



Searching for the Switch: Neural Bases for Perceptual Rivalry Alternations

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Abstract. A midbrain neural basis for the perceptual oscillations of binocular rivalry is suggested on the basis of fMRI studies of rivalry and inferences from the properties of rivalry that cannot be explained from the known properties of primary visual cortical (V1) neurons. The rivalry switch is proposed to activate homologous areas of each cerebral hemisphere alternately, by means of a bistable oscillator circuit that straddles the midline of the ventral tegmentum. This bistable oscillator operates at the same slow rate that is characteristic of perceptual rivalry alternations. Whilst attempting to divert the present preoccupation with cortical mechanisms for rivalry, the new proposal integrates many cortical areas, in keeping with recent evidence that binocular rivalry involves widespread areas of the hemispheres. By linking rivalry to interhemispheric switching mechanisms in this way, the new proposal for the switch makes the prediction that binocular rivalry will be subject to high level influences such as mood and motivation. These predictions are being fulfilled, with rivalry playing an increasing role in the diagnosis and understanding of mood disorders, schizophrenia and other psychiatric conditions.

Key words: binocular rivalry, interhemispheric switch, midbrain oscillator, neural basis

Introduction

The sciences have developed in an order the reverse of what might have been expected ... first the heavens, next the earth, then animal and vegetable life, then the human body, and last of all (as yet imperfectly) the human mind. (Bertrand Russell, 1935, p. 49)

Vision is our best modality, so it is hardly surprising that Russell's outside-to-inside scientific scenario would mean that our most detailed understanding of the brain should be first in the visual domain, which occupies such a large neural territory in primates. Despite the enormous amount of detail available about the functional architecture of the visual areas, primary visual cortex in particular, I am going to present the case that it may be misguided to try to use only these details to seek an understanding of binocular rivalry: the striking perceptual alternation in the face of constant visual stimulation that still provokes investigators to ponder its relation to consciousness, centuries after its discovery.

I will begin with an explanation for my conversion to the until-recently heretical view that the phenomenon of binocular rivalry cannot be explained by the properties of primary visual cortex (V1). This heresy may be all the more surprising as I have spent the last three decades investigating the functional properties of V1. In the past, I was involved in a number of controversies that centered on the question whether V1 could mediate certain sophisticated aspects of visual processing. For example, I defended the thesis that binocular disparity detection is accomplished at this very early stage of visual processing (Barlow *et al.*, 1967; Pettigrew *et al.*, 1968). This was a minority position at first, and took decades before it was generally accepted (see review in Bishop and Pettigrew, 1986). Later I defended other heterodox positions concerned with the extent of V1's developmental plasticity (e.g. Pettigrew, 1978) and initiated the first experiments to test the idea that plasticity in V1 could be influenced by neuromodulators such as noradrenaline and acetylcholine (Pettigrew and Kasamatsu, 1978). Having thus successfully argued that V1 was capable of more complex analysis and synthesis than was thought possible by many at the time (e.g. binocular disparity detection, self organization of receptive field properties in early development), it is therefore somewhat ironic to find myself arguing in the reverse direction in this paper. I am going to make the case that primary visual cortex is inadequate to account for many characteristics of the well-known visual phenomenon called binocular rivalry, even though visual cortex is undoubtedly involved in the process.

As a result of writing this paper and interacting with other authors, as well as the editors, I discovered that it is not so unusual to find those with the same viewpoint, so it is perhaps an exaggeration to call it heretical. It may even be mainstream. Nevertheless, I will stick with the notion of heresy because of the intense emotion, or silence, that seems to be excited when I present the thesis that the oscillatory aspects of rivalry must originate outside V1, especially when I point to the possibility of a sub-cortical oscillator that operates on a hemispheric level.

I think we need to look beyond V1 to explain the puzzle of rivalry. This need can perhaps be brought into focus by the following consideration: – During binocular rivalry there is a striking alternation in perception that occurs in spite of a steadily invariant stimulus. Since the sensory stimulation is constant, is it not a problematical exercise to confine ones' search for the basis of the perceptual oscillation to the early stimulus stream within the structure of the sensory processor itself, where no changes are taking place? Since the period of the oscillation is robust, yet varies considerably between individuals, without any obvious concomitant variation in early visual function, is the early visual pathway the place to look for the source of the oscillation? Some individuals with perfectly normal vision do not show rivalry at all under conditions where 95% of the population experience clear alternation. As I will show in this paper, these and many other features of the oscillation cannot be explained in terms of the physiology of V1, but have acceptable explanations if the essential oscillatory aspect of rivalry originates elsewhere in the brain.

The plan of this essay is as follows: I will first detail the 11 or so reasons that I cannot ascribe binocular rivalry entirely to primary visual cortical physiology. Incidentally, many of these reasons were also responsible for my recently being drawn to study rivalry. These include, in particular, the striking effects upon rivalry observed when one manipulates a cerebral hemisphere on one side (Miller *et al.*, 2000). Next I will set out the properties that define the neural oscillator that is driving rivalry and that would therefore constrain its identity. Along with some fMRI experiments and inferences, these constraints suggest that the rivalry oscillator is located, not in the visual cortex, but far away in the sub-cortical neuraxis where it straddles the midline and can act as a bistable oscillator for both hemispheres. I will also discuss our prediction, that split-brain subjects will show rivalry, in terms of the special properties of bistable brainstem oscillators. Then I will describe some recent experiments on binocular rivalry where the effects originate in the *hindbrain*, even farther from primary visual cortex. By drawing attention to the multiplicity of oscillators and their interconnections in the brainstem, these last experiments serve to illustrate the valuable role that the study of binocular rivalry, and the perceptual rivalries in general, may play in illuminating problematical issues of brain function such as mood and consciousness. Finally, I conclude with the suggestion that binocular rivalry is closely linked to all perceptual rivalries and that these are not merely intellectual curiosities for parlour games and psychology textbooks. I will show that a new illusion, Bonneh's motion-induced blindness, has unsuspected properties that link it to perceptual rivalry and thus brings rivalry closer to the realm of normal perception. The findings with the Bonneh illusion suggest that the cyclicity of the rivalries may reflect more routine aspects of perception's neural basis that deal with the ever-present ambiguity of sensory input, not just the vacillations of a "confused adolescent" (Blake, 2001).

Reasons Why V1 Cannot Account for All the Features of Binocular Rivalry

1. V1 NEURONS CONTRADICT THE MONKEY'S PERCEPTION DURING BINOCULAR RIVALRY

The results of these experiments in behaving monkeys are compelling (Leopold & Logothetis, 1996). The key observation involves the behavior of an orientation selective V1 neuron while a trained monkey reports his/her perceptual alternations during binocular rivalry to Horizontal/Vertical orthogonal gratings. For the majority of such neurons in V1, there is no relation between the pattern of firing and the monkey's signaled percept. For example, while the monkey reports a perceptual switch from horizontal to vertical, a V1 neuron selectively responsive to horizontal, unaffected by the switch, goes on firing vigorously to the horizontal stimulus presented to one eye, despite the monkey's report of its absence. In other words, orientation-selective V1 neurons, with their legendary reliability and specificity, strongly contradict the monkey's perception during rivalry. This is not absence of evidence, as argued by those who have tried to reconcile this evidence with a V1

locus of rivalry. Instead, the behavior of most V1 neurons flatly contradicts the rivalry percept and cannot therefore be reasonably argued to be its neural basis.

One has to record from visual areas much further forward in the monkey's visual pathway (e.g. IT cortex), before one finds significant numbers of neurons that follow the monkey's perceptual changes (Sheinberg & Logothetis, 1997).

I am aware of at least two rejoinders to this result by those defending V1 as the site of rivalry: (i) that spike discharges may have become unsynchronized at the perceptual changeover, despite the continuous vigorous firing of the neuron (Munk *et al.*, 1996); (ii) the very small fraction of V1 neurons that show appropriate behavior may be responsible for the percept (Polonsky *et al.*, 2000).

