity. *Proceedings of the National Academy of Sciences USA*, 100(12), 7406–7411.
- Fox, R. (1991). Binocular rivalry. In D. Regan (Ed.), *Vision and visual dysfunction*, Vol. 9: *Binocular vision* (pp. 93–110). Boca Raton, FL: CRC Press.
- Fox, R., & Herrmann, J. (1967). Stochastic properties of binocular rivalry alternations. *Perception & Psychophysics*, 2(9), 432–436.
- Frecska, E., White, K. D., & Luna, L. E. (2004). Effects of ayahuasca on binocular rivalry with dichoptic stimulus alternation. *Psychopharmacology*, 173(1–2), 79–87.
- Freeman, A. W. (2005). Multistage model for binocular rivalry. *Journal of Neurophysiology*, 94(6), 4412–4420.
- Friston, K. (2005). A theory of cortical responses. *Philosophical Transactions of the Royal Society of London B: Biological Sciences*, 360(1456), 815–836.
- Friston, K., & Kiebel, S. (2009). Predictive coding under the free-energy principle. *Philosophical Transactions of the Royal Society of London B: Biological Sciences*, 364(1521), 1211–1221.
- Fry, G. A. (1936). The relation of accommodation to the suppression of vision in one eye. *American Journal of Ophthalmology*, 19, 135–138.
- Fukuda, H., & Blake, R. (1992). Spatial interactions in binocular rivalry. *Journal of Experimental Psychology: Human Perception and Performance*, 18(2), 362–370.
- Furey, M. L., Pietrini, P., & Haxby, J. V. (2000). Cholinergic enhancement and increased selectivity of perceptual processing during working memory. *Science*, 290(5500), 2315–2319.

- George, R. W. (1936). The significance of the fluctuations experienced in observing ambiguous figures and in binocular rivalry. *Journal of General Psychology*, 15(1), 39–61.
- Gigante, G., Mattia, M., Braun, J., & Del Giudice, P. (2009). Bistable perception modeled as competing stochastic integrations at two levels. *PLoS Computational Biology*, 5(7), e1000430. doi: 10.1371/journal.pcbi.1000430
- Goldberg, T. E., & Weinberger, D. R. (2004). Genes and the parsing of cognitive processes. *Trends in Cognitive Sciences*, 8(7), 325–335.
- Graf, E. W., & Adams, W. J. (2008). Surface organization influences bistable vision. *Journal of Experimental Psychology: Human Perception and Performance*, 34(2), 502–508.
- Gregory, R. L. (1997). Knowledge in perception and illusion. *Philosophical Transactions of the Royal Society of London B: Biological Sciences*, 352(1358), 1121–1127.
- Haijiang, Q., Saunders, J. A., Stone, R. W., & Backus, B. T. (2006). Demonstration of cue recruitment: Change in visual appearance by means of Pavlovian conditioning. *Proceedings of the National Academy of Sciences USA*, 103(2), 483–488.
- Hancock, S., & Andrews, T. J. (2007). The role of voluntary and involuntary attention in selecting perceptual dominance during binocular rivalry. *Perception*, 36(2), 288–298.
- Harrison, S., & Backus, B. (2010). Disambiguating Necker cube rotation using a location cue: What types of spatial location signal can the visual system learn? *Journal of Vision*, 10(6), 23. doi: 10.1167/10.6.23
- Hasselmo, M. E., & Sarter, M. (2011). Modes and models of forebrain cholinergic neuromodulation of cognition. *Neuropsychopharmacology*, 36(1), 52–73.
- Hastorf, A. H., & Myro, G. (1959). The effect of meaning on binocular rivalry. *American Journal of Psychology*, 72(3), 393–400.
- Haynes, J.-D., Deichmann, R., & Rees, G. (2005). Eye-specific effects of binocular rivalry in the human lateral geniculate nucleus. *Nature*, 438(7067), 496–499.
- Helmholtz, H. (1867). *Handbuch der physiologischen Optik*, Leipzig: Voss. J. P. C. Southall, 1925 (Trans.), *Helmholtz's treatise on physiological optics*, Vol 3. New York: Optical Society of America.
- Ichihara, S., & Goryo, K. (1978). The effects of relative orientation of surrounding gratings on binocular rivalry and apparent brightness of central gratings. *Japanese Psychological Research*, 20(4), 159–166.
- Jain, A., Fuller, S., & Backus, B. T. (2010). Absence of cue-recruitment for extrinsic signals: Sounds, spots, and swirling dots fail to influence perceived 3D rotation direction after training. *PLoS ONE*, 5(10), e13295. doi: 10.1371/journal.pone.0013295
- Kang, P., & Shevell, S. (2011). Multistable binocular feature-integrated percepts are frozen by intermittent presentation. *Journal of Vision*, 11(1), 5. doi: 10.1167/11.1.5
- Keliris, G. A., Logothetis, N. K., & Tolias, A. S. (2010). The role of the primary visual cortex in perceptual suppression of salient visual stimuli. *Journal of Neuroscience*, 30(37), 12353–12365.
- Kersten, D., Mamassian, P., & Yuille, A. (2004). Object perception as Bayesian inference. *Annual Review of Psychology*, 55, 271–304.
- Kim, C. Y., & Blake, R. (2007). Illusory colors promote interocular grouping during binocular rivalry. *Psychonomic Bulletin & Review*, 14(2), 356–362.
- Klink, P. C., van Ee, R., Nijs, M. M., Brouwer, G. J., Noest, A. J., & van Wezel, R. J. A. (2008). Early interactions between neuronal adaptation and voluntary control determine perceptual choices in bistable vision. *Journal of Vision*, 8(5), 16. doi: 10.1167/8.5.16

- Knierim, J. J., & van Essen, D. C. (1992). Neuronal responses to static texture patterns in area V1 of the alert macaque monkey. *Journal of Neurophysiology*, 67(4), 961–980.
- Kondo, H. M., Kitagawa, N., Kitamura, M. S., Koizumi, A., Nomura, M., & Kashino, M. (2012). Separability and commonality of auditory and visual bistable perception. *Cerebral Cortex*, 22(8), 1915–1922.
- Kovács, I., Papathomas, T. V., Yang, M., & Fehér, A. (1996). When the brain changes its mind: Interocular grouping during binocular rivalry. *Proceedings of the National Academy of Sciences USA*, 93(26), 15508–15511.
- Kulikowski, J. J. (1992). Binocular chromatic rivalry and single vision. *Ophthalmic and Physiological Optics*, 12(2), 168–170.
- Lack, L. C. (1969). The effect of practice on binocular rivalry control. *Perception & Psychophysics*, 6(6B), 397–400.
- Lack, L. C. (1973). Amplitude of visual suppression during the control of binocular rivalry. *Perception & Psychophysics*, 13(3), 374–378.
- Lack, L. C. (1978). *Selective attention and the control of binocular rivalry*. The Hague: Mouton.
- Lee, S. H., & Blake, R. (2004). A fresh look at interocular grouping during binocular rivalry. *Vision Research*, 44(10), 983–991.
- Lehky, S. R. (1988). An astable multivibrator model of binocular rivalry. *Perception*, 17(2), 215–228.
- Lehky, S. R., & Maunsell, J. H. (1996). No binocular rivalry in the LGN of alert macaque monkeys. *Vision Research*, 36(9), 1225–1234.
- Leopold, D. A., & Logothetis, N. K. (1996). Activity changes in early visual cortex reflect monkeys' percepts during binocular rivalry. *Nature*, 379(6565), 549–553.
- Leopold, D. A., Wilke, M., Maier, A., & Logothetis, N. K. (2002). Stable perception of visually ambiguous patterns. *Nature Neuroscience*, 5(6), 605–609.
- Levelt, W. J. M. (1965). *On binocular rivalry*. Soesterberg, The Netherlands: Institute for Perception RVO-TNO.
- Levelt, W. J. (1967). Note on the distribution of dominance times in binocular rivalry. *British Journal of Psychology*, 58(1–2), 143–145.
- Lunghi, C., Binda, P., & Morrone, M. C. (2010). Touch disambiguates rivalrous perception at early stages of visual analysis. *Current Biology*, 20(4), R143–R144.
- Maloney, L. T., Dal Martello, M. F., Sahm, C., & Spillmann, L. (2005). Past trials influence perception of ambiguous motion quartets through pattern completion. *Proceedings of the National Academy of Sciences USA*, 102(8), 3164–3169.
- Mapperson, B., & Lovegrove, W. (1991). Orientation and spatial-frequency-specific surround effects on binocular rivalry. *Bulletin of the Psychonomic Society*, 29(2), 95–97.
- Maruya, K., Yang, E., & Blake, R. (2007). Voluntary action influences visual competition. *Psychological Science*, 18(12), 1090–1098.
- McDougall, W. (1903). III. – The physiological factors of the attention-process (III.). *Mind*, 12(48), 473–488.
- Mednick, S. C., Cai, D. J., Kanady, J., & Drummond, S. P. (2008). Comparing the benefits of caffeine, naps and placebo on verbal, motor and perceptual memory. *Behavioural Brain Research*, 193(1), 79–86.
- Meng, M., & Tong, F. (2004). Can attention selectively bias bistable perception? Differences between binocular rivalry and ambiguous figures. *Journal of Vision*, 4(7), 2. doi: 10.1167/4.7.2

- Meredith, G. M., & Meredith, C. G. (1962). Effect of instructional conditions on rate of binocular rivalry. *Perceptual and Motor Skills*, 15(3), 655–664.
- Miller, S. M., Hansell, N. K., Ngo, T. T., Liu, G. B., Pettigrew, J. D., Martin, N. G. et al. (2010). Genetic contribution to individual variation in binocular rivalry rate. *Proceedings of the National Academy of Sciences USA*, 107(6), 2664–2668.
- Mitchell, J. F., Stoner, G. R., & Reynolds, J. H. (2004). Object-based attention determines dominance in binocular rivalry. *Nature*, 429(6990), 410–413.
- Moreno-Bote, R., Rinzel, J., & Rubin, N. (2007). Noise-induced alternations in an attractor network model of perceptual bistability. *Journal of Neurophysiology*, 98(3), 1125–1139.
- Mudrik, L., Deouell, L. Y., & Lamy, D. (2011). Scene congruency biases binocular rivalry. *Consciousness and Cognition*, 20(3), 756–767.
- Mueller, T. J., & Blake, R. (1989). A fresh look at the temporal dynamics of binocular rivalry. *Biological Cybernetics*, 61(3), 223–232.
- Mumford, D. (1992). On the computational architecture of the neocortex. II. The role of cortico-cortical loops. *Biological Cybernetics*, 66(3), 241–251.
- Nagamine, M., Yoshino, A., Miyazaki, M., Takahashi, Y., & Nomura, S. (2008). Effects of selective 5-HT_{1A} agonist tandospirone on the rate and rhythmicity of binocular rivalry. *Psychopharmacology*, 198(2), 279–286.
- Neisser, U., & Becklen, R. (1975). Selective looking: Attending to visually specified events. *Cognitive Psychology*, 7(4), 480–494.
- Ngo, T. T., Liu, G. B., Tilley, A. J., Pettigrew, J. D., & Miller, S. M. (2007). Caloric vestibular stimulation reveals discrete neural mechanisms for coherence rivalry and eye rivalry: A meta-rivalry model. *Vision Research*, 47(21), 2685–2699.
- Ngo, T. T., Miller, S. M., Liu, G. B., & Pettigrew, J. D. (2000). Binocular rivalry and perceptual coherence. *Current Biology*, 10(4), R134–R136.
- Noest, A. J., van Ee, R., Nijs, M. M., & van Wezel, R. J. A. (2007). Percept-choice sequences driven by interrupted ambiguous stimuli: A low-level neural model. *Journal of Vision*, 7(8), 10. doi:10.1167/7.8.10
- Ooi, T. L., & He, Z. J. (2005). Surface representation and attention modulation mechanisms in binocular rivalry. In D. Alais & R. Blake (Eds.), *Binocular rivalry* (pp. 117–135). Cambridge, MA: MIT Press.
- Ooi, T. L., & He, Z. J. (1999). Binocular rivalry and visual awareness: The role of attention. *Perception*, 28(5), 551–574.
- Ooi, T. L., & He, Z. J. (2003). A distributed intercortical processing of binocular rivalry: Psychophysical evidence. *Perception*, 32(2), 155–166.
- Ooi, T. L., & He, Z. J. (2006). Binocular rivalry and surface-boundary processing. *Perception*, 35(5), 581–603.
- Paffen, C. L., & Alais, D. (2011). Attentional modulation of binocular rivalry. *Frontiers in Human Neuroscience*, 5, 105. doi:10.3389/fnhum.2011.00105
- Paffen, C. L., Alais, D., & Verstraten, F. A. (2006). Attention speeds binocular rivalry. *Psychological Science*, 17(9), 752–756.
- Paffen, C. L., Tadin, D., te Pas, S. F., Blake, R., & Verstraten, F. A. (2006). Adaptive center-surround interactions in human vision revealed during binocular rivalry. *Vision Research*, 46(5), 599–604.
- Paffen, C. L., van der Smagt, M. J., te Pas, S. F., & Verstraten, F. A. (2005). Center-surround inhibition and facilitation as a function of size and contrast at multiple levels of visual motion processing. *Journal of Vision*, 5(6), 8. doi:10.1167/5.6.8

- Paffen, C. L., & Van der Stigchel, S. (2010). Shifting spatial attention makes you flip: Exogenous visual attention triggers perceptual alternations during binocular rivalry. *Attention, Perception, & Psychophysics*, 72(5), 1237–1243.
- Papathomas, T. V., Kovács, I., & Conway, T. (2005). Interocular grouping in binocular rivalry: Basic attributes and combinations. In D. Alais & R. Blake (Eds.), *Binocular rivalry* (pp. 155–168). Cambridge, MA: MIT Press.
- Parasuraman, R., Greenwood, P. M., Kumar, R., & Fossella, J. (2005). Beyond heritability: Neurotransmitter genes differentially modulate visuospatial attention and working memory. *Psychological Science*, 16(3), 200–207.
- Pastukhov, A., & Braun, J. (2008). A short-term memory of multi-stable perception. *Journal of Vision*, 8(13), 7. doi: 10.1167/8.13.7
- Pearson, J., & Brascamp, J. (2008). Sensory memory for ambiguous vision. *Trends in Cognitive Sciences*, 12(9), 334–341.
- Pearson, J., & Clifford, C. W. G. (2004). Determinants of visual awareness following interruptions during rivalry. *Journal of Vision*, 4(3), 6. doi: 10.1167/4.3.6
- Pearson, J., & Clifford, C. W. G. (2005). Mechanisms selectively engaged in rivalry: Normal vision habituates, rivalrous vision primes. *Vision Research*, 45(6), 707–714.
- Polonsky, A., Blake, R., Braun, J., & Heeger, D. J. (2000). Neuronal activity in human primary visual cortex correlates with perception during binocular rivalry. *Nature Neuroscience*, 3(11), 1153–1159.
- Rao, R. P., & Ballard, D. H. (1999). Predictive coding in the visual cortex: A functional interpretation of some extra-classical receptive-field effects. *Nature Neuroscience*, 2(1), 79–87.
- Rokem, A., Landau, A. N., Garg, D., Prinzmetal, W., & Silver, M. A. (2010). Cholinergic enhancement increases the effects of voluntary attention but does not affect involuntary attention. *Neuropsychopharmacology*, 35(13), 2538–2544.
- Rokem, A., Landau, A. N., Prinzmetal, W., Wallace, D. L., Silver, M. A., & D'Esposito, M. (2012). Modulation of inhibition of return by the dopamine D2 receptor agonist bromocriptine depends on individual DAT1 genotype. *Cerebral Cortex*, 22(5), 1133–1138.
- Sheth, B. R., & Pham, T. (2008). How emotional arousal and valence influence access to awareness. *Vision Research*, 48(23–24), 2415–2424.
- Silver, M. A., & Logothetis, N. K. (2004). Grouping and segmentation in binocular rivalry. *Vision Research*, 44(14), 1675–1692.
- Silver, M. A., Shenav, A., & D'Esposito, M. (2008). Cholinergic enhancement reduces spatial spread of visual responses in human early visual cortex. *Neuron*, 60(5), 904–914.
- Sobel, K. V., & Blake, R. (2002). How context influences predominance during binocular rivalry. *Perception*, 31(7), 813–824.
- Sterzer, P., Frith, C., & Petrovic, P. (2008). Believing is seeing: Expectations alter visual awareness. *Current Biology*, 18(16), R697–R698.
- Stuit, S. M., Paffen, C. L. E., van der Smagt, M. J., & Verstraten, F. A. J. (2011). What is grouping during binocular rivalry? *Frontiers in Human Neuroscience*, 5, 117. doi: 10.3389/fnhum.2011.00117
- Su, Y., He, Z. J., & Ooi, T. L. (2009). Coexistence of binocular integration and suppression determined by surface border information. *Proceedings of the National Academy of Sciences USA*, 106(37), 15990–15995.
- Su, Y. R., He, Z. J., & Ooi, T. L. (2011). Seeing grating-textured surface begins at the border. *Journal of Vision*, 11(1), 14. doi: 10.1167/11.1.14

- Thomas, R., Nardini, M., & Mareschal, D. (2010). Interactions between "light-from-above" and convexity priors in visual development. *Journal of Vision*, 10(8), 6. doi:10.1167/10.8.6
- Tong, F., & Engel, S. A. (2001). Interocular rivalry revealed in the human cortical blind-spot representation. *Nature*, 411(6834), 195–199.
- van Bogaert, E. A., Ooi, T. L., & He, Z. J. (2008). The monocular-boundary-contour mechanism in binocular surface representation and suppression. *Perception*, 37(8), 1197–1215.
- van Dam, L. C., & van Ee, R. (2006). The role of saccades in exerting voluntary control in perceptual and binocular rivalry. *Vision Research*, 46(6–7), 787–799.
- van Ee, R. (2009). Stochastic variations in sensory awareness are driven by noisy neuronal adaptation: Evidence from serial correlations in perceptual bistability. *Journal of the Optical Society of America A: Optics, Image Science and Vision*, 26(12), 2612–2622.
- van Ee, R., van Boxtel, J. J., Parker, A. L., & Alais, D. (2009). Multisensory congruency as a mechanism for attentional control over perceptual selection. *Journal of Neuroscience*, 29(37), 11641–11649.
- van Ee, R., van Dam, L. C., & Brouwer, G. J. (2005). Voluntary control and the dynamics of perceptual bi-stability. *Vision Research*, 45(1), 41–55.
- van Holstein, M., Aarts, E., van der Schaaf, M. E., Geurts, D. E., Verkes, R. J., Franke, B. et al. (2011). Human cognitive flexibility depends on dopamine D2 receptor signaling. *Psychopharmacology*, 218(3), 567–578.
- van Lier, R., & de Weert, C. M. M. (2003). Intra- and interocular colour-specific activation during dichoptic suppression. *Vision Research*, 43(10), 1111–1116.
- Wade, N. J. (1973). Binocular rivalry and binocular fusion of after-images. *Vision Research*, 13(5), 999–1000.
- Wade, N. J., & de Weert, C. M. M. (1986). Aftereffects in binocular rivalry. *Perception*, 15(4), 419–434.
- Washburn, M. F., & Gillette, A. (1933). Motor factors in voluntary control of cube perspective fluctuations and retinal rivalry fluctuations. *American Journal of Psychology*, 45(2), 315–319.
- Whittle, P., Bloor, D. C., & Pocock, S. (1968). Some experiments on figural effects in binocular rivalry. *Perception & Psychophysics*, 4(3), 183–188.
- Wilke, M., Logothetis, N. K., & Leopold, D. A. (2006). Local field potential reflects perceptual suppression in monkey visual cortex. *Proceedings of the National Academy of Sciences USA*, 103(46), 17507–17512.
- Wilke, M., Mueller, K. M., & Leopold, D. A. (2009). Neural activity in the visual thalamus reflects perceptual suppression. *Proceedings of the National Academy of Sciences USA*, 106(23), 9465–9470.
- Wilson, H. R. (2003). Computational evidence for a rivalry hierarchy in vision. *Proceedings of the National Academy of Sciences USA*, 100(24), 14499–14503.
- Wong, E. M., & Freeman, A. W. (1999). Colour but not form patterns combine between the eyes. *Australian and New Zealand Journal of Ophthalmology*, 27(3–4), 275–277.
- Wunderlich, K., Schneider, K. A., & Kastner, S. (2005). Neural correlates of binocular rivalry in the human lateral geniculate nucleus. *Nature Neuroscience*, 8(11), 1595–1602.
- Xu, J. P., He, Z. J., & Ooi, T. L. (2010). Surface boundary contour strengthens image dominance in binocular competition. *Vision Research*, 50(2), 155–170.
- Yoon, K. L., Hong, S. W., Joormann, J., & Kang, P. (2009). Perception of facial expressions of emotion during binocular rivalry. *Emotion*, 9(2), 172–182.

- Yu, K., & Blake, R. (1992). Do recognizable figures enjoy an advantage in binocular rivalry? *Journal of Experimental Psychology: Human Perception and Performance*, 18(4), 1158–1173.
- Zhang, P., Jamison, K., Engel, S., He, B., & He, S. (2011). Binocular rivalry requires visual attention. *Neuron*, 71(2), 362–369.
- Zhou, W., Jiang, Y., He, S., & Chen, D. (2010). Olfaction modulates visual perception in binocular rivalry. *Current Biology*, 20(15), 1356–1358.

Binocular rivalry

Cooperation, competition, and decisions*

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This chapter will first examine the neural circuitry necessary to generate binocular rivalry. Such neural circuits entail both neural cooperation within and competition between monocular images. Evidence will also be presented that rivalry must occur at multiple hierarchic levels in the visual system in order to explain relevant data. In light of this, the suggestion that rivalry can elucidate the neural correlates of conscious vision will be challenged. Following this, generalizations of rivalry to competition among multiple spatial patterns will be developed. It will be argued that such generalized rivalry can provide significant insights into the nature of high level visual decisions in the presence of ambiguous or incomplete information.

Neural modeling, binocular rivalry and consciousness

Normally, the two eyes receive correlated but slightly different images of the scene being viewed. The visual cortex has evolved to combine this information into a single view, using the slight discrepancies, termed disparities, to extract information about the third dimension, depth. When each of the two eyes views a radically different pattern (e.g., horizontal stripes in one eye and vertical in the other), however, perception defaults into an alternation between the two monocular views. Known as binocular rivalry, this is a fascinating phenomenon in which observers experience their own brain grappling to interpret the visual world given inconsistent, competing information. As these perceptual alternations originate in the brain in the absence of any stimulus changes, several authors have proposed that binocular rivalry may be useful as a tool to establish neural correlates of conscious vision. Here I shall take a different approach and argue that generalizations of

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rivalry to multiple, partially overlapping patterns can provide key insights into decision networks and thus also provide insights into conscious processing.

A great diversity of techniques at many levels of complexity contributes to our knowledge of brain function in general as well as rivalry. These include molecular neuroscience, membrane biophysics, electrophysiology of individual neurons, brain imaging (functional magnetic resonance imaging, fMRI), and finally behavior (see chapter by Sterzer, this volume). This raises the question: how can information from these levels be integrated into a predictive and explanatory framework? Computation and neural modeling are crucial to this integration task. The typical neural model incorporates from a few to fairly large numbers of neurons that interact with one another via both excitatory and inhibitory synaptic connections. Such networks may be either designed or else trained via learning algorithms to perform in a manner consistent with an organism's behavior. In essence, therefore, neural models serve as the glue fusing multiple levels of description of brain processes into coherent explanations of brain function.

But what does a mathematical neural network model add to a linguistic description of rivalry or conscious processing? Isn't mathematics just another language? We now know from contemporary brain research that the answer is a resounding NO! Far from being another language, mathematics utilizes completely different brain areas (many in parietal cortex) (Dehaene, 1997; Dehaene, Tzourio, Frak, Cohen, & Mazoyer, 1996). Indeed, mathematics, and especially the nonlinear dynamics integral to neural modeling provide a dramatically different mode of understanding that complements language rather than mimicking it. Concepts such as limit cycle oscillations, hysteresis, and bifurcations are now regarded as central to understanding both rivalry and aspects of conscious experience (Wilson, 1999, 2009). In fact, there is an emerging field of neural models designed to elucidate conscious brain processes, and progress is likely to accelerate in this area (Dehaene & Changeux, 1997; Dehaene, Kerszberg, & Changeux, 1998; Dehaene, Sergent, & Changeux, 2003; O'Reilly, 2006; Wilson, 2009). These claims will be developed by first discussing a number of increasingly more complex models of binocular rivalry. This will lead to a generalization of rivalry to interactions among multiple neural groups in a manner that sheds light on aspects of conscious deliberation and decisions in the face of ambiguous or incomplete data.

Models of binocular rivalry

The simplest binocular rivalry network comprises four groups of neurons, as depicted in Figure 1a (Wilson, 2005, 2007). The groups labeled A and B represent monocular cells in primary visual cortex (V1) driven by the left (L) and right (R) eyes respectively. Furthermore, these groups are assumed to be selective for

very different stimulus patterns, such as vertical and horizontal bars respectively. Each group excites (pointed arrows) a distinct inhibitory neuron population (gray circles) which selectively inhibits the other group (arrows with circular heads). In addition, each group incorporates weak excitatory connections (E) incorporating recurrent feedback among neurons within the group, such as those mediating col-linear facilitation (McLaughlin, Shapley, Shelley, & Wielaard, 2000; Polat, Mizobe, Pettet, Kasamatsu, & Norcia, 1998). This is the archetypical network incorporating cooperation in the form of recurrent excitation E and competition between A and B generated by mutual inhibition.

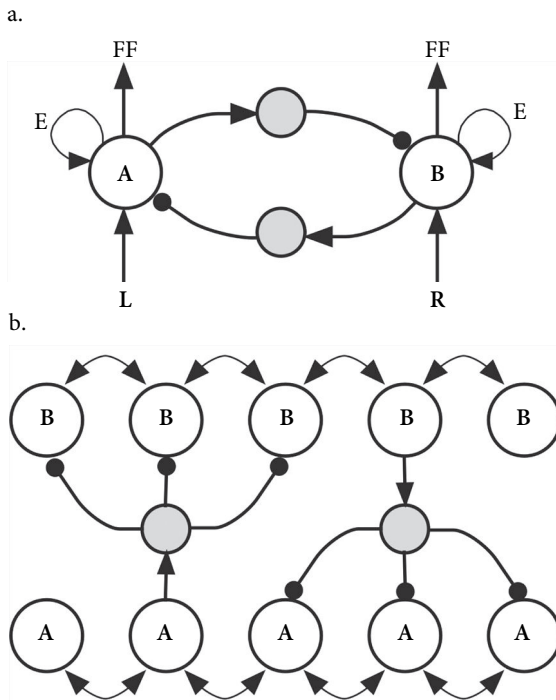


Figure 1. Neural networks for binocular rivalry. (a) Neural populations A and B compete via mutual inhibition mediated by inhibitory neurons indicated by gray circles. L and R represent left and right monocular stimuli, while loops marked E designate cooperative excitatory feedback connections within each group. FF denotes the feedforward output of the model. In this and all subsequent network diagrams, lines terminating in arrowheads designate excitatory connections, while solid black circles at the end of lines indicate inhibitory connections. (b) Spatially extended rivalry network capable of supporting rivalry wave propagation. The recurrent excitatory connections within the A and B neuron groups extend to spatial nearest neighbors. Similarly, the competitive inhibition mediated by the gray neurons has a spatial spread to a range of neurons in the other group. All A and B neurons give rise to such inhibition, although only two are diagrammed for clarity.

The dynamics of this network may be described by appropriate nonlinear differential equations (Wilson, 2007):

$$\tau \frac{dR_A}{dt} = -R_A + S(L + \epsilon R_A - aR_B - gH_A) \quad (1)$$

$$\tau_H \frac{dH_A}{dt} = -H_A + R_A$$

where:

$$S(X) = \frac{[X]_+}{1 + [X]_+^{0.8}} \quad (2)$$

In these equations R_A represents the response firing rate of the A neurons as a function of their level of stimulation, which is given by the nonlinear function $S(X)$. Stimulation of the A neurons results from the indicated combination of left monocular input L , plus ϵR_A (recurrent excitation within the group), minus aR_B (competitive inhibition from the group B neurons), and a subtractive self-polarization term gH_A that is governed by the second differential equation in (1). The nonlinear, sigmoid (S-shaped) function $S(X)$ is plotted in Figure 2a. The expression $[X]_+$ evaluates to zero for $X < 0$ and to X otherwise. This produces a threshold (set to 0.0 here for simplicity). In addition there is a compressive non-linearity in response rate for $X > 0$. This is a form of the Wilson-Cowan equations (Wilson & Cowan, 1972) with $S(X)$ optimized to describe rivalry (Wilson, 2007). Equations analogous to (1) with subscripts A and B interchanged, describe the response, R_B , of the population B neurons.

Key to understanding rivalry dynamics is the balance between recurrent excitation ($+\epsilon R_A$) within a neural population, inhibition from the second population ($-aR_B$), and self-hyperpolarization ($-gH_A$), which is a known characteristic of human and other mammalian cortical excitatory neurons (McCormick & Williamson, 1989). This hyperpolarization is driven by the firing rate of the neurons. Crucially, the time constant $\tau_H \gg \tau$, with values of 700 ms and 15 ms respectively employed in the current simulations. The dynamics of binocular rivalry can now be understood simply by examining the computed response in Figure 2b. Following initiation of stimulation, the Left eye neurons (A), which have a slightly larger stimulus level, become active and suppress the Right eye neurons (B). The A neurons now begin to adapt slowly due to the self-polarizing current, so their firing rate declines until the B neurons are released from inhibition and begin to fire, now suppressing the A neurons. The A neurons now slowly recover from hyperpolarization; the B neurons self-hyperpolarize; and the process repeats itself.

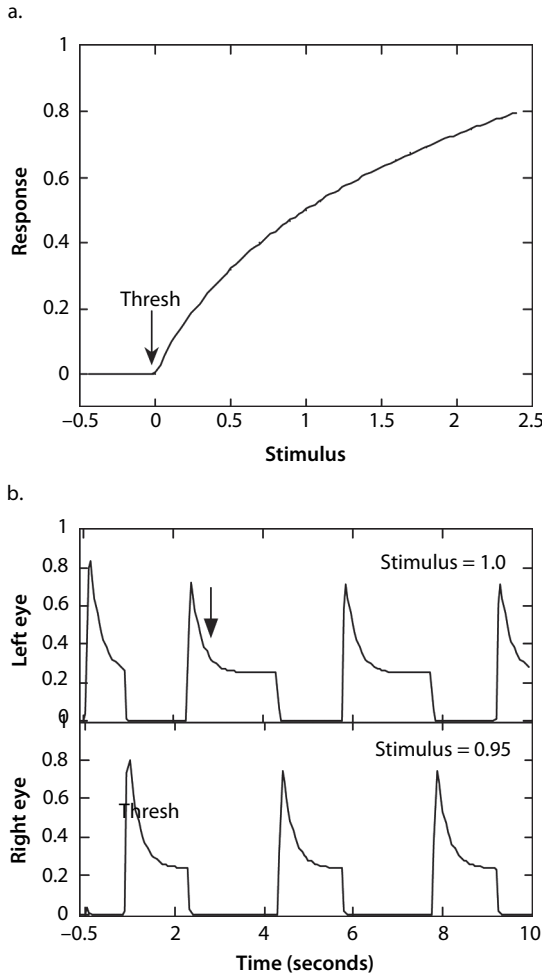


Figure 2. Nonlinear neural response function (a) with threshold (Thresh) and compressive suprathreshold nonlinearity from Equation (2). (b) Rivalry alternations produced by simulations of Equation (1). Left eye neurons receive a slightly stronger stimulus than right eye neurons and therefore generate slightly longer dominance intervals (Level's second law). If all stimulation is stopped for up to 5.0 s at the arrow (about 3.0 s into the simulation), the same neurons remain dominant when stimulation is resumed. This can be repeated multiple times, thus providing evidence for one type of rivalry memory. See text for further details.

From a nonlinear dynamics perspective, the firing rate alternation between A and B neurons represents a limit cycle oscillation. Alternatively, it can be regarded as a winner-take-all victory by one neural group, which sustains its activity via hysteresis until self-hyperpolarization drives it through a bifurcation, when the other group becomes the winner (Wilson, 1999). One can mathematically derive the requirements for this limit cycle (Wilson, 2007). Briefly, the inhibition must be sufficiently strong to suppress the competing pattern; self-excitation must not be strong enough to defeat this suppression; and self-hyperpolarization must ultimately reduce firing rates sufficiently to negate the competitive inhibition. There are three caveats. First, slightly different stimulation levels result in the more strongly stimulated neurons maintaining dominance for a greater portion of the oscillation period (Figure 2b). This is empirically corroborated and known as Levelt's second law (Levelt, 1965). Second, the rivalry alternation periods measured empirically are not precise but show a distribution of durations described by a gamma distribution (Fox & Herrmann, 1967). This is easily incorporated into Equation (1) by adding a noise term to the dH_A/dt equation. Most importantly, as the difference between input stimulation to the A and B neural populations increases, the duration of dominance by the more strongly stimulated group increases until it becomes infinite. At this point a bifurcation occurs, and the network assumes winner-take-all dynamics. This will be important when rivalry is generalized to a model for decisions.

One further aspect of rivalry is important here. Not only are there reliable differences in mean rivalry rates among individuals, but a genetic component has been documented in twin studies (Miller et al., 2010). The rivalry model developed above provides a plausible biological explanation of these correlations. The strength of the self-hyperpolarization denoted by the parameter g in Equation (1) is known to be dependent on the level of modulatory neurotransmitters such as serotonin (McCormick & Williamson, 1989). Previous modeling has shown that variations in the parameter g , controlled by serotonin, can shift the rivalry dominance duration over the range 1.0–5.0 s (Wilson, 2007). As serotonin concentration is modulated by nuclei in the brain stem, it is reasonable to suppose that the efficacy of these nuclei is genetically determined, which would explain both the reliable individual differences in rivalry rates and the strong correlation for identical twins (see chapters by Bressler, Denison, & Silver and Ngo, Barsdell, Law, & Miller, this volume).

It should also be emphasized that binocular rivalry ensues when the two monocular images are too different to be integrated into a stereoscopic view of a three-dimensional world. Thus, rivalry may be viewed as a conflict between incompatible, but equally compelling interpretations of the available visual data. Indeed, there is hysteresis between seeing in three dimensions and experiencing rivalry (Buckthought, Kim, & Wilson, 2008). Thus, there is a bifurcation between

unified perception of the world and rivalry. I will suggest below that rivalry is therefore a paradigm for how the brain deals with equally compelling, but mutually exclusive interpretations of available information.

Extending the basic rivalry model

There are several major extensions of the basic model for binocular rivalry that explain additional empirical results and are also relevant for subsequent interpretation of conscious processing. Three will be briefly mentioned here: hierarchical rivalry networks, spatially distributed rivalry networks, and rivalry memory (see chapter by Brascamp & Baker, this volume).

The discussion above argued that rivalry occurs between monocular neurons in cortical area V1. However, a major challenge to this interpretation was mounted in a paper showing that rivalry dominance for one pattern could outlast roughly seven switches between eyes (Logothetis, Leopold, & Sheinberg, 1996). This would suggest that binocular rivalry durations were stimulus specific rather than eye specific. However, this study required both a 1.5 Hz swap between eyes and an 18.0 Hz on-off flicker of the stimulus in each eye. These unusual dynamical requirements for the phenomenon suggested that it might reflect nonlinear dynamic properties. To demonstrate this, I constructed a two-level hierarchy of rivalry networks by replicating the network in Figure 1a and requiring that the second level be driven by the first level responses (Wilson, 2003). Under normal stimulation conditions, rivalry at the first stage propagated to the second stage and drove rivalry there. Under the flicker and swap conditions, however, inhibition at the first stage was weakened sufficiently so that no rivalry occurred there. However, competitive inhibition at the second stage was still able to operate effectively, so rivalry oscillations occurred at that stage.

Two important points emerge from this example. First, there is evidence that the circuitry for rivalry occurs at a hierarchical series of stages in vision. This is consistent with the notion that more complex, generalized forms of rivalry may provide the basis for competitive decision making at the highest levels of the cortex.

Second, given a hierarchy of rivalry stages in vision, it becomes virtually impossible to use rivalry as a marker to determine the cortical locus of consciousness. Under normal rivalry stimulus conditions the evidence indicates that competition among monocular V1 neurons drives rivalry at all higher stages of the visual system. Strong support for the V1 locus of binocular rivalry has been provided by brain imaging (fMRI) studies showing rivalry in the blind spot representation in V1, which contains exclusively monocular neurons (Tong & Engel, 2001; see chapter by Sterzer, this volume). Thus, activity in the V1 locus

at which binocular rivalry is apparently generated is simply reflected throughout the visual hierarchy via feedforward connections. So evidence for rivalry in multiple higher visual cortical areas has little to say about the locus of consciousness, although it does by definition show that activity in a hierarchy of cortical areas is correlated with rivalry consciousness (see forthcoming companion volume for further discussion).

The second extension of rivalry is to spatially distributed cooperative and competitive networks. Anyone who has experienced rivalry between horizontal bars in one eye and vertical in the other is aware that the patterns do not come and go in a unitary fashion. Rather, when a pattern that was previously suppressed reappears at some locus, that pattern spreads in a wave across the visual field. By restricting rivalry stimuli to circular annuli, we were able to actually measure the speed of rivalry wave propagation psychophysically (Wilson, Blake, & Lee, 2001). When mapped into cortical coordinates, this corresponded to a speed of about 2.0 mm/s. In a masterful subsequent study, Lee, Blake, and Heeger (2007) used fMRI to actually measure the speed of rivalry waves in V1, and this was found to agree closely with the psychophysically estimated value. This direct observation of rivalry waves in V1 further substantiated that early brain region are the driving locus of rivalry under normal conditions.