The first defense requires that we reject the evidence of stimulus drive provided by a vigorous spike discharge, in favor of a new criterion, viz., synchrony between the spike trains of different neurons. Accepting this new criterion as the sole arbiter would fly in the face of the growing evidence from many single unit recording studies in behaving primates (e.g. Bair *et al.*, 2001) that spike discharges signify stimulus strength. However we may feel about the debate on the role of synchrony in binding (Munk *et al.*, 1996), or the likelihood that the anesthetized cat is actually experiencing some form of binocular rivalry, it would seem rash to overturn the positive evidence provided by spike discharges in favor of a more hypothetical possibility that involved measures of synchrony. My own opinion is that the principle of spike synchrony may contribute to the overall pattern of neuronal activity in rivalry by a top-down process (see below), but that we cannot allow this to overturn the evidence provided by vigorous spike discharges if these argue in the opposite direction.

The second defense implies that we should ignore the majority of V1 neurons when making statements about rivalry. If there are so few V1 neurons with the appropriate behavior it is hard to believe that this is a key aspect of V1 function. When appeals have been made in the past to minority classes of neurons in V1, they could usually be related quantitatively to other V1 neurons with similar properties. For example, the most finely-tuned V1 orientation-selective neuron can be related exactly to the population of such tuned neurons (Blasdel *et al.*, 1977). In the present case the minority would have to have qualitatively different properties, completely distinct from the majority that fail to show any connection between percept and firing pattern. And one would still have to deal with the fact that a large number of neurons contradicted the percept. An alternative possibility is that this minority of V1 neurons reflects top-down effects, perhaps via the mechanism of synchrony that has been shown in cat V1 possibly to identify the "active" perceptual alternative. In this way V1 could contribute to the process of rivalry without being the generator of the oscillation.

The demonstration that binocular neurons may show bistable behavior in V1 does not automatically lead to any conclusions about perception in a behaving animal. For this reason I put more weight on the V1 data on rivalry in the behaving monkey than that obtained from anesthetized cats where bistable behavior of

neurons has been reported that might be construed as related to rivalry, but where we have no other evidence about the cat's perceptual state (Sengpiel *et al.*, 1995).

2. THE PERIOD OF THE BINOCULAR RIVALRY CYCLE IS TOO SLOW FOR A V1 PROCESS

The “attentional spotlight” in V1 operates at 30–40 Hz, as measured in serial search tasks (Wolfe *et al.*, 2000; Vidyasagar, 1998). This spotlight moves randomly about at this astonishing speed with no memory of previous locations. Since attention is unitary and the “spot” can therefore be thought of as lighting up only one site at a time, one can see that both visual cortices will be visited randomly but roughly in turn. The spotlight will thus, on average, alternate between V1 in each hemisphere. The attentional spotlight will therefore act as an interhemispheric switch. This foreshadows my discussion about such switches later. If there were strict alternation between V1 on each side, the interhemispheric switch rate would be around 30 Hz. On the whole, binocular rivalry is much slower than this, by an order of magnitude: around 0.5 Hz, depending on some aspects of the stimulus, but never faster than a few Hz.

If V1's attentional spotlight is capable of switching attention between possible sites at 30–40 Hz and normally operates at this speed, why is binocular rivalry so slow if the oscillation originates in V1? Many agree that binocular rivalry is a process like attention which highlights one out of more than one possible alternative, so it therefore surprising that visual cortex would stumble along so slowly on one attentional task when it was so speedy on another. This question is highlighted by the results described below of schizophrenic subjects who can resolve a 30 Hz dichoptic oscillation, but whose phenomenal experience is more than an order of magnitude slower (White *et al.*, 2001). One can have little doubt that V1 is responsible for this extraordinary temporal resolution, which is exactly as one would predict from my analogy to the speed of the attentional serial search spotlight in V1. So one can safely conclude that the much slower perceptual alternation (~1 Hz) that these subjects experience must be originating in some other location that is nevertheless receiving input from V1 but is unable to follow V1's high speed oscillation (30–40 Hz).

It is noteworthy that recent models of binocular rivalry that successfully predict the slow rivalry rate, its robustness and its considerable inter-individual variation, derive these features *from outside the visual system* (Laing *et al.*, 2001).

3. ADAPTATION AFTER-EFFECTS CONFIRM EXTRA-V1 LOCUS OF RIVALRY

A long tradition of experiments with visual after-effects has been able to dissect the levels of the visual pathway at which many psychophysical phenomena are likely to occur. For example, the tilt after-effect is widely believed to occur at the level of orientation-selective neurons in V1. Accordingly, by combining binocular

rivalry and tilt-after-effect in the same experiment, one can decide at what level binocular rivalry takes place in relation to the tilt after-effect. Because of the complexity of the extrastriate visual pathways, it is not possible to be too precise about the extra-striate locus of rivalry suggested from these experiments. There are, moreover, many experiments that have been carried out in this area that are not all in agreement. Nevertheless, it seems clear is that there are many experiments indicating that rivalry takes place beyond the level where the tilt after-effect resides. In other words, according to these experiments binocular rivalry takes place, not in V1, but somewhere beyond that early stage of processing (van der Zwan and Wenderoth, 1994). A similar conclusion is suggested by the results of experiments with the motion after-effect combined with binocular rivalry (van der Zwan, 1993). A similar experiment with color yielded similar results.

There are many studies like this that have attempted to place binocular rivalry at a particular stage in the hierarchy of visual processing, with support being gained in different studies for both the “early”, and “late”, processing points of view. Note that while evidence in support of a “bottom up process” might still be compatible with a locus of rivalry outside V1, the opposite kind of evidence, for “top down processing” cannot be reconciled with a V1 locus and mandates one to look beyond V1. Another example of evidence that contradicts a “bottom-up process” is Howard’s experiment with virtual disparity where binocular rivalry is shown to be at a high level beyond the simple disparity detection that begins in V1 (Howard, 1979).

The conflicting nature of these studies might be resolved with a new paradigm that goes beyond a simple linear progression from V1 to “higher” visual areas, with binocular rivalry located at some controversial point along it. Instead one can imagine an attentional switch that utilizes information from all cortical regions which can phase shift its own intrinsic rhythmicity. In such a paradigm, such as the interhemispheric switch model that I have put forward (Pettigrew and Miller, 1998), neither “early”/“bottom up”, nor “late”/“top down”, points of view are entirely appropriate since the model can have elements of both points of view. Moreover, such complex involvement of many cortical areas, all integrated by a brainstem switch, would probably involve considerable inter-individual variations in the conditions, a prediction that has been confirmed in my own laboratory where we are struck by the enormous variation in individual responses to an identical rivalry display.

4. HEMISPHERIC STIMULATION AND DISRUPTION EXPERIMENTS

An interhemispheric switching model for perceptual rivalry has been proposed that has a large number of testable features (Pettigrew and Miller, 1998). One series of predictions is that manipulations at the level of the cerebral hemispheres would produce concomitant changes in rivalry. This series of experiments has been reported elsewhere (Miller *et al.*, 2000). The main point is that unihemispheric

stimulation by caloric vestibular stimulation, and unihemispheric disruption by single-pulse transcranial magnetic stimulation, both cause striking changes in the pattern of binocular rivalry, with complete reversals of the pattern of predominance produced by hemispheric activation or disruption. These changes are in a direction consistent with the thesis that the alternation between the rivaling perceptual alternatives is the result of attention being switched between hemispheres. For example, in binocular rivalry where horizontal is presented to the right eye and vertical grating to the left, most subjects report a greatly increased time spent seeing horizontal following activation of the left hemisphere. This polarity fits the interpretation that the left hemisphere “prefers” the horizontal pattern (A more accurate way of saying this might be that there are biases in the circuitry of the left hemisphere that would result in preferential activity in favour of the representation of horizontal when faced with the *exclusive or* operation of horizontal vs. vertical). There may be two effects that contribute additively to this hemispheric assignment: (i) horizontal presented to the right eye is more likely to lead to horizontal activation of the left hemisphere because of the generally-recognized increase in effectiveness of contralateral over ipsilateral stimuli in the visual system; (ii) horizontal contours may perhaps be favored by the left hemisphere because of that hemisphere’s recognized predisposition for language execution, a preference which may be linked, in turn, to the much greater number of horizontal over vertical human scripts.