Traveling rivalry waves can be explained by the spatially extended rivalry network depicted in Figure 1b. Here two spatially extended arrays of competing A and B neurons form spatially adjacent recurrent excitatory connections within each array, and the inhibition between arrays mediated by the gray cells likewise spreads to spatially adjacent locations (only two such inhibitory connections are shown for clarity). Wave spread is easily understood using this network (Wilson et al., 2001). Assume that the A neuron on the left has just become active. This will both inhibit a range of B neurons and excite the adjacent A neuron. Thus, A neurons will become active and B neurons will be suppressed as the wave propagates to the right. Subsequently the A neurons will slowly hyperpolarize, and B neuron activity will emerge and propagate. This provides evidence for spatially distributed rivalry networks in vision.

The final important aspect of rivalry networks is the presence of two forms of memory. Suppose that both stimuli to rivalry are turned off immediately after one eye's stimulus becomes dominant, for example at the arrow in Figure 2b. If the stimuli are then turned on 5 s later, the same stimulus (left eye in this case) remains visually dominant. This process can be repeated many times, with the same stimulus remaining dominant for a very long period (Leopold, Wilke, Maier, & Logothetis, 2002). Clearly, rivalry networks have some mechanism for remembering the previously dominant stimulus over these 5 s periods. This has been successfully modeled by assuming that there is a short term increase in the efficacy

of excitatory synapses within the active group, which functions to give this a competitive advantage when the stimuli are again presented (Wilson, 2007). A natural candidate for such short term facilitation would be vesicle docking at the presynaptic membrane.

A second form of rivalry memory has also been reported recently (Klink, Brascamp, Blake, & van Wezel, 2010; see chapter by Klink, van Wezel, & van Ee, this volume). When a subject views rivalry stimuli for a prolonged period of many minutes, the rivalry alternations decrease, and periods in which both stimuli are simultaneously perceived either as a patchwork or plaid become much longer. Further experiments supported the hypothesis that this involves a reduction of inhibitory synaptic strength in the rivalry network. This represents a form of anti-Hebbian or negative learning in which synapses between neurons that cannot be simultaneously active (an inhibitory neuron and the neurons that it is inhibiting) weaken over time. As I suggested in a published commentary, this might be described as: “neurons unwire when they can’t simultaneously fire” (Wilson, 2010). Certainly many more exciting experiments will be driven by these new discoveries. The key point for our purposes is simply that rivalry networks demonstrate forms of plasticity akin to those involved in memory.

To recapitulate, binocular rivalry has been shown to involve both cooperative and competitive interactions between different cell groups. Furthermore, these groups are distributed and interact across space. In addition, stereoscopic vision switches to rivalry precisely when the two eyes present V1 with equally compelling but mutually incompatible information about the nature of the 3D world. Finally, these networks incorporate forms of plasticity and learning. A useful review of binocular vision and rivalry has recently been published (Blake & Wilson, 2011). All these characteristics suggest that generalizations of rivalry networks will be prime candidates for explaining high level decision processes.

Generalized rivalry and deliberative processes

Consider the evolutionary circumstances under which deliberation is valuable. When a course of action must be selected, there is an evolutionary advantage to evaluating all of the available evidence concerning various courses of action before reaching a decision. Such evidence includes current sensory input, memory of similar situations, and the emotional valence contingent on these. When the evidence for one action is vastly greater than that for others, deliberation is not necessary, and there is a metabolic advantage for the brain to act immediately (much like a reflex arc to pain). However, when evidence for several alternatives is almost equal, there is clear advantage to deliberation. In deliberation, an individual first considers

one possible action, then another, then perhaps a third, up to some modest limit. During such deliberation, one typically searches for both further supporting (or refuting) evidence from memories and for emotional cues to the desirability of the action. Sooner or later deliberation results in one course of action.

It is my contention that a generalization of rivalry to incorporate multiple competing patterns provides a plausible and testable model for the neural basis of deliberation (Wang, 2002). Consider the elaborated network in Figure 3. The large box contains three neural populations (A–C), each coupled via recurrent, cooperative excitation E, and all competing via mutual inhibition (arrows ending in solid circles). These populations each receive lower level inputs from high sensory areas such as parietal and temporal lobe visual areas, memory areas for relevant events, and areas conveying emotional valence and potential reward. In addition, there is premotor input reflecting costs and benefits of alternative motor plans. The primary networks in the brain that receive all of these inputs are in prefrontal cortex

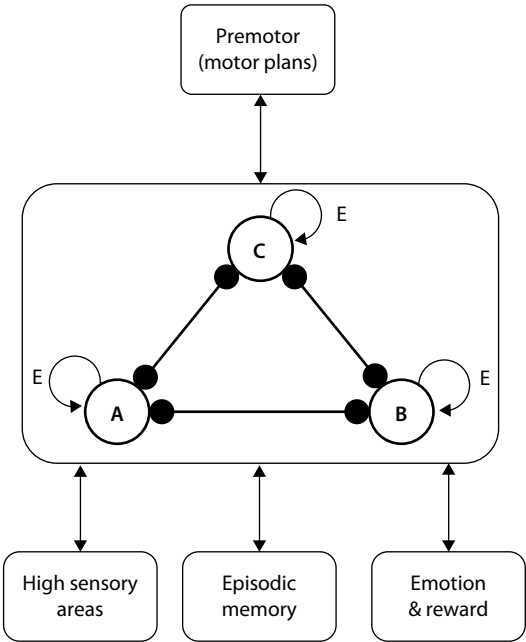


Figure 3. Schematic of multiple rivaling groups (three are shown: A, B, C) hypothesized to be involved in decision-making in prefrontal cortex (PFC). All groups compete via inhibition, and neurons within each group cooperate via recurrent excitation E. These PFC networks receive input from high sensory areas, memory areas, emotion & reward systems, and premotor cortex for motor planning. Active neurons in PFC provide modulatory feedback to their lower level inputs.

(PFC), so I shall hypothesize that the competing network at the top of the figure represents neural populations in PFC. Indeed, there is recent evidence that lateral PFC neurons reflect conscious states during a binocular flash suppression task (Panagiotaropoulos, Deco, Kapoor, & Logothetis, 2012). This agrees with research by Koechlin and Hyafil (2007), who argue that the PFC is “associated with maintaining and switching back and forth between multiple behavioral alternatives in search of optimal behavior” (p. 594).

Let us examine the dynamics of a more complex rivalry network for the hypothetical PFC deliberations. The network illustrated in Figure 4 comprises 15 neurons or neural populations that are differentiated in two dimensions for conceptual clarity. The horizontal dimension contains columns of neurons representing different attributes or actions. For example, if the task is to decide whether a face seen at a distance in a crowd is that of an old friend or enemy, attributes might be head shape, eye separation, nose length, etc. If representing potential actions, columns might describe the direction or magnitude of a sequence of movements. The vertical dimension represents different levels of each attribute. For the face example, squarish, elliptical, or circular head shapes; narrow (e.g., George W. Bush), average, or wide eye spacing, and so on. For the action example: left, straight, or right locomotion. This is obviously a very small number of attributes and levels, but it suffices to illustrate the dynamics of generalized rivalry.

Connectivity within the network incorporates both cooperative excitation and competitive inhibition. On the assumption that each attribute can only assume one level, there must be mutual inhibition among all units within each vertical column, which is depicted in Figure 4a. Regarding cooperation, the network has learned and stored four patterns, each of which comprises activity in one level neuron for each attribute. One learned pattern is depicted by gray circles in Figure 4b. During the learning it is assumed that each activated neuron comprising a pattern develops reciprocal excitatory connections with all other neurons in the pattern. This can be accomplished via Hebbian learning (Hebb, 1949). The result is illustrated by the double headed arrows in Figure 4b. Finally, this generalization of a cooperative/competitive rivalry network permits patterns to partially overlap. Figure 4c illustrates two additional patterns of attributes marked by horizontal and vertical hatching respectively. Note that the two patterns here have two elements in common, which are cross-hatched. Furthermore, the pattern in Figure 4b partially overlaps each of those in 4c. The fourth learned pattern (not shown) likewise overlaps each of the remaining three.

How does this network perform in response to activation of similar magnitude to each of the patterns? Recall that the inputs are assumed to come from the range of areas shown in Figure 3. Figure 5a illustrates responses driven by slightly different inputs for each pattern. As in normal binocular rivalry between left and

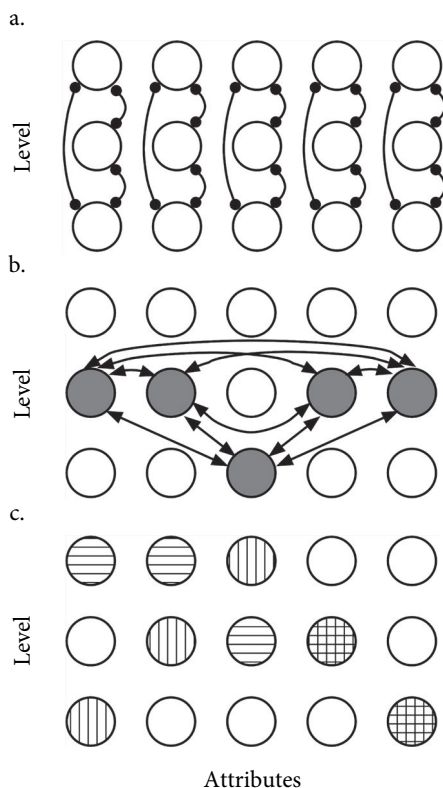


Figure 4. Spatially distributed neural model for pattern competition and decisions in PFC. The network comprises five columns of neurons representing different attributes and three rows representing different levels of each attribute. Each competing pattern is comprised of activity in one level neuron for each attribute. (a) Level neurons for each attribute are mutually inhibitory, reflecting the requirement that only one can be active in any given pattern. (b) Five active attribute neurons (gray) defining one pattern receive mutual recurrent excitatory inputs (arrows) resulting from Hebbian learning. (c) Two other learned patterns are depicted by vertical and horizontal stripes respectively. Note that these two patterns partially overlap as reflected by the cross-hatched neurons for the two attributes on the right. Comparison with (b) shows that all three patterns overlap. This network has also learned a fourth pattern (not shown) that also has partial overlap with each of the others. Note that (a), (b), and (c) all represent different aspects of interactions within a single 15 neuron network.

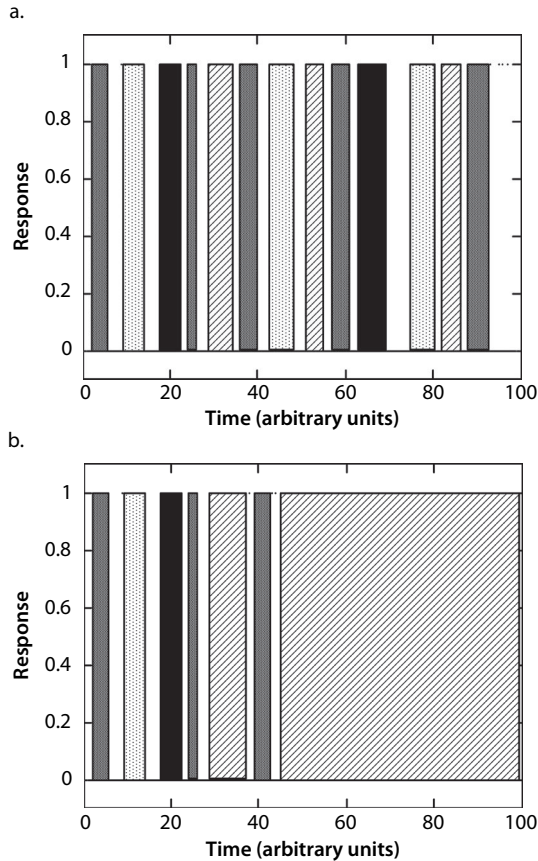


Figure 5. Dominance of different patterns in simulation of network depicted in Figure 4. (a) Time course of dominance alternations among four different competing patterns as shown by different textures and shadings. Lower level inputs to each pattern were similar but not identical in strength. In the absence of any change in input, this complex oscillation will continue ad infinitum. (b) When the diagonally hatched pattern becomes active, it provides modulatory feedback to its input areas that is assumed to slightly increase its input strength. This rapidly leads to a bifurcation to a winner-take-all regime in which this augmented pattern wins, thereby becoming the network decision. See text for further details.

right monocular patterns, the patterns oscillate in dominance, and this cycle repeats itself. However, this response pattern is a generalization in two important ways. First, the oscillation cycles among four patterns rather than two. Second, the patterns share common elements as well as discrepant ones. Finally, when each pattern becomes dominant, it is maintained for a time by the recurrent excitation illustrated for one example in Figure 4b. This indicates that the network exhibits short term memory that is triggered for each of the patterns in turn. Thus, this generalized rivalry model may be construed as a network that considers four possible alternative courses of action or interpretations of sensory data in turn. It should be noted that extensions to five patterns generally resulted in one of the patterns being only occasionally dominant. This suggests agreement with neurophysiology indicating that the capacity limitation of prefrontal and lateral parietal cortex is about four items (Buschman, Siegel, Roy, & Miller, 2011). Whether interaction among four patterns in the model represents a mathematical limit remains to be determined.

The response in Figure 5a shows that generalized rivalry can alternate among at least four distinct, partially overlapping patterns of attributes when all patterns have very similar stimulus levels. Although not illustrated, when only two or three patterns receive similarly high stimulation, while the remainder receive significantly lower stimulation, the competitive alternation switches between just those two or three while the others are permanently suppressed. Finally, if one pattern receives significantly stronger stimulation than all the others, the network switches or bifurcates into a winner-take-all mode, and that pattern switches on permanently. Thus, this generalized rivalry network itself decides how many possible alternative patterns have sufficient evidence to merit further consideration.

The response alternations in Figure 5a do not yet represent a decision, as they continue *ad infinitum*. In fact, this could be regarded as a form of perseveration. For the generalized rivalry network to arrive at a decision, a further ingredient is necessary. Reference to Figure 3 shows that the generalized rivalry network has feedback interactions with high sensory areas, episodic memory, emotional centers, and premotor areas. Given the competitive nature of the rivalry, only the currently active neural population will generate feedback interactions with these other areas. If each neural population represents a potential decision or course of action, it is reasonable to hypothesize that this feedback implements a search for further relevant information from these various input sources. Such further information may be sensory, additional memory traces, emotive, or information about the plausibility of a motor act. This was implemented in simulations of the network as follows. When the diagonally hatched pattern in Figure 5a becomes active, the amount of input information to its elements is augmented by a small amount via this feedback. The other three competing patterns are assumed to

receive no further positive input or to actually receive small decrements to their inputs. An implementation of this simple feedback example is shown in Figure 5b. The first 10 seconds of the simulation are identical to that in 5a, as none of these patterns receive further input. When the diagonally hatched pattern becomes active at about 11 seconds, however, the simulated feedback loop augments its input slightly, so its dominance interval increases relative to the response in 5a. The dark gray pattern then reappears briefly, but now the hatched pattern has strong enough inputs to recover dominance, and it permanently suppresses all other patterns. The network has reached a decision, which is the result of a bifurcation to a winner-take-all dynamical regime.

Several comments are necessary here. First, had the simulated feedback been assigned to one of the other competing patterns, that pattern would eventually have won the competition and suppressed all others. Thus, the network will eventually allow whichever neural population accumulates the greatest amount of positive evidence to represent the decision. Second, it should again be emphasized that the competing populations have some neurons in common as shown in Figure 4c. Finally, it is certainly true that this simulation of feedback loops in producing augmented positive input information in favor of a particular alternative is oversimplified. A more complete model would need to describe the circuitry of the high sensory areas, episodic memory, emotional valence, and premotor networks. That, however, is beyond the scope of this chapter.

Just as in normal binocular rivalry, where alternation rates exhibit reliable individual differences (Miller et al., 2010), it is important to determine whether generalized rivalry can also generate individual differences in reversals. Simulations show that variations of the hyperpolarizing gain factor g in the generalization of Equation (1) can generate greater than a five-fold variation in generalized rivalry reversals, presumably due to differences in neuromodulatory transmitter levels. Thus, at least some differences in individual cognitive styles may be explained by generalized rivalry.

Generalized rivalry and conscious decisions

Here I will argue that generalized rivalry provides a model for conscious, deliberative decision making. When only one alternative course of action has significant support under given circumstances, decisions are rapid, obvious, and need not involve conscious processing. It is when several alternatives seem almost equally desirable that decisions become effortful and deliberative, and this is when feedback loops become important to provide further relevant information in the form of memories, sensory information, emotional valence, and motor efficacy. As argued elsewhere, deliberation has obvious survival value as a form

of cognitive trial and error exploration of alternative actions (Wilson, 2009). This has obvious advantage over acting without deliberation, where incorrect actions may prove debilitating or fatal. Furthermore, it is advantageous to encode episodes of important deliberative decisions in memory so that success or failure of the chosen action can be used for learning and to inform future deliberations. These two advantages appear to be major forces driving the evolution of consciousness.

If generalized rivalry networks are serious candidates for decision making, what aspects of their architecture might plausibly imbue them with consciousness? One aspect seems to be almost universally acknowledged: cooperative and competitive feedback within the network and with its inputs. For example, the dynamic core hypothesis of Edelman and Tononi requires feedback interactions ("reentrant" is their neologism) for consciousness (Edelman & Tononi, 2000). Similarly, feedback has been assigned the critical role by Lamme (2006). Also, Crick and Koch (2003) link consciousness to transient coalitions of neurons that are formed by feedback. Indeed, their concept of competition among transient coalitions of neurons is consistent with the generalized rivalry model developed here.

From the considerations above it is evident that all neuroscientists who have pondered these issues seem to agree that feedback is necessary for consciousness. Excitatory or cooperative feedback binds neuronal assemblies, and inhibitory or competitive feedback selects among them. The alternative is feedforward connections alone, but this is the logical equivalent of a reflex arc. It is hardly conceivable that such would represent conscious processing. This is not to deny that feedforward processing should be useful and sometimes sufficient for determining broad category membership of a stimulus, such as a face, but this is not adequate for consciousness in general.

Is feedback alone sufficient to attribute consciousness, or are there additional requirements? The schematic network in Figure 3 places networks capable of conscious processing at the apex of a hierarchy, which interacts with the highest sensory, memory, and reward networks as well as motor planning networks. This is precisely the location of the "global workspace" modeled by Dehaene and colleagues (Dehaene et al., 1998, 2003). They suggested that the global workspace could be identified with the dorsolateral prefrontal cortex and perhaps also anterior cingulate gyrus. Furthermore, the most anterior aspects of PFC are most highly elaborated in humans and are thought to provide the basis for decision making (Koechlin & Hyafil, 2007). The important implication is that generalized rivalry describes conscious cortical processing only when that processing occurs in PFC (which prefrontal areas or subareas are, of course, empirical issues). Thus, the hypothesis proposed here is that conscious processing requires feedback that always emanates, at least in part, from prefrontal generalized rivalry circuits.