This left hemisphere/horizontal grating assignment by most subjects is also supported by TMS which disrupts the perception of horizontal but not vertical when delivered to the left hemisphere at the appropriate phase of the rivalry cycle (Miller *et al.*, 2000). The occasional subjects with reversed assignment had increased time spent seeing vertical after left hemisphere activation and thus provide a control for the possibility that any lingering residual effects of the caloric stimulation on eye movement (the tests were always delayed until after nystagmus had ceased) would differentially reduce the vertical grating’s visibility.

When oblique stimuli are used for binocular rivalry, the results of unihemispheric activation or disruption are comparable to those seen with horizontal/vertical rivalry, with marked changes in predominance of one alternative percept over the other. This result with obliques supports the interpretation that eye movements cannot be used to explain the change in bias resulting from unihemispheric stimulation, like the occasional subjects who increase their preference for vertical gratings, rather than horizontal gratings. In the oblique case however, it is never possible to predict an individual result in advance. There appears to be random individual assignment of alternative percepts to hemisphere. After left hemisphere activation, roughly half of our sample of 28 subjects increased the time in binocular rivalry seeing left-leaning obliques and half increased time spent seeing right-leaning obliques. This random assignment of hemisphere to perceptual alternative was also observed with another kind of perceptual rivalry, the Necker cube. Random assignment of alternative percept to hemisphere may help explain

the absence of evidence for hemispheric switching in scanning studies with perceptual rivalry. Since most fMRI studies pool across subjects, hemispheric effects will tend to cancel out as a result of the random assignment of many rivalrous alternatives (with the notable exception of horizontal and vertical).

One weakness of these experiments, in terms of the interhemispheric switch model, was a failure to show reciprocal and consistent changes as a result of manipulations of the right hemisphere. Recent work has solved some of the technical problems associated with manipulations of the right hemisphere and shown that it is possible to obtain exactly reciprocal effects upon rivalry by manipulations of right and left hemisphere. There were two related problems associated with the right hemisphere: viz., (i) an apparent greater temporal resolution or higher speed of oscillation; and (ii) an area in right frontal cortex that is very active during the ambiguous stimulation of rivalry (Lumer *et al.*, 1999) and might be thought of as providing the command "Dither!" to match the complementary command from the homologous frontal region on the left side, "Choose!" Since caloric stimulation of the right hemisphere acts for a long time and, more importantly, would continuously activate the right frontal "dither" area, it is not surprising that this is a problematical maneuver in manipulations of rivalry. In contrast, TMS can obviate these problems with time, particularly if the TMS pulse is preprogrammed on the basis of a very regular rivalry cycle so that some TMS pulses occur exactly at the phase-shift, without the double delay from phase-shift to perception and from perception to button press. By using a very regular rivalry cycle and preprogrammed TMS pulses instead of pulses triggered at the subject's button press signaling a phase-shift, equal and opposite effects are seen in both hemispheres.

A note on hemispheres and hemifields is appropriate here. Perhaps the most frequent question that arises about the unihemispheric activation and disruption experiments and the interhemispheric switching model of rivalry concerns how one can rival between hemifields when binocular rivalry involves conflicting stimuli on corresponding retinal loci. One referee even admitted to ignoring this corpus of work, involving dozens of subjects subjected to state-of-the-art hemispheric manipulations, because of difficulties in understanding how both hemispheres could be involved in a phenomenon like binocular rivalry that required stimulation of corresponding points on each retina!

The problem here is the conception, from text book diagrams of homonymous hemianopias, that each cortical hemisphere represents only the contralateral hemifield, with a razor-sharp decussation between hemifields. In fact, because of the phenomenon of nasotemporal division (Balkemore, 1969) there is considerable binocular overlap, even at the earliest level in V1, where a region about 1 deg. wide, enough to straddle the fovea, is represented bilaterally (Stone, 1966, 1973). So, even in a split brain subject with all interhemispheric communication cut, there will still be binocular overlap at the fovea used predominantly for our visual inspection (it takes considerable training for subjects to report on rivalry targets off the fovea). In normal subjects with the corpus callosum intact, this overlap increases

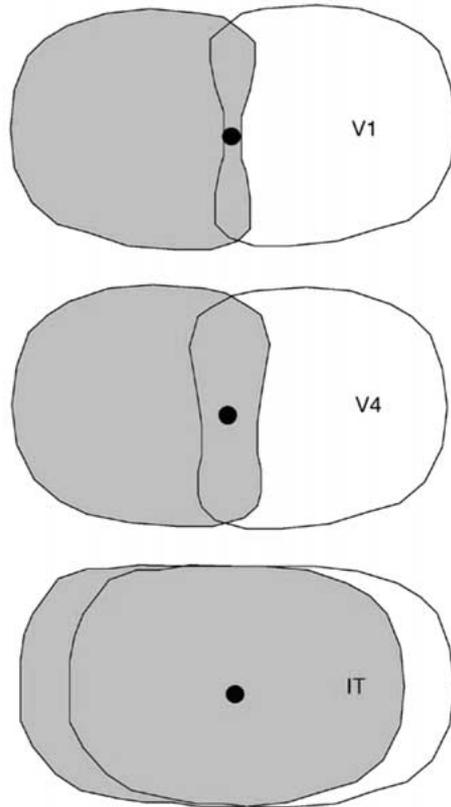


Figure 1. Nasotemporal Overlap of Hemifields at Three Levels in the Visual Pathway: In primary visual cortex the decussation of retinal ganglion cells passes through the edge of the fovea (black circle), rather than through its center, thus giving a region about 1 deg. wide that is represented in both hemispheres. Nasotemporal overlap increases at subsequent levels in the visual hierarchy because of callosal connections, until it is around 5 deg. in V4 and virtually the whole of the binocular visual field in inferotemporal cortex (IT). Note that although the edge of the decussation is sharp, giving rise to a homonymous hemianopia if one hemisphere is lesioned, there is sufficient overlap between each edge of the decussation that foveal stimuli are projected to both hemispheres. In the experiments on binocular rivalry described here, the rivaling targets were small and foveal and thus activated both hemispheres, even in V1.

at each level in the visual hierarchy, For example, it is around 5 deg. in area MT and includes virtually the whole of the binocular visual field in area IT (Gross *et al.*, 1993). These overlapping projections across the midline are topographically orderly in subjects with normal binocular vision, so that rivalrous stimuli presented just to the left of the midline will stimulate corresponding retinal locations, and excite rivalry, in both the left hemisphere (perhaps surprisingly, as a result of nasotemporal overlap) as well as the right (as expected from textbook anatomy). In experiments in my laboratory, we use a small foveal target that we know, from

the anatomy I have just described, will be represented in both hemispheres, even if one is considering only V1, the earliest site where rivalry is currently being argued. Even larger targets that extend beyond the fovea will be bilaterally represented in “higher” visual cortical areas.

This kind of thinking comes easily to me after years of working with the intricacies of the owl’s visual pathway, which organizes superimposed cortical maps of both eyes by complicated, but beautifully ordered, midline-crossing connections (Pettigrew, 1986). This small excursion into the neuroanatomy of binocular overlap illustrates that cerebral hemispheres are not equivalent to hemifields and shows how important it is to be flexible, and not too rigidly concrete, in thinking if one is to understand the global effects on rivalry. More anterior locations appear to have complementary representations in the two hemispheres arranged in dyads that are even more metaphorical than the connections I have just described for uniting the visual fields of both eyes (e.g. go vs stop; choose vs dither; deny vs. accept; group vs ungroup etc.).