Rivalry and its generalization certainly exist at multiple cortical levels from V1 on, and there are thus both cooperative and competitive interactions throughout the cortical hierarchy. So why is it necessary that prefrontal activity is critical for conscious processing? The issue goes back to the question whether feedback alone suffices for consciousness. This has been answered succinctly by Cohen and Dennett (2011), who posed a conceptual experiment in which an individual's cortical color areas (e.g., V4) received inputs but were prevented from providing any output to the rest of the brain. Their conclusion is that as the individual would not be conscious of color, there could be no scientific meaning to the question whether V4 itself (which has feedback connections both internally and to its inputs) is nevertheless conscious.

An even more dramatic argument against feedback as sufficient for conscious experience would involve isolation of the retina. The retina is well known to contain several feedback loops involved in light adaptation, yet severing the optic nerve does produce total blindness. In agreement with Cohen and Dennett, there is no way to evaluate the hypothesis that the isolated retina is conscious, so it is a scientifically meaningless question.

It bears mention that Lamme (2006) sets up a false dichotomy regarding consciousness by asking: "Is it the involvement of the frontoparietal network, as global workspace theory suggests, or is it the recurrency?" (p. 499). He then falsely concludes that it is the recurrent processing alone that defines conscious brain operations. Clearly, the conjunction of both is entirely possible: activity in a prefrontal global workspace in conjunction with recurrent processing provides a testable model for consciousness, as is emphasized by Cohen and Dennett (2011).

Simply stated, it is only in prefrontal areas where short term memory, long term memory, results of sensory processing, emotional valence, and premotor planning are linked recurrently to one another. In agreement with global workspace theory (Dehaene et al., 1998), all of these ingredients are argued here to be necessary for conscious evaluation of competing plans of action.

Discussion

In this paper I have developed the hypothesis that conscious decision processes can be elucidated by a generalized rivalry model. This model contains cooperative interactions instantiated in positive feedback, competitive interactions resulting from inhibition, plus feedback to multiple sources of input (see Figure 3). Generalized rivalry has all the properties of a decision process. First, if available evidence strongly favors one course of action, the network immediately chooses that course and suppresses all alternatives via inhibition. When from two to four

alternatives receive quite similar evidential support, the network produces a generalized rivalry oscillation in which first one and then another alternative temporarily wins the competition and sends feedback signals to high level information and emotional sources in search of further support. If one of the generalized rivalry alternatives receives sufficient additional support from this feedback process, it will eventually win the competition via a bifurcation from an oscillatory state to a winner-take-all state.

A network making decisions based on a feedback mediated search for additional evidence may seem to be overly rational in nature. Two further considerations are relevant here. First, the network incorporates feedback to emotional centers, so part of the search for additional evidence involves searching for “what feels best” under the circumstances. However, even this emotional component does not automatically imply irrationality. As Hurley, Dennett and Adams (2011) argue: “the emotions are rational, but the [emotional] system is a heuristic driver of behavior” (p. 82). By this I take them to mean that emotional valence is very often (but not always) an accurate indicator of a reasonably optimal course of action. Thus, generalized rivalry may be construed as a rational decision strategy incorporating emotions.

The generalized rivalry model is a natural extension of binocular rivalry models that have been studied extensively using mathematics, psychophysics, and fMRI (e.g., Lee et al., 2007; Wilson, 2003, 2005, 2007; Wilson et al., 2001). Thus, the goal of the generalized rivalry model is to make explicit the analogy between high level, conscious decision processes and very low level monocular V1 processes that generate an oscillation in an attempt to resolve a perceptual incompatibility in the domain of depth perception. There is the further requirement that conscious decisions must involve generalized rivalry in prefrontal areas. This means that even though rivalry-type processes are likely ubiquitous in cortical hierarchies (Wilson, 2003), that does not imbue all areas with consciousness. In other words, it is not just rivalry driven by recurrent connections that produces conscious experience; the representations that are rivaling also matter, and the relevant ones only come together in PFC.

The generalized rivalry model is consistent with the global neuronal workspace model (Dehaene et al., 1998) and also with the emphasis on cooperation and competition via recurrent connections in other models of consciousness (Crick & Koch, 2003; Edelman & Tononi, 2000). However, the emphasis on the competitive process complete with the ability of competing patterns to share elements in common enables generalized rivalry to provide new insights into the neural substrate of complex decisions. For example, the different neural groups in the network in Figure 4 need not all be in the same prefrontal area. Thus, different conscious decisions may involve competition among different groups of neurons in different

areas sharing little or nothing in common. Indeed, there is recent fMRI evidence that different types of decisions involve different, but partially overlapping pre-frontal areas (Mitchell et al., 2009).

Given the similarity of the generalized rivalry model to the global neuronal workspace (GNW) model, it is also worth considering how they differ. Both contain recurrent excitatory connections mediating neuronal cooperation, and both also contain inhibitory competitive interconnections. However, much of GNW has focused on modeling the threshold for entrance of perceptual information into consciousness. As summarized recently (Dehaene & Changeux, 2011), entry into consciousness occurs when stimulation of GNW is sufficiently strong to activate its feedback connections, thereby stabilizing the GNW activity as a short term memory state. No mechanism for rivalry between competing alternate states is explicitly discussed. Thus, GNW in its current state can be viewed as operating in a dynamical subspace of generalized rivalry in which winner-take-all dynamics obtain. Although earlier work (Dehaene et al., 1998) does enable pattern switching within GNW, this only occurs as a result of a strong negative evaluation. Thus, GWM does not currently incorporate the dynamics for spontaneous and repeated rivalry alternation among neural patterns, although this could be incorporated in future models.

There are also other probabilistic neural decision models in the literature, typified by diffusion models, which share some aspects of the current model but do not generate rivalry. For example, Wang's (2002) model incorporates two competing excitatory neural populations that compete via a single inhibitory neuron pool. That model is formally a winner-take-all model which generates slow dynamics in arriving at a winner when the competing excitatory populations have similar input levels. As the generalized rivalry model presented here can produce both complex rivalry oscillations and winner-take-all behavior, the Wang (2002) model may be thought of as occupying a particular dynamical subspace of generalized rivalry. In addition, diffusion models of decision processes (Ratcliff & McKoon, 2008) may also be viewed as residing in a winner-take-all dynamical subspace of generalized rivalry with the addition of noise. It has already been shown that very similar inputs to competitors in a winner-take-all model result in a much slower approach to winning (Wilson, 1999).

Little has been said about the nature of the reciprocal connections between the generalized rivalry model in Figure 3 and the relevant memory, emotion, sensory, and motor areas. This is a problem that has been examined in greater detail in global workspace models by Dehaene et al. (2003). One point that these authors emphasize seems incontrovertible. Feed-forward excitation to the generalized rivalry network should involve depolarizing ion channels such as AMPA receptors. Feedback excitation, on the other hand, should involve modulatory amplification

such as is produced by NMDA receptors. The reason for this becomes obvious if the input levels are regarded as providing evidence to the generalized rivalry decision network. The input evidence should result in direct excitation of competitive, rivaling patterns. Feedback excitation, however, should not manufacture new evidence; rather, it should amplify additional weak information that is already present. In addition, modulatory feedback via NMDA receptors may provide one source of learning resulting from difficult perceptual decisions. Further elucidation of the roles of recurrent modulatory inputs presents an ongoing challenge to neural modeling.

One challenge to the very notion of conscious decisions comes from fMRI data showing that the brain can make a particular decision as much as 10 seconds before the subject becomes aware of the decision (Soon, Brass, Heinze, & Haynes, 2008). This would seem to question whether decisions are ever conscious, or whether consciousness is simply an epiphenomenon consequent upon a decision. It is important to note, however, that an unusual task was employed. The subject simply had to decide at random when to push one or the other of two buttons. Thus, there was absolutely no utility in conscious deliberation, and a random number generator could easily have performed the task. It is important to acknowledge that there are sometimes cases in which the optimal decision is to behave as randomly as possible, and this has been partially captured under the rubric of "Machiavellian Intelligence" (Byrne & Whiten, 1997). In such cases, it has been conjectured that higher cortical levels trigger an appropriate subordinate network to bifurcate into a chaotic regime, which would provide a deterministic network an effective way of generating apparently random behavior (Wilson, 1999). If the brain utilizes that procedure under these experimental conditions, then prefrontal areas could not be consciously aware of the decision until after it had been made. Thus, my suggestion is that pre-conscious decisions revealed by fMRI in the Soon et al. (2008) study are a consequence of the random nature of the decision task employed by the investigators. Further work will be needed to evaluate this possibility.

The goal of this chapter has been to extend the circuitry thought to be responsible for binocular rivalry in V1 to higher levels of the cortex, culminating in generalized rivalry in prefrontal areas as a model for conscious decisions. Such network replications at subsequent cortical levels could easily have evolved under natural selection, thus providing a framework for the evolution of conscious behavior. It is important to realize that all mammals have a PFC; it is just relatively larger in humans. Thus, the definition of consciousness as requiring prefrontal activity with recurrent prefrontal interactions and recurrent interactions with high sensory areas, emotional areas, memory areas, and premotor areas, certainly implies that all mammals (or at least all social mammals) are conscious. My

dog is certainly conscious by these criteria, and his behavior shows it. This does not imply that all mammals are also self-conscious, and the evidence suggests that probably only great apes and humans have this capability. Neither does it imply that conscious processes are comparable in detail across species. The issue of consciousness in birds, for example, seems to be answered in the affirmative by the gray parrot, Alex (Pepperberg, 2008). However, the avian equivalent of PFC remains to be determined.

As an interesting aside here, there is evidence that even fruit flies (*Drosophila*) exhibit a form of binocular rivalry (data summarized by Miller, Ngo, & van Swinderen, 2012; see chapter by Ngo et al., this volume). Thus, the neural circuitry subserving rivalry may be of fairly early evolutionary origin and may plausibly have provided survival value to all animals confronted with perceptual decisions. This is not to impute conscious processes to *Drosophila*, but only to emphasize that rivalry has been around for long enough to evolve as a substrate for conscious brain circuitry.

In conclusion, generalized rivalry provides a testable model of conscious decision making under difficult or ambiguous circumstances. It incorporates cooperation, competition, and feedback to brain areas performing memory, emotive, sensory, and motor planning functions. This, I take to be the essence of Dennett's (1996) contention:

Mental contents become conscious not by entering some special chamber in the brain, not by being transduced into some privileged and mysterious medium, but by winning the competitions against other mental contents for domination in the control of behavior, and hence for achieving long lasting effects. (p. 155)

Thus, a philosophic and scientific consensus may be emerging in which generalized rivalry and global workspaces within PFC will play an increasingly dominant role in defining and elucidating conscious brain processes.

References

- Blake, R., & Wilson, H. R. (2011). Binocular vision. *Vision Research*, 51(7), 754–770.
- Buckthought, A., Kim, J., & Wilson, H. R. (2008). Hysteresis effects in stereopsis and binocular rivalry. *Vision Research*, 48(6), 819–830.
- Buschman, T. J., Siegel, M., Roy, J. E., & Miller, E. K. (2011). Neural substrates of cognitive capacity limitations. *Proceedings of the National Academy of Sciences USA*, 108(27), 11252–11255.
- Byrne, R. W., & Whiten, A. (1997). Machiavellian intelligence. In A. Whiten, & R. W. Byrne (Eds.), *Machiavellian intelligence II: Extensions and evaluations* (pp. 1–23). Cambridge, NY: Cambridge University Press.

- Cohen, M. A., & Dennett, D. C. (2011). Consciousness cannot be separated from function. *Trends in Cognitive Sciences*, 15(8), 358–364.
- Crick, F., & Koch, C. (2003). A framework for consciousness. *Nature Neuroscience*, 6(2), 119–126.
- Dehaene, S. (1997). *The number sense*. Oxford: Oxford University Press.
- Dehaene, S., & Changeux, J.-P. (1997). A hierarchical neuronal model for planning behavior. *Proceedings of the National Academy of Sciences USA*, 94(24), 13293–13298.
- Dehaene, S., & Changeux, J.-P. (2011). Experimental and theoretical approaches to conscious processing. *Neuron*, 70(2), 200–227.
- Dehaene, S., Kerszberg, M., & Changeux, J.-P. (1998). A neuronal model of a global workspace in effortful cognitive tasks. *Proceedings of the National Academy of Sciences USA*, 95(24), 14529–14534.
- Dehaene, S., Sergent, C., & Changeux, J. P. (2003). A neuronal network model linking subjective reports and objective physiological data during conscious perception. *Proceedings of the National Academy of Sciences USA*, 100(14), 8520–8525.
- Dehaene, S., Tzourio, N., Frak, V. R. L., Cohen, L. M. J., & Mazoyer, B. (1996). Cerebral activations during number multiplication and comparison: A PET study. *Neuropsychologia*, 34(11), 1097–1106.
- Dennett, D. C. (1996). *Kinds of minds: Toward an understanding of consciousness*. New York: Basic Books.
- Edelman, G. M., & Tononi, G. (2000). *A universe of consciousness*. New York: Basic Books.
- Fox, R., & Herrmann, J. (1967). Stochastic properties of binocular rivalry alternations. *Perception & Psychophysics*, 2(9), 432–436.
- Hebb, D. O. (1949). *The organization of behavior*. New York: John Wiley & Sons.
- Hurley, M. M., Dennett, D. C., & Adams, R. B. (2011). *Inside jokes: Using humor to reverse-engineer the mind*. Cambridge, MA: MIT Press.
- Klink, P. C., Brascamp, J. W., Blake, R., & van Wezel, R. J. (2010). Experience-driven plasticity in binocular vision. *Current Biology*, 20(16), 1464–1469.
- Koechlin, E., & Hyafil, A. (2007). Anterior prefrontal function and the limits of human decision-making. *Science*, 318(5850), 594–598.
- Lamme, V. A. F. (2006). Towards a true neural stance on consciousness. *Trends in Cognitive Sciences*, 10(11), 494–501.
- Lee, S.-H., Blake, R., & Heeger, D. J. (2007). Hierarchy of cortical responses underlying binocular rivalry. *Nature Neuroscience*, 10(8), 1048–1054.
- Leopold, D. A., Wilke, M., Maier, A., & Logothetis, N. K. (2002). Stable perception of visually ambiguous patterns. *Nature Neuroscience*, 5(6), 605–609. <http://dx.doi.org/10.1038/nn0602-851>
- Levelt, W. J. M. (1965). *On binocular rivalry*. Soesterberg, The Netherlands: Institute of Perception.
- Logothetis, N. K., Leopold, D. A., & Sheinberg, D. L. (1996). What is rivalling during binocular rivalry? *Nature*, 380(6575), 621–624.
- McCormick, D. A., & Williamson, A. (1989). Convergence and divergence of neurotransmitter action in human cerebral cortex. *Proceedings of the National Academy of Sciences USA*, 86(20), 8098–8102.
- McLaughlin, D. C., Shapley, R., Shelley, J., & Wielaard, D. J. (2000). A neuronal network model for macaque primary visual cortex (V1): Orientation selectivity and dynamics in the input layer 4Ca. *Proceedings of the National Academy of Sciences USA*, 97(14), 8087–8092.

- Miller, S. M., Hansell, N. K., Ngo, T. T., Liu, G. B., Pettigrew, J. D., Martin, N. G. et al. (2010). Genetic contribution to individual variation in binocular rivalry rate. *Proceedings of the National Academy of Sciences USA*, 107(6), 2664–2668.
- Miller, S. M., Ngo, T. T., & van Swinderen, B. (2012). Attentional switching in humans and flies: Rivalry in large and miniature brains. *Frontiers in Human Neuroscience*, 5, 188. doi: 10.3389/fnhum.2011.00188
- Mitchell, D. G. V., Luo, Q., Avny, S. B., Kasprzycki, T., Gupta, G., Chen, G. et al. (2009). Adapting to dynamic stimulus-response values: Differential contributions of inferior frontal, dorsomedial, and dorsolateral regions of prefrontal cortex to decision making. *Journal of Neuroscience*, 29(35), 10827–10834.
- O'Reilly, R. C. (2006). Biologically based computational models of high-level cognition. *Science*, 314(5796), 91–94.
- Panagiotaropoulos, T. I., Deco, G., Kapoor, V., & Logothetis, N. K. (2012). Neuronal discharges and gamma oscillations explicitly reflect visual consciousness in the lateral prefrontal cortex. *Neuron*, 74(5), 924–935.
- Pepperberg, I. M. (2008). *Alex & me: How a scientist and a parrot uncovered a hidden world of animal intelligence – and formed a deep bond in the process*. New York: Harper.
- Polat, U., Mizobe, K., Pettet, M. W., Kasamatsu, T., & Norcia, A. M. (1998). Collinear stimuli regulate visual responses depending on cell's contrast threshold. *Nature*, 391(6667), 580–584.
- Ratcliff, R., & McKoon, G. (2008). The diffusion decision model: Theory and data for two-choice decision tasks. *Neural Computation*, 20(4), 873–922.
- Soon, C. S., Brass, M., Heinze, H.-J., & Haynes, J.-D. (2008). Unconscious determinants of free decisions in the human brain. *Nature Neuroscience*, 11(5), 543–545.
- Tong, F., & Engel, S. A. (2001). Interocular rivalry revealed in the human cortical blind spot representation. *Nature*, 411(3834), 195–199.
- Wang, X.-J. (2002). Probabilistic decision making by slow reverberation in cortical circuits. *Neuron*, 36(5), 955–968.
- Wilson, H. R. (1999). *Spikes, decisions, and actions: Dynamical foundations of neuroscience*. Oxford: Oxford University Press.
- Wilson, H. R. (2003). Computational evidence for a rivalry hierarchy in vision. *Proceedings of the National Academy of Sciences USA*, 100(24), 14499–14503.
- Wilson, H. R. (2005). Rivalry and perceptual oscillations: A dynamical synthesis. In D. Alais, & R. Blake (Eds.), *Binocular rivalry* (pp. 317–335). Cambridge, MA: MIT Press.
- Wilson, H. R. (2007). Minimal physiological conditions for binocular rivalry and rivalry memory. *Vision Research*, 47(21), 2741–2750.
- Wilson, H. R. (2009). Requirements for conscious visual processing. In M. Jenkin, & L. R. Harris (Eds.), *Cortical mechanisms of vision* (pp. 399–417). Cambridge, NY: Cambridge University Press.
- Wilson, H. R. (2010). Binocular rivalry: Neurons unwire when they can't simultaneously fire. *Current Biology*, 20(17), R715–R717.
- Wilson, H. R., Blake, R., & Lee, S.-H. (2001). Dynamics of travelling waves in visual perception. *Nature*, 412(6850), 907–910.
- Wilson, H. R., & Cowan, J. D. (1972). Excitatory and inhibitory interactions in localized populations of model neurons. *Biophysical Journal*, 12(1), 1–24.