5. CIRCADIAN, MOOD AND HIGH-ORDER EFFECTS ON BINOCULAR RIVALRY

It will not be possible to review this large body of data completely here. Its message is that binocular rivalry can be influenced in ways that even the most creative individuals will have difficulty in relating back to the properties of V1. Take the experiment of Breese (1899) that examined motor output and binocular rivalry with red and green targets. If the subject was asked to clench his/her fists, or otherwise engage the motor system, the predominance (proportion of time spent seeing one alternative during rivalry) of red increases dramatically (at the expense of green)! This is a puzzling result if one clings to V1 interpretations of rivalry, if for no other reason than the lack of any obvious connection with motor functions, let alone the further problem of the color assignment. On the other hand, this result fits readily into a more global framework for rivalry, since we know that the clenching will tend to activate the left hemisphere. There are hints from many sources that the left hemisphere may innately prefer red over green, just as it may prefer horizontal over vertical. I have already discussed the language-horizontal connection. The connection between the left hemisphere and red is also indirect, but is supported by a remarkable convergence of observations from comparative neurology, which has shown appropriate asymmetries between both the hemispheres and even between the eyes (cone photoreceptor differences between the eyes of birds are consistent with a greater sensitivity to movement and to red on the part of the right eye (Hart, 2000)) and from introspective studies over the millennia in three great religions that have all converged in the same direction on an association between action, heat, red, horizontal, far etc and the right side of the body (i.e. the left cerebral hemisphere, given the decussation between cerebral hemisphere and output) compared with inaction, cold, green, vertical, near etc and the left side/right hemisphere respectively (see www.uq.edu.au/nig/jack/jack.html for an illustration of this from

Parfionovitch *et al.*, 1992). In other words, the Breese result fits an interhemispheric switch context better than a V1 context.

This hemispheric interpretation of the Breese two-color experiment based on comparative inference is supported by Marina Pavloskaya, who is working on perceptual rivalry in patients with parietal lesions. When the right eye is shown a red horizontal grating and the left eye is shown a vertical green grating, the patients all report a constantly present horizontal red grating, a result consistent both with a role for hemispheric switching in rivalry and with the assignment of red/horizontal to the left hemisphere.

Similarly, one can show mood changes that are correlated strongly with binocular rivalry, with right hemisphere predominance associated with negative emotions such as fear, depression and grief, while left hemisphere predominance is associated with confidence, well-being and euphoria. The pattern of rivalry can reveal an underlying mood disturbance, with for example, negative emotions being associated with greater time seeing vertical and therefore greater presumed activity of the right hemisphere.

The predominance ratio of binocular rivalry also varies on a circadian schedule. If one wakes a sleeper in the hours before dawn, there is a strong preponderance for vertical in H/V rivalry, indicating a right hemisphere bias that may be consonant with the right hemisphere bias thought to accompany the increased REM episodes just before waking. This circadian variation of the predominance ratio of binocular rivalry continues throughout the day and can be correlated with mood changes. In rapid cycling mood disorder, some subjects show a striking variation in the predominance ratio over a time scale of minutes that is well-correlated with mood, as short periods of vertical (presumed right hemisphere) predominance are accompanied by bursts of negative emotion such as anxiety, fear or depression.

Many of these results may have been ignored because of the difficulties of explaining them in the current paradigm of V1 locus for rivalry. Taken together they support the need to venture further afield than V1. It is possible to imagine that release of a neuromodulator, such as serotonin and norepinephrine, into visual cortex might produce all these mood- and state-related changes in rivalry. In this way one could avoid the need to go outside V1. The problem with this explanation is that there is absolutely no evidence to suggest that neuromodulators would have any such specific, eye dominance-reversing effects on V1, despite studies that have examined the effects of serotonin and norepinephrine in V1. This literature on the role of amine modulators in visual is extensive and still growing. As I pointed out in the introduction, I also contributed extensively to it (see for example Kasamatsu *et al.*, 1999), but there is no evidence within it that application of monoamines can cause such dramatic changes in predominance as are seen on a circadian basis or as a result of unihemispheric activation.

6. MOSAICISM EXPERIMENTS

The mechanism for binocular rivalry is capable of reconstructing a complete perceptual representation using constituent fragments derived separately from each eye's image. This was first shown by Diaz-Caneja (1925) and there have been a number of confirmations (Ngo *et al.*, 2000) and elaborations since (Kovacs *et al.*, 1996). I find it hard to imagine how V1 could organize this kind of reconstruction. The early processing that characterizes V1 has not been described to involve the use of the complex forms that result from these reconstructions. Moreover, I know of no mechanism in V1 that could select the appropriate fragments from each eye to take part in the reconstruction. These experiments would only be compatible with V1 processing if one erected an elaborate top-down scheme to bring about the reconstruction. Top-down arrangements to explain rivalry are common and I have suggested this kind of mechanism myself elsewhere in this paper to help account for the apparent involvement of V1 in aspects of rivalry that also seem to require input from higher-order processes. But then one would still have to explain why it was not the higher executive function that was responsible for the rivalry rather than V1!

7. EYE SWAPPING EXPERIMENTS: V1 CONTRADICTS PERCEPTUAL ALTERNATIONS

Liquid crystal shutters enable one to exchange the conflicting images presented to each eye at any frequency while maintaining rivalrous stimulation on each retina. At frequencies between 1 Hz and 10 Hz we know that V1 neurons will be responsive to the changes produced by every swap, yet the subject's perception alternates at its usual, much slower, pace, unaffected by the swaps (Logothetis and Leopold, 1999; White, 2001). This result is exactly what would be predicted from the results of recording from V1 neurons during rivalry. The experiment should have added power in the eyes of those skeptical of the monkey single unit data (such as Polonsky *et al.*, 2000, who raise the monkey-hominid divide) because it relies directly on the report of a human subject. I have no doubts that human V1 neurons will be responding as vigorously as monkey V1 to these rapid swaps, so one must venture beyond V1 to account for the much slower perceptual alternations.

Some subjects rival slowly when the rivalrous stimuli are alternated at even more rapid rates between the eyes. The gradual decrease in the rate of their perceptual alternations as the rate of eye swapping increases suggests a form of aliasing. Under these conditions some schizophrenic subjects can "see" rivalrous alternations at around 1 Hz when the rate of eye swapping is as high as 30 Hz! (White *et al.*, 2001). These results again emphasize the high speed of some of the underlying visual events that we presume must be in V1, compared with the much slower speed of the perceptual alternations.

As with Point 2 raised already, these observations involve a direct contradiction between the high temporal frequency of modulated activity of V1 neurons and the

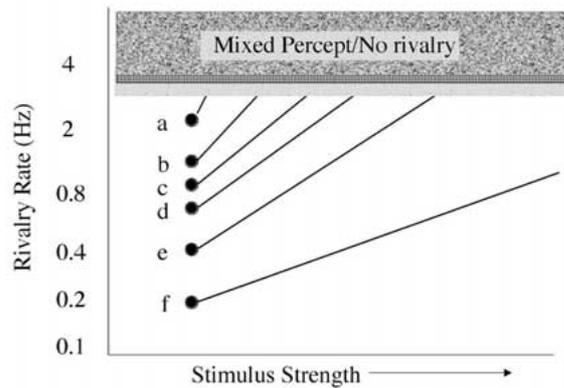


Figure 2. Effect of Stimulus Strength on Binocular Rivalry Rate: Increasing stimulus strength, (by increasing contrast, spatial frequency, velocity), leads to an increase in rivalry rate. This effect is least in individuals with the slowest rivalry rate (example f), who have a relatively shallow slope on the curve relating stimulus strength to rivalry rate. At very high rivalry rates, perception changes from rivalrous alternations to a continuous mixed percept (such as grid or crosshatch in this case where the rivalrous stimuli were horizontal and vertical gratings). Fast switchers (e.g., example a) show the steepest increase in rate as a function of strength. Although there is individual variation in the transition from rivalry to mixed percept, there is a broad ceiling at around 4 Hz that suggests that there is a fusional frequency limit for rivalry in this range.

low temporal frequency of perceptual alternation. We are not merely dealing with the absence of evidence for alternation from V1 at the subject's perceived rivalry rate. Rather, the high speed of the presumed neuronal alternations in V1 directly contradicts the percept and so can hardly be used as the percept's basis.