The future of binocular rivalry research

Reaching through a window on consciousness

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Binocular rivalry is often considered an experimental window on the neural processes of consciousness. We propose three distinct approaches to exploit this window. First, one may look through the window, using binocular rivalry as a passive tool to dissociate unaltered sensory input from wavering perceptual output. Second, the mechanisms underlying binocular rivalry may yield detailed knowledge of the neuronal underpinnings of binocular vision and increase the value of rivalry as a tool to study consciousness. Finally, smart experimental manipulations allow experimenters to ‘reach through the window’ and interact with mechanisms of conscious visual perception. Within this distinction, we discuss the major open questions in binocular rivalry research and examine how recent technological developments may be incorporated in future studies.

1. Introduction

The integration of visual information from two eyes leads to perceptual advantages such as stereopsis and enhanced contrast sensitivity. Binocular integration is however not always beneficial and does not occur when the two retinal patterns are substantially different. In that case, rather than perceiving a mixture of the two patterns, observers typically report a stream of perceptual fluctuations in which each of the two patterns is perceived exclusively dominant for a few seconds, after which it fades from awareness and the other pattern becomes dominant. This phenomenon of perceptual fluctuations is called binocular rivalry because it resembles an ongoing competition for dominance between the visual patterns in the two eyes and their corresponding neuronal representations (Blake & Logothetis, 2002). In this chapter

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we briefly summarize how scientific interest in the binocular rivalry phenomenon has developed and propose how recent technological advances and novel experimental results create opportunities for the future of binocular rivalry research.

1.1 A window on consciousness

The fluctuations in the content of perceptual awareness that arise during binocular rivalry despite the constant visual input into the eyes has advocated the use of this paradigm in studying the neuronal basis of conscious visual perception (Crick & Koch, 1990; Leopold & Logothetis, 1996). Visual processing starts as soon as photons hit the retina, but somewhere along the neuronal processing chain from stimulus to percept, the brain must ‘decide’ what the content of perceptual awareness is going to be. While this generic notion holds for all visual input, the mechanisms responsible for these perceptual choices are especially revealing when the same sensory input can evoke distinctly different conscious percepts. It is this characteristic of binocular rivalry that has earned it the qualification of ‘a window on consciousness’ (Logothetis, 1999). The realization that binocular rivalry can be used as a tool to study the neural correlates of consciousness is, however, a relatively recent development in the history of binocular rivalry research. Since the first systematic description of binocular rivalry appeared in the literature (Wheatstone, 1838), the paradigm has been used to investigate many different aspects of perceptual processing (Alais, 2012).

1.2 A brief history of binocular rivalry research

Before we unfold our ideas for future directions in binocular rivalry research, we will briefly summarize the history of binocular rivalry research. Because far more comprehensive overviews of the (early) history of binocular rivalry research can be found in this volume (see chapter by Wade & Ngo) and elsewhere (Alais, 2012), our summary will merely provide a coarse description of how the questions typically addressed with binocular rivalry experiments have evolved over the years. This coarse timeline will later function as the basis of our proposal to divide the field of binocular rivalry research into three distinct subfields, each with their own specific research aims and most suitable experimental approaches.

The invention of the mirror stereoscope by Charles Wheatstone in the 19th century marks the first significant boost in broad scientific interest for binocular rivalry (Wheatstone, 1838). In the decades that followed the introduction of the stereoscope, binocular rivalry was predominantly studied as a peculiar perceptual phenomenon. The main questions that were addressed in binocular rivalry

research in those days concerned the reason why binocular rivalry occurred in the first place and the phenomenon's relation to binocular fusion and stereoscopic depth perception (for a recent review, see Blake & Wilson, 2011). Some of the early observations describe aspects of binocular rivalry that are still present in contemporary binocular rivalry research, including the occurrence of piecemeal rivalry (Meenes, 1930; Wheatstone, 1838), the spatiotemporal profile of perceptual alternations (Wheatstone, 1838), the correlation between stimulus strength and predominance (Breese, 1899), and the extent to which perception is under an observer's voluntary control (Breese, 1899; Helmholtz, 1867; Wheatstone, 1838). During a revival of interest in binocular rivalry in the second half of the 20th century, researchers started using the phenomenon as a tool to study other psychological phenomena such as differences between the sexes (Kaufer & Riess, 1960), cultural differences between observers (Bagby, 1957; LoSciuto & Hartley, 1963), or personality aspects (Bokander & Radeborg, 1966; Kohn, 1960). In the meantime, the systematic investigation of binocular rivalry continued. Notable contributions in this area are the work of Fox on the suppression aspect of binocular rivalry (Fox, 1963), Levelt's studies on the relation between stimulus strength and predominance (Levelt, 1965), and Whittle's experiments on the effects of perceptual grouping (Whittle, 1963). Heavily influenced by Hubel and Wiesel's seminal series of publications on the anatomy and physiology of the visual cortex (for a review, see Hubel & Wiesel, 1998), this branch of research aimed to incorporate the newly discovered concepts of ocular dominance and binocular combination in their theories of binocular rivalry and stereopsis (e.g., Blake, 1989).

Research in the late nineties of the previous century challenged the early idea of binocular rivalry as a pure competition between eyes. Paradigms in which binocular rivalry images were rapidly switched between the eyes demonstrated that an additional level of pattern rivalry must exist at cortical processing stages where eye-of-origin information is lost (Logothetis, Leopold, & Sheinberg, 1996). While the debate as to what is actually rivaling in binocular rivalry and where in the brain the associated perceptual conflicts are resolved is still very much alive (see Blake & Wilson, 2011; Watanabe et al., 2011), there is now a broadly accepted consensus that binocular rivalry can involve different levels of processing depending on the precise stimulus characteristics (Blake & Logothetis, 2002; Ooi & He, 2003; Tong, Meng, & Blake 2006; van Boxtel & Koch, 2012).

The application of binocular rivalry as a tool to study other aspects of psychology took a noteworthy turn near the end of the 20th century when it was proposed as a potent method to study the neurobiological underpinnings of consciousness in general and visual awareness in particular (Crick & Koch, 1998; Koch & Braun, 1996). Interestingly, the publication of this proposition roughly coincided with the introduction of functional magnetic resonance imaging (fMRI) in the cognitive

neurosciences (Belliveau et al., 1991). With fMRI, researchers could now measure (a derivative of) neuronal activity in an entire brain, non-invasively and at relatively high spatial resolution. An overview of imaging studies on binocular rivalry is available elsewhere in this volume (see chapter by Sterzer, this volume), but it is clear that ever since its first appearance on the scene, functional neuroimaging has played a prominent role in binocular rivalry research, especially when researchers aimed to find neural concomitants of visual awareness.

Now, at the start of the 21st century, binocular rivalry has found its way into the clinic, demonstrating slower switching rates in patients with bipolar disorder (Krug, Brunskill, Scarna, Goodwin, & Parker, 2008; Miller et al., 2003; see chapter by Ngo, Barsdell, Law, & Miller, this volume). The future of binocular rivalry research is bright, with an ever-expanding number of studies (Baker, 2010) and numerous technological advances in the last few years that have opened up many potentially interesting pathways for future studies.

2. The future of binocular rivalry research

It is always difficult to predict the future of a research field in a context that evolves as rapidly as the neurosciences. Some technological developments, however, seem particularly suitable for application in binocular rivalry research. In the following sections we will discuss several of these advances and relate them to specific types of binocular rivalry research. Suggestions for future directions range from classic topics in binocular rivalry to more novel questions inspired by recent findings from both binocular rivalry and other fields of neuroscience.

2.1 A challenge on three fronts

The broad range of possibilities for future binocular rivalry research asks for a sound research strategy. In keeping with the metaphor of binocular rivalry as an experimental window on consciousness, we propose three distinct branches of binocular rivalry experiments (Figure 1). First, the most obvious function of a window is that it allows an observer to see what is happening on the other side of a wall. Because binocular rivalry allows the experimenter to ‘observe’ the neuronal mechanisms involved in converting sensory input into perceptual output, this is what earned the paradigm its qualification of a ‘window on consciousness’.

A second branch of binocular rivalry research involves the rivalry mechanism itself. To return to the window metaphor, the functionality of a window may be most efficiently exploited if the operator knows how the window works. While the

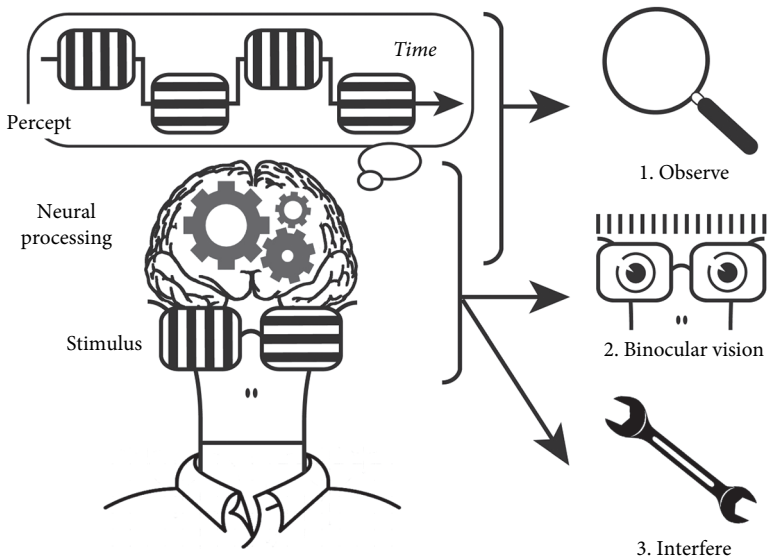


Figure 1. Three branches of binocular rivalry research. Binocular rivalry (left panel) involves a stimulus of incompatible images presented to the individual eyes (here horizontal and vertical line patterns). In the brain, complex neuronal processing converts the visual input into a conscious percept (indicated by the thought cloud). Over time, perception fluctuates between the two individual images. We propose the future of binocular rivalry research to focus on three intimately related areas (right panels). These areas are (1) the observation of perceptual and neuronal dynamics during fluctuations in awareness; (2) the binocular rivalry mechanism itself and its relation to other aspects of binocular vision; and (3) interference with neural processing, either via stimulus manipulations or by brain stimulation.

biological mechanisms involved in binocular rivalry are far more complex than the mechanistic properties of a window, the same principle applies and experimenters that study consciousness with binocular rivalry have much to gain from a deeper understanding of the binocular rivalry mechanism itself. Despite, the long tradition in studying the neural underpinnings of the binocular rivalry phenomenon and the vast body of existing literature on the topic, there is still a lot that we do not know about the neural mechanisms and brain structures involved.

The third branch of binocular rivalry research takes elements of the first two and could be coarsely summarized as ‘interfering with the functional mechanisms of consciousness’. While the passive observation of a process has the advantage of encountering it in its most natural, unperturbed state, it also limits the amount of

information that can be derived about the underlying operational mechanisms. Alternatively, active interference with such a process will likely reveal much more information than can ever be inferred from mere observation. In terms of the window metaphor, one could imagine such an approach as actively reaching through the window to interfere with the ongoing mechanisms of consciousness rather than just observing them passively.

With these three branches of binocular rivalry research in mind we can now turn to some recent theoretical and technological developments in neuroscience and discuss their relevance for each of the proposed binocular rivalry approaches.

2.2 Observing streams of consciousness

Passive observation of the unperturbed mechanisms that shape visual awareness will yield most information if the recording techniques can measure activity in large portions of the brain simultaneously and with high spatiotemporal resolution. In the past, broad spatial focus and high measuring resolution have often been mutually exclusive, but improvements of existing, as well as the development of novel, imaging methods have greatly expanded these possibilities. In addition, some recent findings on the dynamic perceptual phenomenology of binocular rivalry may open the door to a whole new range of behavioral and imaging experiments.

2.2.1 *Transitions, traveling waves and nucleations*

Much of the existing binocular rivalry research treats the perceptual phenomenology of alternating percepts as a more or less binary process in which either one or the other percept is exclusively dominant at any time. While this approach has certainly revealed much about the perceptual dynamics involved in rivalry, its focus on dominance episodes overlooks the transition period as a fundamental property of binocular rivalry. It has been argued that the two hallmark features of binocular rivalry are *mutual exclusivity* and *reversibility* (Klink, van Wezel, & van Ee, 2012a; Leopold & Logothetis, 1999; Long & Toppino, 2004). Mutual exclusivity entails that observers perceive either one, or the other perceptual interpretation, but not both. Alternatively, one could say that exclusivity concerns the content of perception and thus deals with the episodes of temporary stable dominance (Klink et al., 2012a). The reversibility aspect, pertains to the occurrence of perceptual alternations, and thus to the transitions between episodes of exclusive dominance. These transitions seem especially interesting for questions about neural correlates of conscious perception because they mark the moment when ‘the brain changes its mind’ and constructs new conscious percepts from the same sensory input.

It has long been known that perceptual alternations in binocular rivalry are not instantaneous (Wheatstone, 1838). Instead, a currently dominant percept often appears to be 'swept into suppression' by a wave-like intrusion of the alternative percept. Systematic investigation of these traveling transition waves has only started recently (Wilson, Blake, & Lee, 2001), but has already resulted in valuable information about the neural correlates of perceptual alternations during binocular rivalry. Most notably, the perceptual experience of dominance-altering waves traveling through the visual field has been shown to coincide with similar waves of neural activity traveling over the retinotopic maps of early visual cortices (Lee, Blake, & Heeger, 2005, 2007). In addition, these cortical waves of activity were abolished by diverting attention away from the visual stimulus in V2 and V3, but remained present in V1 (Lee et al., 2007), lending support for the involvement of hierarchical stages of cortical processing involved in binocular rivalry (Blake & Logothetis, 2002; Wilson 2003). Two distinct aspects of transition waves will likely turn out to be informative about different aspects of their neuronal basis. First, the location within the visual field where the wave is instigated (Naber, Carter, & Verstraten, 2009; Paffen, Naber, & Verstraten, 2008; Stuit, Verstraten, & Paffen, 2010), or the 'nucleation site' (van Ee, 2011), may reflect important inhomogeneities in neuronal properties throughout retinotopic cortical areas. A thorough investigation of this aspect of binocular rivalry requires a focus on the initial moments of rivalry. Indeed, experimental paradigms aimed at explaining the onset of rivalry have strongly gained in popularity over recent years, albeit mostly for an entirely different reason (Carter & Cavanagh, 2007; Klink et al., 2008a; Leopold, Wilke, Maier, & Logothetis, 2002; Pearson & Brascamp, 2008) (see also Section 2.3.2). The second interesting aspect of perceptual transition waves is their spatiotemporal dynamics. The speed and directional pattern with which dominance waves propagate through visual space (Knapen, van Ee, & Blake, 2007; Wilson et al., 2001) combined with the fact that similar waves of activity can be observed in visual cortex (Lee et al., 2005) may reveal essential aspects of cortical connectivity.

Renewed interest in the properties of perceptual transitions may inspire a whole new range of psychophysical experiments and the paradigms developed in these behavioral studies will likely be fit for neuroimaging and neurophysiological experiments as well.

2.2.2 *fMRI*

In the few years that functional magnetic resonance imaging (fMRI) has been available to record brain activity, it has established itself as a force to reckon with in binocular rivalry research (Knapen, Brascamp, Pearson, van Ee, & Blake, 2011; Lee et al., 2007; Polonsky, Blake, Braun, & Heeger, 2000; Tong, Nakayama, Vaughan,

& Kanwisher, 1998; Wunderlich, Schneider, & Kastner, 2005). Both the technique itself and the associated data analysis procedures are, however, still under development. The first fMRI experiments typically used scanners with magnetic field strengths of 1.5 Tesla, allowing a resolution of about $2 \times 2 \times 2$ mm. With stronger magnetic fields, higher signal to noise ratios and better spatial resolutions can be obtained. While 3 Tesla scanners are now relatively common, the latest generation high field fMRI scanners even boost magnetic fields of 7 Tesla or more, resulting in spatial resolutions at the level of cortical columns (Yacoub, Shmuel, Logothetis, & Ugurbil, 2007). For binocular rivalry, these advanced resolutions seem especially promising because monocular neurons that represent input from only one eye are organized in ocular dominance columns based on their eye-of-preference (Horton & Hedley-Whyte, 1984; Hubel & Wiesel, 1969). It would provide a broad view of neural processing from stimulus to percept if activity patterns of monocular and binocular neurons could simultaneously be recorded throughout visual cortex and correlated with perception during binocular rivalry.

The development of robust analysis methods to deal with the large amounts of data generated with fMRI is perhaps an even more important objective than the technical improvement of scanning resolution (Logothetis, 2008; Poldrack, 2012). Fundamentally flawed conclusions drawn from inadequate statistical data analysis or circular reasoning are a widespread problem in cognitive neuroimaging and appropriate solutions are now being suggested to resolve this issue (Bennett, Baird, Miller, & Wolford, 2010; Poldrack, 2012). Furthermore, if fMRI is used in combination with binocular rivalry to investigate how the evolution of neural activity throughout the brain correlates with the dynamics of perception, it does not suffice to limit data analysis to what is sometimes called 'blobology' (Poldrack, 2012); finding a brain area where average activity fluctuations correlate with perception and call it 'a neural correlate'. Instead, it would be more interesting to take patterns of activation into account. While global patterns may reveal aspects of functional connectivity (Ramsey et al., 2010), patterns on a more local scale have been shown to encode information that cannot be extracted from averaged activity alone (Kriegeskorte, Goebel, & Bandettini, 2006).

Functional near-infrared spectroscopy (fNIRS) is relatively new technique that, like fMRI, measures brain oxygenation (Izzetoglu et al., 2005). It does so by detecting the absorption of near-infrared light noninvasively directed at the brain. fNIRS has lower spatial resolution than fMRI, but a better temporal resolution. More importantly however, it offers a cheap, portable and relatively motion-resistant method to detect hemodynamic responses that may in the future become a viable alternative for fMRI in studying, for instance, developmental aspects of binocular rivalry in children.

2.2.3 MEG/EEG

Whereas fMRI is the most broadly used brain imaging technique, it has a rather low temporal resolution. This is perhaps the primary reason why magnetoencephalography (MEG) is rapidly gaining popularity as a temporally sensitive functional neuroimaging tool. Unlike fMRI, which measures changes in blood flow or blood oxygenation as an indirect measure of neural activity, MEG registers the weak magnetic fields induced by the actual electrical signals within populations of neurons. This allows sub-millisecond temporal resolution, but comes at the cost of spatial resolution. Moreover, MEG can only record brain activity at the scalp surface, and while spatial resolutions in the order of millimeters can be obtained with post-hoc dipole analysis, the signal will always remain superficial.

Recent binocular rivalry MEG studies have reported early spatial and temporal aspects of neural activity during perceptual alternations (e.g., Kamphuisen, Bauer, & van Ee, 2008). In the future though, a combination of data obtained from the same observers with fMRI and MEG under the same experimental conditions promises to offer a spectacularly detailed record of the spatiotemporal dynamics of neural activity throughout the brain (Horwitz & Poeppel, 2002).

A similar exciting combination of techniques that we may expect to see more of in the future is the combination of fMRI and electroencephalography (EEG). Like MEG, EEG has excellent temporal resolution at the cost of poor spatial performance. Unlike MEG however, EEG does not require big machines to register brain activity which means that EEG signals can in fact be recorded inside the MRI scanner (Ritter & Villringer, 2006). This approach allows the simultaneous monitoring of the neural processes involved in rivalry with both high spatial and high temporal resolution. The particular advantage of having the EEG signal in addition to the whole brain scans from the fMRI lies in the possibility to employ so-called frequency-tagging paradigms (that are possible with MEG) in which each eye's stimulus is flickering at a different frequency. Fluctuation in the power of these stimulus-specific frequencies in the EEG-signal recorded from occipitally placed electrodes reflects the perceptual dominance cycles evoked by the rivalry (Brown & Norcia, 1997; Lansing, 1964; Lawwill & Biersdorf, 1968). As such, the EEG signal thus represents an objective measure of the subjective process of perception that can be correlated with the spatial information from the fMRI signal to unravel the neural correlates of conscious visual perception.

In addition to the value of MEG and EEG in combination with fMRI, there are some topics in rivalry where these methods by themselves may be the appropriate experimental tools. While fMRI research has demonstrated the involvement of a hierarchical set of brain areas in binocular rivalry (e.g., Lee et al., 2007), EEG and MEG may pinpoint the temporal characteristics of the dynamic neural information processing in networks of areas throughout the brain.

2.2.4 *Electrophysiology*

It is currently not possible to directly measure single neuron activity non-invasively. Single neuron activity in humans can occasionally be recorded in patients equipped with intracranial electrode grids in preparation of brain surgery (Kreiman, Fried, & Koch, 2002), but these opportunities are relatively rare and the location of electrodes is on such occasions optimized for the pending surgical procedure, not for a rivalry experiment. For this reason, single-unit activity during binocular rivalry is generally recorded in animals, preferably non-human primates, because their brains (and in particular their visual cortices) closely resemble those of humans.

While recording the activity of a single neuron provides a remarkably detailed insight in the dynamic response properties of that particular cell (Logothetis, 1998), it omits the responses of many other potentially relevant neurons. The classic way to overcome this constraint is to repeat the experiment many times and record from a large population of different neurons (Logothetis & Schall, 1989). However, with the increased availability of computational resources it is now becoming more common to record activity with large multi-electrode grids rather than with single electrodes. Elaborate spike-sorting algorithms can split up signals according to individual source neurons. This approach not only saves the experimenter time by measuring activity from many neurons at once, it also allows an evaluation of interneuronal activity relations (Gail, Brinksmeier, & Eckhorn, 2004; Wilke, Logothetis, & Leopold, 2006). In the specific case of binocular rivalry it would, for instance, be very interesting to see how the activity of individual cells in primary visual cortex relates to the activity of cells in later cortical areas. The progression of activity over cortex associated with perceptual traveling waves of dominance discussed in Section 2.2.1 would also be an excellent topic to investigate with large multi-electrode grids to allow the detection of neural activity in a direct way rather than the indirect approach of fMRI.

On a side-note, it is not yet clear at all how the different measures of neural activity like spikes, local field potentials, and fMRI responses correspond to one another (Logothetis, 2003; Logothetis, Pauls, Augath, Trinath, & Oeltermann, 2001). There is an urgent need for multimodal recording approaches, both to establish this relation and to decipher how information is encoded in different forms of neural activity.

2.2.5 *Two-photon imaging*

Two-photon excited microscopy is a relatively new, but rapidly developing, method to simultaneously record the activity of populations of neurons with single cell resolution or better (Svoboda & Yasuda, 2006). By recording the

amount of light that is emitted by neurons labeled with calcium concentration or voltage-sensitive fluorescent dyes and excited with laser-light, neuronal activity can be measured up to a depth of one millimeter. Furthermore, the choice of marker allows a distinction between excitatory and inhibitory cells (Hofer et al., 2011). At the moment, the technique is predominantly used with smaller animals like mice (Stosiek, Garaschuk, Holthoff, & Konnerth, 2003), rats (Kerr, Greenberg, & Helmchen, 2005), zebra finches (Roberts, Tschida, Klein, & Mooney, 2010), or ferrets (Li, van Hooser, Mazurek, White, & Fitzpatrick, 2008) because they easily fit under a microscope, but solutions for two-photon imaging in monkeys are being developed as well (Heider, Nathanson, Isacoff, Calaway, & Siegel, 2010). Ocular dominance plasticity is a popular topic for two-photon imaging studies in mice (Hofer, Mrsic-Flogel, Bonnhoeffer, & Hübener, 2006). Binocular rivalry research may benefit from advances in this field and apply similar imaging techniques to obtain spatiotemporally detailed recordings from populations of tens of neurons located in multiple cortical layers. These studies may complement existing work with optical imaging of intrinsic signals (Sengpiel, Freeman, Bonnhoeffer, & Blakemore, 2001) and voltage-sensitive dyes (Wen & Zhang, 2009) that have related the characteristics of binocular rivalry to the dynamic activation patterns in large ensembles of cortical neurons. In addition to being capable of imaging detailed activity fluctuations in large cell ensembles, two-photon microscopy also has a high enough spatial resolution to visualize axons, dendrites and even the location of synapses (Holtmaat & Svoboda, 2009). Combining structural information with high-resolution activity patterns may eventually become valuable in revealing the neuronal mechanism of visual awareness.

2.3 Mechanisms of binocular rivalry: How the window works

With the increasing use of binocular rivalry as a convenient tool to study the neural mechanisms of consciousness, some of the fundamental questions about the binocular rivalry mechanism itself may have moved into the background. It is however conceivable that the answers to several of these questions will be essential for the interpretation of any neural correlate of consciousness revealed with binocular rivalry. We therefore argue that a second branch of binocular rivalry research should dedicate itself to the investigation of binocular rivalry as an under-defined perceptual phenomenon and attempt to unravel its basic functional and neuronal properties. In the next few paragraphs, a number of longstanding questions as well as several novel findings will be discussed as potentially fruitful topics of interest for this branch of research.

2.3.1 *Stereopsis*

While the ‘rivalry’ aspect in binocular rivalry may attract most interest in the phenomenon, the ‘binocular’ aspect may actually be more interesting from a functional point of view. The question how stereopsis and rivalry can coexist in a single neuronal organization of binocular vision has been a prominent issue ever since the discovery of binocular rivalry (Andrews & Purves, 1997; Blake, Yang, & Wilson, 1991; Grossberg, Yazdanbakhsh, Cao, & Swaminathan, 2008; Livingstone, 1996; Wolfe, 1986). Striking observations of binocular rivalry in the absence of binocular conflict due to a temporal separation of the rival images (O’Shea & Crassini, 1984; van Boxtel, Alais, Erkelens, & van Ee, 2008), and binocular fusion of stimuli that would generally instigate rivalry (Yang, Rose, & Blake, 1992) suggest an intricate relation between fusion and rivalry. Even though our knowledge of the complex neurophysiological mechanisms of stereopsis has increased tremendously over the past few years (Blake & Wilson, 2011), binocular rivalry and non-rivaling binocular vision are still predominantly studied in relative isolation, with only a limited number of studies directly addressing the issue (Andrews & Lotto, 2004; Andrews & Purves, 1997; Blake & Camisa, 1978; Blake et al., 1991; Buckthought & Mendola, 2011; Buckthought & Wilson, 2007; Treisman, 1962). We believe that both research fields may greatly benefit from each other’s progress and that, especially with novel imaging techniques, chances are now better than ever to pinpoint how the brain decides whether to fuse information from two eyes or engage in binocular rivalry.

2.3.2 *Computational modeling*

One area of research where mechanisms of stereopsis and binocular vision are already being combined on a regular basis is computational modeling. A solid tradition of model-driven experimental work in binocular rivalry research has resulted in a plethora of binocular rivalry models that explain (parts of) the phenomenon at a wide range of conceptual levels (Freeman, 2005; Kalarickal & Marshall, 2000; Lehky, 1988; Mueller, 1990; Noest et al., 2007; Seely & Chow, 2011; Stollenwerk & Bode, 2003; Wilson, 2007). We do not foresee a definitive, universally accepted, computational model of binocular vision or binocular rivalry anytime soon, but experience with existing models teaches that, on many occasions, (counterintuitive) model predictions can be instrumental in getting to understand functional and physiological mechanisms.

Recently, so-called ‘percept-choice’ or ‘onset-rivalry’ models have yielded important novel insights in the formation of the initial percept at the onset of binocular rivalry (Carter & Cavanagh, 2007; Noest et al., 2007). We have made the distinction between the *reversibility* and *mutual exclusivity* aspects of binocular rivalry (see Section 2.2.1) and argued that reversibility may be the most interesting

feature when studying fluctuations in visual awareness. Mutual exclusivity, on the other hand, may be probed best at the onset of rivalry, when the brain ‘chooses’ a dominant percept. This choice process can be studied with sequences of briefly interrupted stimuli in which stimulus onsets are repeated many times (Leopold et al., 2002). The percept-choice paradigm has already been instrumental in demonstrating forms of perceptual memory and spatial relations in binocular rivalry (Brascamp et al., 2008; Brascamp, Pearson, Blake, & van den Berg, 2009; de Jong, Knapen, & van Ee, 2012; Klink et al., 2008a; Klink, Noest, Holten, van den Berg, & van Wezel, 2009; Knapen, Brascamp, Adams, & Graf, 2009; Pastukhov & Braun, 2008) and the underlying neurophysiology (Klink, Oleksiak, Lankheet, & van Wezel, 2012b), but in the future it may also reveal information about more generic questions of visual decision-making.

An overview of the role of computational evidence in binocular rivalry research can be found in the chapter by Wilson (this volume). We are confident that computational studies will remain crucial in providing testable predictions about the functional mechanisms and neural substrates of binocular rivalry in the future.

2.3.3 *Plasticity*

Functional conceptualizations and computational models of binocular rivalry generally contribute fluctuations in awareness to a combination of the effects of adaptation, inhibition and neural noise (Seely & Chow, 2011; van Ee, 2009). Without going into too much detail, these explanations usually assume that neuronal populations coding for conflicting stimulus features engage in a competition for conscious representation in which they actively inhibit the activity of their rival populations while their own noisy activity levels are subject to neuronal fatigue that reduces their responsiveness. While the effective strength of mutual inhibition in such a mechanism will be the product of the driving activity and the inhibitory efficacy, the gain of the proposed inhibitory connectivity is often (implicitly) assumed to be constant. Recent findings, however, demonstrate a form of plasticity in the binocular rivalry mechanism that implies a recalibration of inhibitory efficacy based on recent perceptual history (Klink, Brascamp, Blake, & van Wezel, 2010).

In this study, researchers explicitly focused on the transition periods between periods of exclusive percepts. As we noted before, these transitions are often erroneously classified as instantaneous switches from one dominant percept to the other. In reality, transition periods can however have significant durations and take a range of qualitatively different forms that are all mixtures of the two exclusive percepts (Blake, O’Shea, & Mueller, 1992; Hollins, 1980; Klink et al., 2010; Yang, Rose, & Blake, 1992). The occurrence and duration of mixture percept transition

periods can be regarded as an indication of the inhibitory efficacy between the neuron populations that represent these exclusive percepts (Hollins, 1980). When binocular rivalry exposure was prolonged to more than half an hour, considerably longer than typically used presentation durations of several minutes, the mixture periods became progressively longer, indicating a decrease in inhibitory efficacy (Klink et al., 2010). Additional experiments revealed that this apparent loss of inhibition was highly selective to the eye-of-origin and to the stimulus features. It also showed that it could not be attributed to straightforward fatigue because it required selective exposure to binocularly matching stimuli to recover to baseline values rather than that it recovered passively.

Other forms of plasticity in binocular rivalry affect the rate at which percepts fluctuate in dominance (Lack, 1969; Suzuki & Grabowecky, 2007; van Ee, 2005), the relative dominance of visual information presented to a previously deprived eye (Lunghi, Burr, & Morrone, 2011), or even the ability to experience binocular rivalry altogether (Lack, 1978). Together, these plasticity phenomena demonstrate the dynamic nature of the binocular visual system, a feature that may be important for interocular contrast-gain control during binocular summation and the coexistence of binocular rivalry and stereopsis. A focus on visual plasticity may furthermore be helpful for the study of adult brain plasticity, the same way research on ocular dominance has been helpful for the field of neuronal development (Katz & Crowley, 2002).

2.3.4 *Genetics*

The temporal dynamics of binocular rivalry have been vigorously investigated and it has long been known that the rate of perceptual fluctuations, while relatively stable within observers, can differ greatly between observers (Aafjes, Hueting, & Visser, 1966). Inspired by the observation that alternation rates are generally slower in patients with bipolar disorder (Krug et al., 2008; Miller et al., 2003; Pettigrew & Miller, 1998), a heritable mental disorder, a recent study aimed to find out whether there could be a genetic component to the individual differences in alternation rate (Miller et al., 2010). When alternation rates were measured in a large sample of monozygotic and dizygotic twins they indeed revealed a substantial genetic contribution, a finding that was later confirmed with a broader range of rivalry stimuli (Shannon, Patrick, Jiang, Bernat, & He, 2011), and complemented by a demonstrated correlation between brain structure and alternation rate (Kanai, Bahrami, & Rees, 2010). Not only do these findings open up possibilities to use binocular rivalry alternation rates as a diagnostic endophenotype for bipolar disorder, they also suggest that important determinants of the specific neuronal machinery of binocular rivalry are encoded in our DNA. This notion asks for the introduction of molecular biology

in binocular rivalry research. Animal models like *Drosophila melanogaster* that are easily accessible to genetic manipulations and for which evidence of rivalry characteristics has repeatedly been shown, will likely become fruitful tools in this direction of research (Miller, Ngo, & van Swinderen, 2012). Such a completely novel experimental approach may reveal many previously unexplained aspects of binocular rivalry in the future. Elsewhere in this volume the genetic contribution to rivalry is discussed in more detail (see chapters by Ngo et al. and Bressler, Denison, & Silver, this volume).

2.4 Reaching through a window on consciousness

For the third branch of binocular rivalry research, we return to the use of rivalry as a window on the neural processes of visual awareness. This time, however, we ask for a more experimentally proactive approach. Instead of passively observing these processes, we propose to interfere with them and investigate how closely controlled experimental manipulations may alter perceptual experience and neural processing during binocular rivalry. Such manipulations can range from simple stimulus variations to invasive interference with specific aspects of neural processing. Each of these perturbations and the corresponding consequences may potentially help in determining whether certain processes are merely correlates of consciousness or whether they are essential for its constitution (Miller, 2007).

2.4.1 Human psychophysics

With the availability of modern imaging possibilities, there is a danger of underappreciating the value of human psychophysical tools in binocular rivalry research. Even though one cannot directly measure brain activity with psychophysics, psychophysical experiments can teach us much about the mechanisms of perception, especially when they are combined with computational modeling and thorough knowledge of neurophysiology and neuroanatomy. Psychophysical experiments systematically investigate the relation between stimulus and perception or behavior. They thus look at processes from a functional point of view, which is the only viewpoint relevant to the observing organism. In addition, many inventive experimental paradigms in binocular rivalry research were originally developed in a psychophysical setting, but have later been used in imaging experiments. A detailed overview of psychophysical techniques can be found in the chapter by Brascamp and Baker (this volume), accompanied by a discussion of general pitfalls and possibilities. Here, we merely stress the importance of 'simple' psychophysics for the technologically advanced future of binocular rivalry research and point out some of the most promising novel approaches.

In psychophysics, binocular rivalry stimuli are typically presented to an observer in a dark and quiet room, isolated from any form of context. With this situation as a starting point, any additional context can be regarded as a manipulation of the pathway from stimulus to awareness. An extensive overview of studies that have shown how the brain uses spatial, temporal, and crossmodal contexts, or even ‘internal states’ like emotional or attentional load to interpret perceptual ambiguities is available elsewhere (Klink et al., 2012a; see chapter by Bressler et al., this volume). Here we will only briefly touch upon some of the most promising approaches. The temporal characteristics of binocular rivalry are not only being exploited in the onset paradigms mentioned in Section 2.3.2 and the frequency tagging approach discussed in Section 2.2.2, but they may also reveal sequential processing steps in rivalry resolution and possibly the involvement of feedback connectivity (e.g., Bartels & Logothetis, 2010; van Boxtel, Knapen, Erkelens, & van Ee, 2008). Explorations in multimodal interactions have also begun to make their way into binocular rivalry research (Blake, Sobel, & James, 2004; Conrad, Bartels, Kleiner, & Noppeney, 2010; Lunghi, Binda, & Morrone, 2010; van Ee, van Boxtel, Parker, & Alais, 2009; Zhou, Jiang, He, & Chen, 2010) and we expect a lot from these approaches in unraveling general processes of perceptual selection and binding. Spatial context effects on the other hand have been investigated in binocular rivalry for quite some time (e.g., Fukuda & Blake, 1992; Sobel & Blake, 2002), but the relatively new nucleation and traveling wave approaches mentioned in Section 2.2.1 can provide important new insights in the spatial instigation and progression of perceptual fluctuation.

A whole new class of experiments have started to use binocular rivalry as a tool to investigate the unconscious processing of sensory information (Lin & He, 2008) and the interaction between attention and awareness (Brascamp, van Boxtel, Knapen, & Blake, 2010; Koch & Tsuchiya, 2007; Lamme, 2003; van Boxtel, Tsuchiya, & Koch, 2010). Such studies frequently use a form of rivalry dubbed continuous flash suppression (Tsuchiya & Koch, 2005), where one eye is presented with a highly salient, rapidly changing, stimulus that suppresses a far less salient image in the other eye for minutes at a time (Figure 2a), much longer than the typical suppression duration in conventional binocular rivalry. As research interest in this field of unconscious perceptual processing is rapidly growing, there is increasing demand for binocular rivalry as a tool to manipulate which sensory input is consciously perceived. However, as we argued in Section 2.1, such instrumental use of binocular rivalry can only benefit from a better understanding of the binocular rivalry mechanism itself.

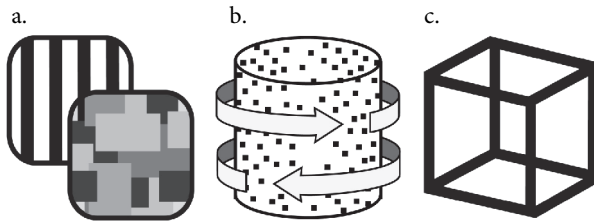


Figure 2. Other rivalry stimuli. (a) Continuous flash suppression is a special case of binocular rivalry where a highly salient, dynamic, image in one eye (e.g., a dynamic Mondrian pattern), suppresses a static image in the other eye for much longer periods than is the case with equally salient stimuli. (b) In ambiguously rotating structure-from-motion cylinders, the impression of a three-dimensional object arises from a two-dimensional projection of dots moving as if they are located on the surface of a rotating transparent cylinder. Lacking depth information, the rotation direction is ambiguous. (c) A Necker cube lacks depth cues, rendering its three-dimensional orientation ambiguous.