8. BRAIN SCANNING STUDIES

There have been a number of fMRI scanning studies of binocular rivalry and perceptual rivalry. Very few of these studies have been able to preserve phase information because of the relatively rapid phase shifts of rivalry compared with the usual much longer block durations and the sluggish hemodynamic response in fMRI. One might have thought that the large number of perceptual phase shifts signaled by the subject would be sufficient to collate the scanned data from the brain, but the fMRI BOLD signal is slow, taking many seconds compared with the usually shorter duration of the phase changes. Results are often pooled from different subjects and from both hemispheres that I would predict to have opposite hemispheric patterns of activation during rivalry. This would lead to cancellation of some significant effects such as interhemispheric switching and would caution those who wanted to draw conclusions about the absence of evidence of brain effects of rivalry. Nevertheless, all these studies are remarkable for the widespread activation outside V1. Both frontal and parietal areas are active during the

perceptual switch, whereas the activation of V1 during the perceptual switches of rivalry is quite comparable to that observed with similar visual patterns, but not presented in a rivalrous fashion. Perhaps the clearest fMRI study involved Nancy Kanwisher's detailed knowledge of the face area in the fusiform gyrus (FFA) that she examined with colleagues while subjects experienced "face/place" rivalry, produced by conflicting stimulation with a face presented to one eye and a house presented to the other. In phase with the perceptual shift from face to place, they found that activation clearly alternated between FFA and the parahippocampal gyrus, where other work had shown activation by "place" (Tong *et al.*, 1999). As clear as this study is, one can question its generality to all other cases of perceptual rivalry, particularly those involving more "symmetrical" alternatives such as the two perspectives of a Necker cube or two orthogonal orientations. It seems unlikely to me that symmetrical alternative interpretations of the same kind of stimulus would be encoded, like face and place, in functionally distinct cortical areas, rather than within a single area, or between functionally equivalent cortical areas on opposite sides of the brain.

It has been claimed on the basis of fMRI studies that binocular rivalry is "resolved" in V1 (Polonsky *et al.*, 2000), but the data have not enabled me to resolve this issue in my own mind, mostly because it is difficult to see a clear relationship between the perceptual phase changes and the hemodynamic changes, but in addition because there is so much left unexplained by this simple view (*viz.* the eleven points raised here).

Two scanning studies each used "tags" to help track the progress of neuronal processing for each eye during binocular rivalry, without having any guarantee that the tracks defined by the tags were actually connected to the neuronal processing paths for rivalry. Polonsky *et al.* (2000) used a "tag" based upon a much lower contrast in one eye, which gave a readily visible fMRI signature, while Srinivasan *et al.* (1999) flickered each eye's stimulus at different rates, thus providing a readily visible signature that could be resolved in temporally-precise MEG. As ingenious as these tagging techniques are, the underlying assumption can be questioned. There are so many parallel paths for visual information to travel that one can have no certainty that the rivalry process and the "tag" will travel the same way. Indeed, increasing work suggests that the conscious aspect of rivalry is mediated by P-processes while the M-pathway may contribute to unconscious aspects of rivalry, such as the timing of the switch (Carlson and He, 2000). Whatever the outcome of these experiments on the M- and P-pathways in rivalry, this work emphasizes that it is naive to think that a single "tag" will faithfully reveal all the processes underlying rivalry. We already know, from the experiments on eye swapping described in point 7, that the subject's rivalrous perception of alternations may be at a much lower frequency than the high-speed alternations taking place in V1. If these V1 oscillations fail to reach the conscious level of rivalry, why should one expect a similarly high frequency, flickered, tag to survive to the crucial later stages of the rivalry process where one might be able to locate its oscillator?

9. A PARALLEL BETWEEN THE MECHANISMS OF ALL PERCEPTUAL RIVALRIES, INCLUDING BINOCULAR RIVALRY

There is a growing view (e.g. Andrews and Purves, 1997), shared by myself, that binocular rivalry is not just a curiosity, only to be brought out for parlor room discussion, student demonstrations and vigorous debates about its neural mechanism. In this view, ambiguity is an ever-present problem in sensory processing that may be addressed by oscillatory switching mechanisms to protect against the possibility of decision-making becoming locked into a single alternative. In this view, binocular rivalry is part of perceptual rivalry in general, albeit with special features that recommend it for study. One of these special features is the difficulty most subjects have in willing one eye's alternative to take over. Since we do not normally have separate conscious control over each eye's channel, data from binocular rivalry (a few "essential alternators" with abnormal binocular vision excepted) are very noise-free compared with those collected from other rivalrous alternations such as the Necker cube where it is easier for the subject to exercise conscious control over the perspective chosen to enter perception.

Once one takes account of this convenient aspect of binocular rivalry, I am not sure that it is very different from other rivalries, a view that I adopted after working with Bonneh's illusion which is equally as difficult to influence by will as is binocular rivalry (this can be viewed at www.keck.ucsf.edu/~yoram/mib.html). At first sight, this illusion seems to share no obvious similarity with rivalry because the alternative perceptual states are not mutually exclusive, nor are they obvious to inspection of the pattern before the effect sets in. The stationary, constant yellow discs disappear and reappear as the swirling cloud of blue points is continuously visible. My first inkling that this process was like binocular rivalry came from studying Bonneh's illusion in a number of subjects that covered a broad range of binocular rivalry rates and predominance. Strikingly, there was a tight correlation between individual values on both phenomena. For example, one individual, by far the most euphoric following the recent birth of a son and career success, had the group's strongest left hemisphere bias (i.e., horizontal predominance) and also had the greatest proportion of time when the yellow disc was invisible. He also had the same switch rate on both phenomena. At the other end of the scale, a mildly depressed individual had a strong right hemisphere bias (marked vertical predominance on H/V rivalry) and had an extremely short disappearance time of the yellow discs, as well as similar, slow switch rates on both phenomena. In keeping with these two examples that I have chosen for illustration, the correlation between both the switch rate and the predominance/disappearance time was high for a large group of subjects studied with both binocular rivalry and the Bonneh illusion.

This tight link between the properties of the switch in both phenomena was further supported by studies of the hemispheric basis of Bonneh's illusion. These showed that disappearance of the yellow discs is a left hemisphere phenomenon,

because disruption induced by TMS causes the reappearance of the discs if delivered to the left hemisphere at the time of their disappearance. The regular cyclicality of the Bonneh phenomenon is such that one can even time the TMS to anticipate the subject's button press indicating a phase change in perception. This regularity is just as great as it is for binocular rivalry and is proving to be a valuable adjunct to the measurement of rivalry rate for clinical purposes that does not require both eyes to be functioning nor high visual acuity. The regularity of the cycle also permitted a new kind of experiment where the TMS was delivered in a pre-programmed sequence based on a prior examination of the subject's switch cycle. In this way some TMS pulses could be delivered, on the average, exactly at the phase transition, anticipating the subject's button press instead of being subject to the dual delays inherent in perception of the switch and then the reaction time to button press. With this increased precision in timing, which was very disturbing to the subjects, who had the feeling that their decision-making process was being interfered with, we were able for the first time to get clear reciprocal effects from TMS of the Right hemisphere. In other words, Left TMS during the disappearance phase caused it to shorten, while Right TMS had no effect during that phase. In contrast, Right TMS delivered in the appearance phase caused it to shorten while Left TMS had no effect. This balanced phase-specific, hemisphere-specific effect is hard to explain without recourse to some form of the hemisphere switching model.