2.4.2 *Transcranial magnetic stimulation*

Instead of interfering with the processes of conscious perception by manipulating stimulus conditions, one may also try to directly influence the activity of the involved neurons. One way of doing this is with transcranial magnetic stimulation (TMS; see chapter by Thomson & Fitzgerald, this volume). With this technique, a locally applied, rapidly changing, magnetic field induces weak electrical currents in the brain that can cause neurons to become active or silent, depending on the precise stimulation paradigm. A comprehensive review of recent brain stimulation experiments during rivalry can be found in the chapter by Ngo et al. (this volume), but for the future of binocular rivalry research, TMS and related non-invasive stimulation techniques will be most informative if some aspects of the technique can be improved. One basic problem is the rather coarse spatial specificity of the stimulation that disrupts processing in relatively large patches of cortex. Another issue is that there is no detailed understanding of the physiological consequences of TMS (Bestmann, 2008). This may however not be a deal-breaker. A minimal functional interpretation of TMS as interfering with ongoing neural processing is enough to make TMS a valuable research tool. Besides, the combination of TMS with fMRI (another technique for which the physiological underpinnings are not entirely resolved, see Section 2.2.3) or EEG, provides a powerful non-invasive approach to study causal relations between activity patterns in different areas of the brain (Driver, Blankenburg, Bestmann, Vanduffel, & Ruff, 2009). TMS thus has the potential of becoming an important tool in unraveling both the necessity and sufficiency of specific neural processes in visual perception and binocular rivalry.

2.4.3 *Microstimulation*

Invasive forms of brain stimulation like electrical microstimulation can be used in animal models and the occasional human patient (Bak et al., 1990). Binocular rivalry essentially confronts the brain with a perceptual conflict in which it eventually ‘chooses’ a dominant percept. Similar perceptual decisions between options with equal or close to equal sensory support have been shown to be highly susceptible to the influence of microstimulation (Cohen & Newsome, 2004). Stimulating only a very limited number of neurons has been shown to alter perceived motion direction (Salzman, Murasugi, Britten, & Newsome, 1992), heading direction (Britten & van Wezel, 1998), and depth perception (DeAngelis, Cumming, & Newsome, 1998). If the subjective appearance of such basic features can be altered with microstimulation, it should also be possible to influence the perceptual choices between two competing binocular rivalry stimuli by subtly stimulating subsets of neurons. If microstimulation is combined with additional imaging techniques, it may reveal the complex recurrent connectivity within and between functional brain networks.

2.4.4 *Photostimulation*

In addition to electrical stimulation, recent advances have promoted a rapid growth in popularity of photostimulation as a novel neuronal interference technique. Photostimulation is used in animal models, both *in vitro* and *in vivo*, and allows precisely targeted neuronal stimulation. The variant that is most likely to be useful for binocular rivalry in the near future is optogenetics, Nature magazine’s ‘Method of the Year 2010’ (Deisseroth, 2010). In optogenetics, light sensitive ion channels are genetically built into the membranes of a specific class of neurons. If these channels are illuminated with precisely controlled light of a specific wavelength and flicker frequency, these ion channels open or close, depending on their protein compounds. With operational control over ion channels, an experimenter can effectively switch a neuron on or off with the flick of a light switch. While initial studies were limited to rodents, the method has now also been applied to non-human primates (Han et al., 2009), opening up possibilities of combining it with behavioral paradigms in which awake behaving monkeys are exposed to binocular rivalry while the activity of specific groups of neurons, either in visual cortex or elsewhere, are experimentally controlled.

3. Concluding remarks

Binocular rivalry is a popular tool in the scientific study of consciousness because it dissociates stable, unchanged, visual stimulation from fluctuations in visual awareness. Other types of visual ambiguities exhibit a similar behavior without the need to present conflicting information to the two eyes (Leopold & Logothetis, 1999). Stimuli like the Necker cube, or ambiguously rotating structure-from-motion cylinders embody a competition between mutually exclusive, three-dimensional perceptual interpretations based on two-dimensional projections that lack explicit depth information (Figure 2b and 2c). It has been argued, that while different types of visual ambiguities are likely resolved by different cortical neurons and at different cognitive levels, the operational principles may to a certain extent be comparable (Klink, van Ee, & van Wezel, 2008b).

The primary difference between these perceptual rivalry stimuli and binocular rivalry is that the same phenomenological experience of alternating perception emerges without involving of the complex neuronal organization of binocular vision. It thus avoids the issue of interocular interactions and focuses purely on the (cortical) perceptual conflict between competing interpretations of the stimulus. It is, however, unclear whether suppressing (part of) a visual stimulus from awareness, as is the case in binocular rivalry, is the same as suppressing a perceptual interpretation while still using all the available visual information. In addition, the techniques that most effectively suppress visual input from awareness, like continuous flash suppression, actually exploit the binocular visual system. Clearly, perceptual rivalry and binocular rivalry both have their advantages and disadvantages in studying the neural underpinnings of conscious visual perception and the choice of stimuli and experimental paradigm will ultimately depend on the specific research question that is to be addressed. Both types of rivalry will however continue to be valuable tools in studying the neuronal basis of visual awareness. The similarities and differences between them, complemented by the increasing knowledge of the neuronal underpinnings of binocular vision and object perception, may in fact prove to be highly informative about the brain mechanisms that shape visual awareness.

The technological developments discussed in this chapter make it possible to register neuronal activity at many different processing levels. Each method comes with its own advantages and disadvantages, making it increasingly prudent to combine techniques and explore multimodal recording possibilities. Care should however be taken that all these exciting new technological possibilities do not distract us from the fact that the binocular rivalry mechanism itself remains poorly understood. We therefore proposed a distinction between three intimately

related branches of binocular rivalry research that each offer specific possibilities for future research (Box 1). Novel imaging techniques will further promote the use of binocular rivalry as a window on the processes of visual awareness, while ongoing efforts aimed at understanding the mechanisms of binocular rivalry itself and its relation to stereopsis will continue to advance our understanding of visual processing. Finally, we invite binocular rivalry researchers to reach through the window on consciousness, interact with the underlying neuronal processes, and learn the neuronal language of consciousness.

Box 1. Major opportunities on three fronts

While we propose a wide range of possibilities for future binocular rivalry research throughout this chapter, here we tentatively select one topic for each branch of research that we currently believe to have most potential.

1. New animal models and optical imaging techniques

The rapid rise in studying visual perception with optical imaging techniques in rodents (Grewe & Helmchen, 2009) offers great opportunities for the ‘observation’ of binocular rivalry processes. While it may be more difficult to obtain perceptual reports from these animals (it is currently not known if they even experience binocular rivalry), the amount of detail that can potentially be obtained about patterns of activity and involved neural structures is unprecedented. In addition, this line of research can provide a lot of information about the stereopsis vs rivalry issue as basic (binocular) vision experiments are already quite common in this field. Expanding the technique to non-human primates and combining imaging with stimulation paradigms allows this approach to be useful for all three branches of binocular rivalry research.

2. Plasticity and inhibition link binocular rivalry and stereopsis

The observation of plasticity in inhibitory efficacy during binocular rivalry (Klink et al., 2010) may move interest in binocular rivalry towards the transition periods. On the computational side, it urges new models to incorporate more adaptive neuronal interactions that may bridge the gap between stereopsis and rivalry. The focus on neuronal processes that mediate perceptual alternations and correlating those with perceptual experience may also inspire new psychophysical, physiological and imaging experiments.

3. Multisensory context as interference on the stimulus side

A straightforward way of interfering with binocular rivalry processing is to add context to the stimulus. Because we live in a multimodal world, the brain employs mechanisms of multimodal integration to establish rich perceptual experiences (Ernst & Bühlhoff, 2004). These mechanisms can be exploited in binocular rivalry to reveal the functional mechanisms of perceptual awareness. Such endeavors have recently started to appear in the literature (e.g., Conrad et al., 2010; Lunghi et al., 2010; van Ee et al., 2009; Zhou et al., 2010), but we expect more revealing findings to emerge from this field in the future.

References

- Aafjes, M., Hueting, J. E., & Visser, P. (1966). Individual and interindividual differences in binocular retinal rivalry in man. *Psychophysiology*, 3(1), 18–22.
- Alais, D. (2012). Binocular rivalry: Competition and inhibition in visual perception. *Wiley Interdisciplinary Reviews: Cognitive Science*, 3(1), 87–103.
- Andrews, T. J., & Lotto, R. B. (2004). Fusion and rivalry are dependent on the perceptual meaning of visual stimuli. *Current Biology*, 14(5), 418–423.
- Andrews, T. J., & Purves, D. (1997). Similarities in normal and binocularly rivalrous viewing. *Proceedings of the National Academy of Sciences USA*, 94(18), 9905–9908.
- Bagby, J. W. (1957). A cross-cultural study of perceptual predominance in binocular rivalry. *Journal of Abnormal and Social Psychology*, 54(3), 331–334.
- Bak, M., Girvin, J. P., Hambrecht, F. T., Kufta, C. V., Loeb, G. E., & Schmidt, E. M. (1990). Visual sensations produced by intracortical microstimulation of the human occipital cortex. *Medical & Biological Engineering & Computing*, 28(3), 257–259.
- Baker, D. H. (2010). Visual consciousness: The binocular rivalry explosion. *Current Biology*, 20(15), R644–R646.
- Bartels, A., & Logothetis, N. K. (2010). Binocular rivalry: A time dependence of eye and stimulus contributions. *Journal of Vision*, 10(12), 3. doi:10.1167/10.12.3
- Belliveau, J. W., Kennedy, D. N., McKinsty, R. C., Buchbinder, B. R., Weisskoff, R. M., Cohen, M. S. et al. (1991). Functional mapping of the human visual cortex by magnetic resonance imaging. *Science*, 254(5032), 716–719.
- Bennett, C. M., Baird, A. A., Miller, M. B., & Wolford, G. L. (2010). Neural correlates of interspecies perspective taking in the post-mortem Atlantic Salmon: An argument for proper multiple comparisons correction. *Journal of Serendipitous and Unexpected Results*, 1(1), 1–5.
- Bestmann, S. (2008). The physiological basis of transcranial magnetic stimulation. *Trends in Cognitive Sciences*, 12(3), 81–83.
- Blake, R. (1989). A neural theory of binocular rivalry. *Psychological Review*, 96(1), 145–167.
- Blake, R., & Camisa, J. (1978). Is binocular vision always monocular? *Science*, 200(4349), 1497–1499.
- Blake, R., & Logothetis, N. K. (2002). Visual competition. *Nature Reviews Neuroscience*, 3(1), 13–21.
- Blake, R., O'Shea, R. P., & Mueller, T. J. (1992). Spatial zones of binocular rivalry in central and peripheral vision. *Visual Neurosciences*, 8(5), 469–478.
- Blake, R., Sobel, K. V., & James, T. W. (2004). Neural synergy between kinetic vision and touch. *Psychological Science*, 15(6), 397–402.
- Blake, R., & Wilson, H. (2011). Binocular vision. *Vision Research*, 51(7), 754–770.
- Blake, R., Yang, Y. D., & Wilson, H. R. (1991). On the coexistence of stereopsis and binocular rivalry. *Vision Research*, 31(7–8), 1191–1203.
- Bokander, I., & Radeborg, K. (1966). The solution of perceptual conflict between stereoscopically presented facial photographs. *Psychological Research Bulletin*, 6(3), 1–10.
- Brascamp, J. W., van Boxtel, J. J. A., Knapen, T. H. J., & Blake, R. (2010). A dissociation of attention and awareness in phase-sensitive but not phase-insensitive visual channels. *Journal of Cognitive Neuroscience*, 22(10), 2326–2344.

- Brascamp, J. W., Knapen, T. H. J., Kanai, R., Noest, A. J., van Ee, R., & van den Berg, A. V. (2008). Multi-timescale perceptual history resolves visual ambiguity. *PLoS ONE*, 3(1), e1497. doi: 10.1371/journal.pone.0001497
- Brascamp, J. W., Pearson, J., Blake, R., & van den Berg, A. V. (2009). Intermittent ambiguous stimuli: Implicit memory causes periodic perceptual alternations. *Journal of Vision*, 9(3), 3. doi: 10.1167/9.3.3
- Breese, B. B. (1899). On inhibition. *Psychological Monographs*, 3(1), 1–65.
- Britten, K. H., & van Wezel, R. J. A. (1998). Electrical microstimulation of cortical area MST biases heading perception in monkeys. *Nature Neuroscience*, 1(1), 59–63.
- Brown, R. J., & Norcia, A. M. (1997). A method for investigating binocular rivalry in real-time with the steady-state VEP. *Vision Research*, 37(17), 2401–2408.
- Buckthrought, A., & Mendola, J. D. (2011). A matched comparison of binocular rivalry and depth perception with fMRI. *Journal of Vision*, 11(6), 3. doi: 10.1167/11.6.3
- Buckthrought, A., & Wilson, H. R. (2007). Interaction between binocular rivalry and depth in plaid patterns. *Vision Research*, 47(19), 2543–2556.
- Carter, O. L., & Cavanagh, P. (2007). Onset rivalry: Brief presentation isolates an early independent phase of perceptual competition. *PLoS ONE*, 2, e343. doi: 10.1371/journal.pone.0000343
- Cohen, M. R., & Newsome, W. T. (2004). What electrical microstimulation has revealed about the neural basis of cognition. *Current Opinion in Neurobiology*, 14(2), 169–177.
- Conrad, V., Bartels, A., Kleiner, M., & Noppeney, U. (2010). Audiovisual interactions in binocular rivalry. *Journal of Vision*, 10(10), 27. doi: 10.1167/10.10.27
- Crick, F., & Koch, C. (1990). Towards a neurobiological theory of consciousness. *Seminars in the Neurosciences*, 2, 263–275.
- Crick, F., & Koch, C. (1998). Consciousness and neuroscience. *Cerebral Cortex*, 8(2), 97–107.
- DeAngelis, G. C., Cumming, B. G., & Newsome, W. T. (1998). Cortical area MT and the perception of stereoscopic depth. *Nature*, 394(6694), 677–680.
- Deisseroth, K. (2010). Optogenetics. *Nature Methods*, 8(1), 26–29.
- de Jong, M. C., Knapen, T., & van Ee, R. (2012). Opposite influence of perceptual memory on initial and prolonged perception of sensory ambiguity. *PLoS ONE*, 7(1), e30595. doi: 10.1371/journal.pone.0030595
- Driver, J., Blankenburg, F., Bestmann, S., Vanduffel, W., & Ruff, C. C. (2009). Concurrent brain-stimulation and neuroimaging for studies of cognition. *Trends in Cognitive Sciences*, 13(7), 319–327.
- Ernst, M. O., & Bühlhoff, H. H. (2004). Merging the senses into a robust percept. *Trends in Cognitive Sciences*, 8(4), 162–169.
- Fox, R. (1963). *An analysis of the suppression mechanism in binocular rivalry*. (Doctoral dissertation, University of Cincinnati, 1963).
- Freeman, A. W. (2005). Multistage model for binocular rivalry. *Journal of Neurophysiology*, 94(6), 4412–4420.
- Fukuda, H., & Blake, R. (1992). Spatial interactions in binocular rivalry. *Journal of Experimental Psychology: Human Perception and Performance*, 18(2), 362–370.
- Gail, A., Brinksmeier, H., & Eckhorn, R. (2004). Perception-related modulations of local field potential power and coherence in primary visual cortex of awake monkey during binocular rivalry. *Cerebral Cortex*, 14(3), 300–313.
- Grewe, B. F., & Helmchen, F. (2009). Optical probing of neuronal ensemble activity. *Current Opinion in Neurobiology*, 19(5), 520–529.

- Grossberg, S., Yazdanbakhsh, A., Cao, Y., & Swaminathan, G. (2008). How does binocular rivalry emerge from cortical mechanisms of 3-D vision? *Vision Research*, 48(21), 2232–2250.
- Han, X., Qian, X., Bernstein, J. G., Zhou, H.-H., Franzesi, G. T., Stern, P. et al. (2009). Millisecond-timescale optical control of neural dynamics in the nonhuman primate brain. *Neuron*, 62(2), 191–198.
- Heider, B., Nathanson, J. L., Isacoff, E. Y., Callaway, E. M., & Siegel, R. M. (2010). Two-photon imaging of calcium in virally transduced striate cortical neurons of behaving monkey. *PLoS ONE*, 5(11), e13829. doi: 10.1371/journal.pone.0013829
- Helmholtz, H. (1867). *Handbuch der physiologischen Optik*, Leipzig: Voss. J. P. C. Southall, 1962 (Trans.), *Helmholtz's treatise on physiological optics*, Vol 3. New York: Dover Publications Inc.
- Hofer, S. B., Ko, H., Pichler, B., Vogelstein, J., Ros, H., Zeng, H. et al. (2011). Differential connectivity and response dynamics of excitatory and inhibitory neurons in visual cortex. *Nature Neuroscience*, 14(8), 1045–1052.
- Hofer, S. B., Mrsic-Flogel, Th. D., Bonhoeffer, T., & Hübener, M. (2006). Lifelong learning: Ocular dominance plasticity in mouse visual cortex. *Current Opinion in Neurobiology*, 16(4), 451–459.
- Hollins, M. (1980). The effect of contrast on the completeness of binocular rivalry suppression. *Perception & Psychophysics*, 27(6), 550–556.
- Holtmaat, A., & Svoboda, K. (2009). Experience-dependent structural synaptic plasticity in the mammalian brain. *Nature Reviews Neuroscience*, 10(9), 647–658.
- Horton, J. C., & Hedley-Whyte, E. T. (1984). Mapping of cytochrome oxidase patches and ocular dominance columns in human visual cortex. *Philosophical Transactions of the Royal Society of London B: Biological Sciences*, 304(1119), 255–272.
- Horwitz, B., & Poeppel, D. (2002). How can EEG/MEG and fMRI/PET data be combined? *Human Brain Mapping*, 17(1), 1–3.
- Hubel, D. H., & Wiesel, T. N. (1969). Visual area of the lateral suprasylvian gyrus (Clare-Bishop area) of the cat. *Journal of Physiology*, 202(1), 251–260.
- Hubel, D. H., & Wiesel, T. N. (1998). Early exploration of the visual cortex. *Neuron*, 20(3), 401–412.
- Izzetoglu, M., Izzetoglu, K., Bunce, S., Ayaz, H., Devaraj, A., Onaral, B. et al. (2005). Functional near-infrared neuroimaging. *IEEE Transactions on Neural Systems and Rehabilitation Engineering*, 13(2), 153–159.
- Kalarickal, G. J., & Marshall, J. A. (2000). Neural model of temporal and stochastic properties of binocular rivalry. *Neurocomputing*, 32–33, 843–853.
- Kamphuisen, A., Bauer, M., & van Ee, R. (2008). No evidence for widespread synchronized networks in binocular rivalry: MEG frequency tagging entrains primarily early visual cortex. *Journal of Vision*, 8(5), 4. doi: 10.1167/8.5.4
- Kanai, R., Bahrami, B., & Rees, G. (2010). Human parietal cortex structure predicts individual differences in perceptual rivalry. *Current Biology*, 20(18), 1626–1630.
- Katz, L. C., & Crowley, J. C. (2002). Development of cortical circuits: Lessons from ocular dominance columns. *Nature Reviews Neuroscience*, 3(1), 34–42.
- Kaufer, G., & Riess, B. F. (1960). Stereoscopic perception as a tool in psychotherapeutic research. *Perceptual and Motor Skills*, 10(3), 241.
- Kerr, J. N. D., Greenberg, D., & Helmchen, F. (2005). Imaging input and output of neocortical networks in vivo. *Proceedings of the National Academy of Sciences USA*, 102(39), 14063–14068.