In summary, the Bonneh phenomenon can be regarded as a form of denial, where the existence of the yellow discs is disregarded in favor of the rival hypothesis about the coherent moving cloud of complementary color and depth. The fact that both binocular rivalry and Bonneh's illusion have the same cyclicality, period and predominance, and that both behave similarly when one hemisphere is manipulated, all suggest that the fundamental aspects of the underlying oscillator are the same in each case. If one accepts this thesis, then the high level aspects of the Bonneh illusion, such as the palpable disappearance of groups of targets in line with Gestalt principles, for example (Bonneh *et al.*, 2001), would tend to align binocular rivalry to that higher level too. The striking disappearance of the yellow discs also emphasizes why a cyclic phenomenon like this form of rivalry might be present, but escape attention, in everyday life. Since denial, by definition, involves some active disregard or elimination of sensory input, one can see that the state of mind that accompanies the denial (i.e. the left hemisphere's constructive activity) is hardly likely to make the subject acutely aware of that hemisphere's role in the phenomenon! One is reminded of Ramachandran's subject, unable to avoid denial because of right hemisphere damage, who reveals the construction to us, but not herself, by exclaiming "And I did it with both hands!" when she related how she had tied her shoe laces together for the reward offered by the experimenter, even though she was paralyzed on the left side and quite unable to carry out the task (Ramachandran and Blakeslee, 1998).

This line of reasoning is strengthened by the observation that a number of perceptual rivalries, binocular rivalry included, seem to share a common oscillator mechanism, based on the fact that rates of these different rivalries are similar in the same individual, despite the 40 fold inter-individual variation in rate. Moreover, our preliminary data indicate that these different forms of cyclic perception all show similar mood-related variations in the predominance ratio of the component phases, as predicted from the hemispheric model.

10. GENETIC AND INTER-INDIVIDUAL VARIATION IN RIVALRY RATE AND PROPORTION OF NON-RIVALRY THAT CANNOT BE ATTRIBUTED TO VARIATION IN V1 FUNCTION

By a process called “phase normalization” many workers in binocular rivalry eliminate what I consider to be one of the most fascinating aspects of binocular rivalry: its rate. In a sample of 300 subjects, I observed a range of variation of around 40, despite a robustly stable rate in each individual that could be measured up to 3 years later with 85% reliability so long as the stimulus apparatus was the same. Given the association of abnormal rates with mood disorder, the rate variation has important implications for psychiatry (Pettigrew and Miller, 1998; Miller *et al.*, 2000; Pettigrew *et al.*, 2001). It is difficult to account for this rich variation in terms of V1 properties, particularly because there are no hints from my own extensive work on “slow switchers” that there is any connection between an altered rate of switching and any accepted V1 function (such as stereo and vernier acuity). Given the machine-like precision of V1, not to mention its very high speed in varying attention in tasks like serial search, it is remarkable that such wide individual variability in rivalry rate would not be accompanied by variations in some other function in V1, if rivalry rate were attributable to V1.

Another marked inter-individual variation is in the proportion of time spent seeing both alternatives simultaneously. In the H/V rivalry set-up that I use routinely, some subjects spend most of the time seeing a grid or cross-hatch and very little time in rivalry. This proportion can be increased by maneuvers such as increasing the strength of the stimulus, as well as by getting the subject to laugh (see below), but is otherwise fairly constant in an individual over time. Rare individuals (around 1%) fail to show any binocular rivalry at all, showing 100% grid perception. These young, fit individuals have perfectly normal vision on a variety of tests, so it is difficult to argue that they differ in some fundamental aspect of V1 processing that is responsible for the lack of rivalry. There is no explanation for all these individual variations in time spent in rivalry that can be derived from V1 physiology. On the other hand, as I explain below, there are a number of possible explanations based on brainstem-forebrain organization.

11. CRICK AND KOCH'S ARGUMENT ABOUT VISUAL CONSCIOUSNESS

Crick and Koch (1995) argue that V1 operations are not conscious, a line of argument that is quite parallel to the one that I have been developing. But note one difference. My stand leaves open the possibility that V1 might mediate awareness of other visual phenomena apart from rivalry, while they would argue that we are not aware of any V1 operations. This is philosophical territory that I would prefer to leave to the philosophers, but it does bear directly on the issue of V1's involvement in rivalry.

I am impressed with Goodale's subject (Humphrey and Goodale, 1998) who lacks conscious awareness of some visual processes as a result of damage of V1 and the subsequent ventral stream, but who retains extraordinary, unconscious visual abilities as a result of a surviving dorsal visual stream. Based on these considerations I would guess that the dorsal stream might be involved in signaling the switching process, whose phase changes are completely unconscious and unpredictable in most subjects, while the ventral stream might be responsible for the more "conscious", identifiable aspects of rivalry. A recent study came to a similar conclusion, if one can loosely interchange dorsal stream for magno- and ventral stream for parvo- while bearing in mind the cross-talk known to occur between the two parallel streams. (Carlson and He, 2000).

Sleuthing the Location and Properties of the Rivalry Oscillator

If one accepts my argument that rivalry is a manifestation of a neural oscillator, an important question concerns the location and properties of that oscillator. I believe that one can narrow these down by a consideration of all the properties of rivalry that might result from the oscillator.

1. INTRINSICALLY SLOW OSCILLATION

Given the renowned speed of temporal processes in the visual system, with serial search oscillators and critical fusion frequencies in the tens of hertz, to take two examples, it is remarkable that rivalry alternations are so slow, around 1 Hz. This suggests that the underlying synaptic mechanisms might also involve relatively slow processes, like the ~ 1 sec PSPs that characterize aminergic synapses. This suggestion is further reinforced by the fact that rivalry does not occur for briefly-flashed dichoptic stimuli, which have to be continuously present for at least a few hundred milliseconds before rivalry begins (see review in Blake *et al.*, 1991).

2. ROBUST RATE WITH HIGH HERITABILITY

Test-retest and MZ twin studies of the rivalry cycle show high reliability and heritability, better than 0.8 (Pettigrew and Miller, 1998), indicating a robust oscillator with a high degree of genetic control. The picture of robustness and reproducibility

might seem to be marred by the diverse values for the rivalry cycle that can be found in the literature. The reasons for this apparent noise are two-fold: (i) There is marked inter-individual variation in the rivalry cycle, covering a 40-fold range from 0.5 s to 20 s in my sample of around 300 normal subjects. (ii) The rivalry cycle length is inversely proportional to stimulus strength. This effect is complex and is greatest in “fast switchers” who may show a greater than fourfold increase in rivalry cycle from the highest to the lowest stimulus strength. This effect, of increasing switch rate with increasing stimulus strength, is not explained, but may be related to the fact that weaker stimuli involve more “inference” and therefore a greater contribution from more anterior regions of cortex where the interhemispheric switch rate is slower. This suggestion concerning anterior “inference” and posterior “realism” is made more explicit in Figure 4 where I have set out our rudimentary knowledge of the interhemispheric switches and where one can see a gradient of increasing switch rate from frontal to occipital cortex.

3. SHARP TRANSITIONS

When I emphasize this feature of rivalry, with sharp transitions between the comparatively long-lived rivaling states, some of my colleagues have protested because transitions often seem sloppy to them, with gradual or hesitant changeover between the rivalrous percepts. My point is that perceptual transitions *can* be razor sharp, even if there are other times when the transitions are more gradual, passing for example through the mixed intermediate “grid” state. Since I have a long period of oscillation, the instantaneous change (perceived as lasting less than a tenth of a second) is particularly striking to me, coming as it does at the end of ten seconds or more of constant percept. In these circumstances the transition time is certainly very brief compared with the total duration of the percept. This kind of change is reminiscent of the bistable oscillators that have been so well-studied in invertebrate neural systems (e.g. Rowat and Selverston, 1997).

4. HEMISPHERIC EFFECTS

Two completely different, independent hemispheric activation techniques, caloric vestibular stimulation and single pulse transcranial magnetic stimulation, both produce changes in the predominance (ratio of time spent in the two alternatives during rivalry). (Miller *et al.*, 2000). Reversing the stimulated hemisphere reverses the effect (Miller *et al.*, 2000). The effect is specific for both the phase of the perceptual alternation and for the hemisphere, defying any explanation apart from interhemispheric switching. In the initial experiments, there was not much evidence for any effects of stimulating or disrupting the right hemisphere compared with the striking effects on the left, but more recent experiments with greater preci-

sion in time show clear effects of right hemisphere disruption and complementary, phase-specific effects in both hemispheres.

Patients with right parietal lesions show rivalry changes that are also consistent with interhemispheric switching in that perceptual alternation is abolished by a unihemispheric lesion and replaced with a single percept that favors horizontal over vertical and red over green (in accordance with other evidence of these predispositions by the left hemisphere during rivalry).

5. INFLUENCED BY SSRIS ETC.

Rivalry is strongly affected by mood-altering drugs such as the SSRI antidepressants, which change the predominance to favor the horizontal/left hemisphere in H/V binocular rivalry (JDP, personal observations). These observations suggest that the oscillator can be biased toward one or other hemisphere by local serotonin concentrations.

6. AFFECTED IN TIME WITH MOOD AND SLEEP

As already mentioned, the rivalry bias (or per cent *predominance* of one alternative compared with the other) varies in the same subject as a function of time of day (waking from sleep in the early morning hours gives a vertical bias in our set-up, with vertical to right eye and horizontal to left eye) and as a function of mood (vertical bias is associated with depressed mood). I have often surprised subjects by accurately commenting on their mood state using the rivalry data when there have been no outward signs. It is extraordinary that rivalry, a phenomenon that has been considered as largely visual, has such a large mood-related component.

7. GAMMA DISTRIBUTION OF INTERVALS

The gamma distribution has been used to diagnose *bona fide* rivalry and to distinguish it from malingering, particularly in behaving monkeys where indirect measures of conscious state are all that are available. The generation of a gamma distribution of intervals involves an asymmetry in the thresholding process of the neuronal oscillator responsible (Rowat and Selverston, 1997). While a number of mechanisms can generate a gamma distribution, a recognized and empirically validated circuit is the bistable oscillator with mutually-inhibitory connections. Moreover, schizophrenic subjects show a bimodal distribution of intervals in binocular rivalry that cannot be fitted to a gamma distribution (White *et al.*, 2001; Miller *et al.*, 2001). This strikingly different interval distribution is accompanied by other changes in the rivalry switch, such as an ability to follow eye swapping to very high frequencies. These complexities of the switch could constrain its identity, by requiring that rapid V1 inputs, for example, be added to the gamma distribution of rivaling schizophrenics up to the frequency limit imposed by the switch.

8. CHANGED FREQUENCY FOLLOWING CORTICAL LESIONS

Visual cortical lesions produce dramatic reductions in the rate of binocular rivalry (Poeppel *et al.*, 1978). In contrast, bilateral frontal lesions usually cause a prolongation of the nasal cycle associated with frontal cortex, but produce the opposite effect on rivalry, an increase in rate (Pettigrew, unpublished). Right unilateral frontal lesions can slow the switch, presumably by involving the same right frontal area (that I call the “dither!” area) identified as very active in scanning studies of rivalry and ambiguity. These effects, involving frontal-occipital compensation and the involvement of widespread cortical regions, suggest that the switch must have a global, integrative kind of connectivity.

9. HINDBRAIN EFFECTS

Laughter consistently abolishes binocular rivalry (Pettigrew, 2000). This is a consequence of the emotional release and not a physical consequence of transient head movement, which can interfere with rivalry under some conditions. Theatrical or forced laughter does not mimic the effect of real laughter in abolishing rivalry. Binocular rivalry produced with orthogonal grating afterimages on each retina, and therefore immune to movement, also disappears with laughter. Mirth without head-shaking laughter likewise increases the incidence of periods where rivalry ceases. Sudden decreases in emotional tension of other kinds can have the same effect, just as cataplexy is triggered by such events (Lai and Siegel, 1988). The neural circuitry underlying cataplexy is beginning to be elucidated and involves a hindbrain nucleus that projects forward to the forebrain as well as back to spinal cord. TMS of the cerebellum has the same effect on binocular rivalry as laughter, in keeping with the cataplexy circuit. These findings suggest that the site of rivalry is also the target of inputs from the hindbrain that can eliminate the rivalry, perhaps by providing simultaneous input to both sides of the switch and thereby stopping the alternation.

10. INDIVIDUAL VARIATION IN DEGREE OF RIVALRY

Some individuals do not show any binocular rivalry at all, instead experiencing both of the alternative percepts simultaneously (Pettigrew, 2000). In addition, subjects vary in the threshold at which a lowered stimulus strength will result in the apparent cessation of rivalry and the simultaneous perception of both alternatives (Liu *et al.*, 1992). It seemed strange to us that both increasing and decreasing the stimulus strength would each lead to a loss of rivalry, so we have been looking at this issue in detail. It seems that the loss of rivalry at low contrast is a different phenomenon, with only superficial similarity to the loss of rivalry at very high stimulus strengths (Hekel and Pettigrew, 2001). The low contrast phenomenon is more like mosaic rivalry in that horizontal and vertical are not seen simultaneously in the same place, with the uncertainty that results from the low contrast leading to a percept where both orientations are thought to be present, but not at any

particular location on careful inspection. In contrast, the “grid” percept at high stimulus strengths is seen as clearly overlapping horizontal and vertical contours, with prominent right angles.

Decreased stimulus strength can also abolish rivalry, as well as considerably slowing the rate before rivalry breaks down, so I have suggested a mechanism that could account for this effect. One could imagine that a weak stimulus has higher uncertainty and might therefore be more dependent upon higher processes like memory and imagination than a stronger stimulus that might drive posterior visual cortical processes directly. If the frontal regions switch more slowly (as the evidence suggests) one would therefore expect a low strength stimulus to be associated with slower switching. Why very low strength stimuli should also fail to produce rivalry is more mysterious, although this failure might be regarded as some kind of extrapolation to the infinitely slow rivalry rate expected at the lowest stimulus strength. Work in progress in my laboratory (Hekel, in preparation) suggests that the apparent losses of rivalry at both high and low stimulus strengths are unrelated phenomena that share a subjective similarity that does not stand up to closer examination. The failure of H/V rivalry at high stimulus strengths appears to reflect the upper temporal limit of rivalrous alternations that can be perceived. This interpretation is supported by Keith White’s experiments with eye swapping and rivalry where aliasing or beat frequency phenomena are elicited systematically as the rate of dichoptic alternation is increased (White *et al.*, 2001). High-speed dichoptic alternations are clearly having an effect on the system, but rivalry is incapable of following at high speeds that exceed the limit around a few hertz. I have already pointed out the surprising slowness of this limit when it is compared with other temporal limits in the visual system, which are an order of magnitude faster.

In contrast, the apparent failure at low stimulus strength may be a different phenomenon that seems to share features with patchwork rivalry, where the patches are so numerous and the stimulus so uncertain that the subject reports the presence of the orthogonal orientations simultaneously over the whole display, even though the two orientations cannot actually be perceived to cross over at any location. For this reason it may superficially resemble the grid perception that occurs above the temporal limit of rivalry at high stimulus strengths. Note that in this latter case there are visible intersections between horizontal and vertical contours at all locations in the display, a percept that our limited number of subjects are so far not willing to admit in the low contrast case. The task of reporting rivalry becomes very difficult at low stimulus strengths we think, not only because rivalry may slow down and cease, but because the stimulus becomes so weak that it is difficult to rule out what we think is a likely interpretation: viz., that patchwork rivalry is now occurring at every resolvable location in the display. Given the very different appearance of the H/V rivalry display at high- versus low-stimulus strength, we do not think it appropriate to view both apparent losses of rivalry as related phenomena, even if the explanation I have just provided needs modification as we study more subjects,

bearing in mind once again the considerable variation in individual perception of precisely the same rivalry display.