- Klink, P. C., Brascamp, J. W., Blake, R., & van Wezel, R. J. A. (2010). Experience-driven plasticity in binocular vision. *Current Biology*, 20(16), 1464–1469.
- Klink, P. C., van Ee, R., Nijs, M. M., Brouwer, G. J., Noest, A. J., & van Wezel, R. J. A. (2008a). Early interactions between neuronal adaptation and voluntary control determine perceptual choices in bistable vision. *Journal of Vision*, 8(5), 16. doi:10.1167/8.5.16
- Klink, P. C., van Ee, R., & van Wezel, R. J. A. (2008b). General validity of level's propositions reveals common computational mechanisms for visual rivalry. *PLoS ONE*, 3(10), e3473. doi:10.1371/journal.pone.0003473
- Klink, P. C., Noest, A. J., Holten, V., van den Berg, A. V., & van Wezel, R. J. A. (2009). Occlusion-related lateral connections stabilize kinetic depth stimuli through perceptual coupling. *Journal of Vision*, 9(10), 20. doi:10.1167/9.10.20
- Klink, P. C., Oleksiak, A., Lankheet, M. J. M., & van Wezel, R. J. A. (2012b). Intermittent stimulus presentation stabilizes neuronal responses in macaque area MT. *Journal of Neurophysiology*, 108(8), 2101–2114.
- Klink, P. C., van Wezel, R. J. A., & van Ee, R. (2012a). United we sense, divided we fail: Context-driven perception of ambiguous visual stimuli. *Philosophical Transactions of the Royal Society of London B: Biological Sciences*, 367(1591), 932–941.
- Knapen, T., Brascamp, J., Adams, W. J., & Graf, E. W. (2009). The spatial scale of perceptual memory in ambiguous figure perception. *Journal of Vision*, 9(13), 16. doi:10.1167/9.13.16
- Knapen, T., Brascamp, J., Pearson, J., van Ee, R., & Blake, R. (2011). The role of frontal and parietal brain areas in bistable perception. *Journal of Neuroscience*, 31(28), 10293–10301.
- Knapen, T., van Ee, R., & Blake, R. (2007). Stimulus motion propels traveling waves in binocular rivalry. *PLoS ONE*, 2(1), e739. doi:10.1371/journal.pone.0000739
- Koch, C., & Braun, J. (1996). Towards the neuronal correlate of visual awareness. *Current Opinion in Neurobiology*, 6(2), 158–164.
- Koch, C., & Tsuchiya, N. (2007). Attention and consciousness: Two distinct brain processes. *Trends in Cognitive Sciences*, 11(1), 16–22.
- Kohn, H. (1960). Some personality variables associated with binocular rivalry. *Psychological Record*, 10, 9–13.
- Kreiman, G., Fried, I., & Koch, C. (2002). Single-neuron correlates of subjective vision in the human medial temporal lobe. *Proceedings of the National Academy of Sciences USA*, 99(12), 8378–8383.
- Kriegeskorte, N., Goebel, R., & Bandettini, P. (2006). Information-based functional brain mapping. *Proceedings of the National Academy of Sciences USA*, 103(10), 3863–3868.
- Krug, K., Brunskill, E., Scarna, A., Goodwin, G. M., & Parker, A. J. (2008). Perceptual switch rates with ambiguous structure-from-motion figures in bipolar disorder. *Proceedings of the Royal Society of London B: Biological Sciences*, 275(1645), 1839–1848.
- Lack, L. C. (1969). The effect of practice on binocular rivalry control. *Perception & Psychophysics*, 6(6B), 397–400.
- Lack, L. C. (1978). *Selective attention and the control of binocular rivalry*. Mouton, The Hague.
- Lamme, V. A. F. (2003). Why visual attention and awareness are different. *Trends in Cognitive Sciences*, 7(1), 12–18.
- Lansing, R. W. (1964). Electroencephalographic correlates of binocular rivalry in man. *Science*, 146(3649), 1325–1327.
- Lawwill, T., & Biersdorf, W. R. (1968). Binocular rivalry and visual evoked responses. *Investigative Ophthalmology*, 7(4), 378–385.

- Lee, S.-H., Blake, R., & Heeger, D. J. (2005). Traveling waves of activity in primary visual cortex during binocular rivalry. *Nature Neuroscience*, 8(1), 22–23.
- Lee, S.-H., Blake, R., & Heeger, D. J. (2007). Hierarchy of cortical responses underlying binocular rivalry. *Nature Neuroscience*, 10(8), 1048–1054.
- Lehky, S. R. (1988). An astable multivibrator model of binocular rivalry. *Perception*, 17(2), 215–228.
- Leopold, D. A., & Logothetis, N. K. (1996). Activity changes in early visual cortex reflect monkeys' percepts during binocular rivalry. *Nature*, 379(6565), 549–553.
- Leopold, D. A., & Logothetis, N. K. (1999). Multistable phenomena: Changing views in perception. *Trends in Cognitive Sciences*, 3(7), 254–264.
- Leopold, D. A., Wilke, M., Maier, A., & Logothetis, N. K. (2002). Stable perception of visually ambiguous patterns. *Nature Neuroscience*, 5(6), 605–609.
- Levelt, W. J. M. (1965). On binocular rivalry. (Doctoral dissertation, University of Leiden, 1965).
- Li, Y., van Hooser, S. D., Mazurek, M., White, L. E., & Fitzpatrick, D. (2008). Experience with moving visual stimuli drives the early development of cortical direction selectivity. *Nature*, 456(7224), 952–956.
- Lin, Z., & He, S. (2008). Seeing the invisible: The scope and limits of unconscious processing in binocular rivalry. *Progress in Neurobiology*, 87(4), 195–211.
- Livingstone, M. S. (1996). Differences between stereopsis, interocular correlation and binocularity. *Vision Research*, 36(8), 1127–1140.
- LoSciuto, L. A., & Hartley, E. L. (1963). Religious affiliation and open-mindedness in binocular resolution. *Perceptual and Motor Skills*, 17(2), 427–430.
- Logothetis, N. K. (1998). Single units and conscious vision. *Philosophical Transactions of the Royal Society of London B: Biological Sciences*, 353(1377), 1801–1818.
- Logothetis, N. K. (1999). Vision: A window on consciousness. *Scientific American*, 281(5), 69–75.
- Logothetis, N. K. (2003). The underpinnings of the BOLD functional magnetic resonance imaging signal. *Journal of Neuroscience*, 23(10), 3963–3971.
- Logothetis, N. K. (2008). What we can and what we cannot do with fMRI. *Nature*, 453(7197), 869–878.
- Logothetis, N. K., Leopold, D. A., & Sheinberg, D. L. (1996). What is rivalling during binocular rivalry? *Nature*, 380(6575), 621–624.
- Logothetis, N. K., Pauls, J., Augath, M. A., Trinath, T., & Oeltermann, A. (2001). Neurophysiological investigation of the basis of the fMRI signal. *Nature*, 412(6843), 150–157.
- Logothetis, N. K., & Schall, J. D. (1989). Neuronal correlates of subjective visual perception. *Science*, 245(4919), 761–763.
- Long, G. M., & Toppino, T. C. (2004). Enduring interest in perceptual ambiguity: Alternating views of reversible figures. *Psychological Bulletin*, 130(5), 748–768.
- Lunghi, C., Binda, P., & Morrone, M. C. (2010). Touch disambiguates rivalrous perception at early stages of visual analysis. *Current Biology*, 20(4), R143–R144.
- Lunghi, C., Burr, D. C., & Morrone, C. (2011). Brief periods of monocular deprivation disrupt ocular balance in human adult visual cortex. *Current Biology*, 21(14), R538–R539.
- Meenes, M. (1930). A phenomenological description of retinal rivalry. *American Journal of Psychology*, 42(2), 260–269.
- Miller, S. M. (2007). On the correlation/constitution distinction problem (and other hard problems) in the scientific study of consciousness. *Acta Neuropsychiatrica*, 19(3), 159–176.
- Miller, S. M., Gynther, B. D., Heslop, K. R., Liu, G. B., Mitchell, P. B., Ngo, T. T. et al. (2003). Slow binocular rivalry in bipolar disorder. *Psychological Medicine*, 33(4), 683–692.

- Miller, S. M., Hansell, N. K., Ngo, T. T., Liu, G. B., Pettigrew, J. D., Martin, N. G. et al. (2010). Genetic contribution to individual variation in binocular rivalry rate. *Proceedings of the National Academy of Sciences USA*, 107(6), 2664–2668.
- Miller, S. M., Ngo, T. T., & van Swinderen, B. (2012). Attentional switching in humans and flies: Rivalry in large and miniature brains. *Frontiers in Human Neuroscience*, 5, 188. doi: 10.3389/fnhum.2011.00188
- Mueller, T. J. (1990). A physiological model of binocular rivalry. *Visual Neurosciences*, 4(1), 63–73.
- Naber, M., Carter, O. L., & Verstraten, F. A. J. (2009). Suppression wave dynamics: Visual field anisotropies and inducer strength. *Vision Research*, 49(14), 1805–1813.
- Noest, A. J., van Ee, R., Nijs, M. M., & van Wezel, R. J. A. (2007). Percept-choice sequences driven by interrupted ambiguous stimuli: A low-level neural model. *Journal of Vision*, 7(8), 10. doi: 10.1167/7.8.10
- Ooi, T. L., & He, Z. J. (2003). A distributed intercortical processing of binocular rivalry: Psycho-physical evidence. *Perception*, 32(2), 155–166.
- O'Shea, R. P., & Crassini, B. (1984). Binocular rivalry occurs without simultaneous presentation of rival stimuli. *Perception & Psychophysics*, 36(3), 266–276.
- Paffen, C. L. E., Naber, M., & Verstraten, F. A. J. (2008). The spatial origin of a perceptual transition in binocular rivalry. *PLoS ONE*, 3(6), e2311. doi: 10.1371/journal.pone.0002311
- Pastukhov, A., & Braun, J. (2008). A short-term memory of multi-stable perception. *Journal of Vision*, 8(13), 7. doi: 10.1167/8.13.7
- Pearson, J., & Brascamp, J. W. (2008). Sensory memory for ambiguous vision. *Trends in Cognitive Sciences*, 12(9), 334–341.
- Pettigrew, J. D., & Miller, S. M. (1998). A “sticky” interhemispheric switch in bipolar disorder? *Proceedings of the Royal Society of London B: Biological Sciences*, 265(1411), 2141–2148.
- Poldrack, R. A. (2012). The future of fMRI in cognitive neuroscience. *Neuroimage*, 62(2), 1216–1220.
- Polonsky, A., Blake, R., Braun, J., & Heeger, D. J. (2000). Neuronal activity in human primary visual cortex correlates with perception during binocular rivalry. *Nature Neuroscience*, 3(11), 1153–1159.
- Ramsey, J. D., Hanson, S. J., Hanson, C., Halchenko, Y. O., Poldrack, R. A., & Glymour, C. (2010). Six problems for causal inference from fMRI. *Neuroimage*, 49(2), 1545–1558.
- Ritter, P., & Villringer, A. (2006). Simultaneous EEG-fMRI. *Neuroscience & Biobehavioral Reviews*, 30(6), 823–838.
- Roberts, T. F., Tschida, K. A., Klein, M. E., & Mooney, R. (2010). Rapid spine stabilization and synaptic enhancement at the onset of behavioural learning. *Nature*, 463(7283), 948–952.
- Salzman, C., Murasugi, C., Britten, K. H., & Newsome, W. T. (1992). Microstimulation in visual area MT: Effects on direction discrimination performance. *Journal of Neuroscience*, 12(6), 2331–2355.
- Seely, J., & Chow, C. C. (2011). The role of mutual inhibition in binocular rivalry. *Journal of Neurophysiology*, 106(5), 2136–2150.
- Sengpiel, F., Freeman, T. C. B., Bonhoeffer, T., & Blakemore, C. (2001). On the relationship between interocular suppression in the primary visual cortex and binocular rivalry. *Brain and Mind*, 2, 39–54.
- Shannon, R. W., Patrick, C. J., Jiang, Y., Bernat, E., & He, S. (2011). Genes contribute to the switching dynamics of bistable perception. *Journal of Vision*, 11(3), 8. doi: 10.1167/11.3.8

- Sobel, K. V., & Blake, R. (2002). How context influences predominance during binocular rivalry. *Perception*, 31(7), 813–824.
- Stollenwerk, L., & Bode, M. (2003). Lateral neural model of binocular rivalry. *Neural Computation*, 15(12), 2863–2882.
- Stosiek, C., Garaschuk, O., Holthoff, K., & Konnerth, A. (2003). In vivo two-photon calcium imaging of neuronal networks. *Proceedings of the National Academy of Sciences USA*, 100(12), 7319–7324.
- Stuit, S. M., Verstraten, F. A. J., & Paffen, C. L. E. (2010). Saliency in a suppressed image affects the spatial origin of perceptual alternations during binocular rivalry. *Vision Research*, 50(19), 1913–1921.
- Suzuki, S., & Grabowecky, M. (2007). Long-term speeding in perceptual switches mediated by attention-dependent plasticity in cortical visual processing. *Neuron*, 56(4), 741–753.
- Svoboda, K., & Yasuda, R. (2006). Principles of two-photon excitation microscopy and its applications to neuroscience. *Neuron*, 50(6), 823–839.
- Tong, F., Meng, M., & Blake, R. (2006). Neural bases of binocular rivalry. *Trends in Cognitive Sciences*, 10(11), 502–511.
- Tong, F., Nakayama, K., Vaughan, J., & Kanwisher, N. (1998). Binocular rivalry and visual awareness in human extrastriate cortex. *Neuron*, 21(4), 753–759.
- Treisman, A. (1962). Binocular rivalry and stereoscopic depth perception. *Quarterly Journal of Experimental Psychology*, 14(1), 23–37.
- Tsuchiya, N., & Koch, C. (2005). Continuous flash suppression reduces negative afterimages. *Nature Neuroscience*, 8(8), 1096–1101.
- van Boxtel, J. J. A., Alais, D., Erkelens, C. J., & van Ee, R. (2008). The role of temporally coarse form processing during binocular rivalry. *PLoS ONE*, 3(1), e1429. doi:10.1371/journal.pone.0001429
- van Boxtel, J. J. A., Knapen, T., Erkelens, C. J., & van Ee, R. (2008). Removal of monocular interactions equates rivalry behavior for monocular, binocular, and stimulus rivalries. *Journal of Vision*, 8(15), 13. doi:10.1167/8.15.13
- van Boxtel, J. J. A., & Koch, C. (2012). Visual rivalry without spatial conflict. *Psychological Science*, 23(4), 410–418.
- van Boxtel, J. J. A., Tsuchiya, N., & Koch, C. (2010). Opposing effects of attention and consciousness on afterimages. *Proceedings of the National Academy of Sciences USA*, 107(19), 8883–8888.
- van Ee, R. (2005). Dynamics of perceptual bi-stability for stereoscopic slant rivalry and a comparison with grating, house-face, and Necker cube rivalry. *Vision Research*, 45(1), 29–40.
- van Ee, R. (2009). Stochastic variations in sensory awareness are driven by noisy neuronal adaptation: Evidence from serial correlations in perceptual bistability. *Journal of the Optical Society of America A: Optics, Image Science, and Vision*, 26(12), 2612–2622.
- van Ee, R. (2011). Percept-switch nucleation in binocular rivalry reveals local adaptation characteristics of early visual processing. *Journal of Vision*, 11(2), 13. doi:10.1167/11.2.13
- van Ee, R., van Boxtel, J. J. A., Parker, A. L., & Alais, D. (2009). Multisensory congruency as a mechanism for attentional control over perceptual selection. *Journal of Neuroscience*, 29(37), 11641–11649.
- Watanabe, M., Cheng, K., Murayama, Y., Ueno, K., Asamizuya, T., Tanaka, K. et al. (2011). Attention but not awareness modulates the bold signal in the human V1 during binocular suppression. *Science*, 334(6057), 829–831.

- Wen, Y., & Zhang, Q. (2009). Ensemble cortical responses to rival visual stimuli: Effect of monocular transient. *Biochemical and Biophysical Research Communications*, 380(1), 105–110.
- Wheatstone, C. (1838). Contributions to the physiology of vision. – Part the first. On some remarkable, and hitherto unobserved, phenomena of binocular vision. *Philosophical Transactions of the Royal Society of London*, 128, 371–395.
- Whittle, P. (1963). *Binocular rivalry*. (Doctoral dissertation, Cambridge University, 1963).
- Wilke, M., Logothetis, N. K., & Leopold, D. A. (2006). Local field potential reflects perceptual suppression in monkey visual cortex. *Proceedings of the National Academy of Sciences USA*, 103(46), 17507–17512.
- Wilson, H. R. (2003). Computational evidence for a rivalry hierarchy in vision. *Proceedings of the National Academy of Sciences USA*, 100(24), 14499–14503.
- Wilson, H. R. (2007). Minimal physiological conditions for binocular rivalry and rivalry memory. *Vision Research*, 47(21), 2741–2750.
- Wilson, H. R., Blake, R., & Lee, S.-H. (2001). Dynamics of travelling waves in visual perception. *Nature*, 412(6850), 907–910.
- Wolfe, J. M. (1986). Stereopsis and binocular rivalry. *Psychological Review*, 93(3), 269–282.
- Wunderlich, K., Schneider, K., & Kastner, S. (2005). Neural correlates of binocular rivalry in the human lateral geniculate nucleus. *Nature Neuroscience*, 8(11), 1595–1602.
- Yacoub, E., Shmuel, A., Logothetis, N., & Ugurbil, K. (2007). Robust detection of ocular dominance columns in humans using Hahn Spin Echo BOLD functional MRI at 7 Tesla. *Neuroimage*, 37(4), 1161–1177.
- Yang, Y., Rose, D., & Blake, R. (1992). On the variety of percepts associated with dichoptic viewing of dissimilar monocular stimuli. *Perception*, 21(1), 47–62.
- Zhou, W., Jiang, Y., He, S., & Chen, D. (2010). Olfaction modulates visual perception in binocular rivalry. *Current Biology*, 20(15), 1356–1358.

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