Candidates for the Interhemispheric Oscillator

So, if we accept these requirements, particularly that it must be able to exercise control over each hemisphere separately, where in the brain might one find a structure with the appropriate properties to be a candidate for the interhemispheric oscillator? Where would one find a bistable oscillator with sharp transitions between relatively long phases, relatively slow and prolonged synaptic effects that would limit the frequency at which both sides of the oscillator fused, where there was global kind of telencephalic connectivity that would reflect activity in all cortical regions including V1, where there was an effect upon the oscillation of overall mood and motivational state, where there was individual variation in the conditions under which the bistable oscillator was disabled and where the oscillator was affected by mood-altering medications that affect indolaminergic and catecholaminergic function?

One could bring inputs to the visual system from other diverse brain regions to handle these different aspects, as a recent model does. In this model, the bistable oscillation is a feature of higher order visual cortical neurons and the other features, such as the inter-individual variation in switch rate, originate elsewhere (Laing *et al.*, 2001). Because there seems to be a relation between many different kinds of perceptual rivalry, I would prefer to look in the first instance for a single site that might be able to account for the complexity of rivalry, rather than have to bring inputs from diverse neural sites. Even if one adopts such a model with recourse to different inputs from outside the visual system, it would still be necessary to go back to those diverse sources to understand how they produced these changes in rivalry. I consider it preferable to find a model that might have all of these diverse properties in the smallest set(s) of neurons.

While these features do not narrow down the search to a great degree, it is clear that there are a number of paired midline structures in the neuraxis that would fit this description, in the hypothalamus, the midbrain tegmentum, the raphe system, the locus coeruleus and the medulla. These are illustrated in Figure 3, where it can be seen that putative interhemispheric switch rate varies considerably, from thousands of seconds in the hypothalamus, to a few tens of milliseconds in caudal midbrain. This gradient of switch rate from anterior pole of the brain to the caudal midbrain is also consonant with the other observations that suggest that the more anterior regions of cortex switch more slowly than posterior regions. Information is still sketchy on this point, but the figure shows the known cases, with a very slow switch in medial prefrontal cortex linked to the nasal cycle of the hypothalamic arcuate nucleus (period of 2–3 hrs) and more rapid oscillation as one moves posteriorly to the visual cortex (where the 30 msec period is the fastest known). Recent work has shown that the circadian clock, the suprachiasmatic nucleus of the hypo-

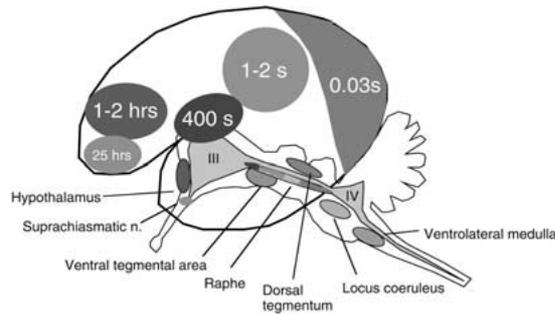


Figure 3. Gradient of Switch Rates in the Putative Interhemispheric Switches: Summary of the sketchy knowledge available about brainstem bistable oscillators and their cortical targets. Note that there is a rough gradient of switch rate in the brainstem, from caudal midbrain to hypothalamus that matches a similar caudal-to-frontal gradient of switch rate in the neocortex. Because this information is still fragmentary (for example, some reviewers did not agree that there is a high speed oscillator driving V1 that is responsible for the extraordinary speed of the attentional spotlight of serial search) there may be even more resistance to my postulating the dorsal tegmentum as the site of the oscillator in this diagram. Nevertheless, this information grows in the direction that I have indicated, with recent confirmation of my prediction that even the hypothalamic suprachiasmatic nucleus (SCN) can act as a switch. While this piece was being written, new evidence emerged that the SCN of the hypothalamus can act as a bistable oscillator to bring about interhemispheric switching in the time scale of days (de la Iglesia *et al.*, 2000).

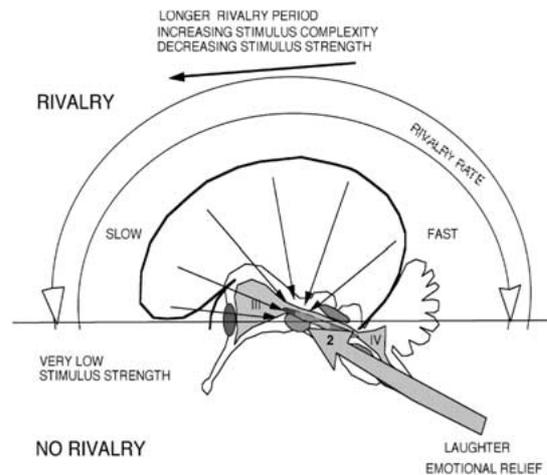


Figure 4. Interrelationship of the Oscillators that might be Involved in Rivalry: The role of this diagram is to try to account for the individual variation in switch rate, as well as that fact that some individuals do not rival at all, seeing instead a mixed percept at all times. Since all individual tested can be induced to “abandon” rivalry by emotional releasers such as getting them to laugh, perhaps the individuals who never experience rivalry can be related to this temporary loss of rivalry in normals. Emotional releasers such as laughter are also effectors of cataplexy, whose hindbrain-midbrain circuitry is becoming known. A midbrain switch, such as the ventral tegmentum, might thus be “balanced” or “centered” by such releasers. At the least, the diagram maps out the rivalry phenomena that have to be accounted for and emphasizes the difficulties of so doing if one confines one’s attention to the properties of V1.

thalamus (SCN), can also act as an interhemispheric bistable oscillator when it is subject to continuous light, although the exact target region in frontal cortex is not yet clear (de la Iglesia, 2000). This extraordinary, slow interhemispheric cycle from the SCN emphasizes both the general concept of interhemispheric oscillators while at the same time illustrating the very slow time scale that one may expect from such oscillators in the hypothalamus.

VTA AS THE RIVALRY OSCILLATOR

From the point of view of the timing involved, the best candidate for the binocular rivalry oscillator is the ventral tegmental area, where the switch rates are in the appropriate range of seconds and where there is evidence of striking coupling of the oscillation of the neural structure with the perceptual switches (Pettigrew *et al.*, 2001). In these studies, a small region of the medial VTA was observed to flash in time with perceptual switches during binocular rivalry on individual 1 sec fMRI images, without the need for averaging (see movie at www.uq.edu.au/nug/jack/VTA.html). Remarkable features of this signal were its timing (not delayed by the many seconds typical of a hemodynamic response) and its magnitude (around 20–30% instead of the usual 1–2% BOLD signal obtained from cortical venous drainage). Local release from dopaminergic VTA neurons as well as the high Mn(II) ion levels in this part of the brain could account for the remarkably high fMRI signal generated, given the well-documented powerful effects of amines in quenching the MRI signal from water (Cohen *et al.*, 2000). Dopaminergic VTA neurons also have dendro-dendritic DA synapses that could mediate reciprocal inhibition across the midline, even though there appear not to be midline-crossing axon collaterals (Pickel, 2000). If these dopaminergic dendro-dendritic synapses have a long time course, as might be expected from the ~ 1 sec PSPs generated at axo-dendritic dopaminergic synapses, then this property of the VTA would explain the slowness of rivalry that is so surprising when it is compared with the relatively high speed of transient visual processes like flicker and attention. The complex properties of dopaminergic VTA neurons could easily account for the host of complex properties of rivalry. For example, the replacement of alternation by simultaneous bilateral activation that is inferred by the abolition of rivalry in laughter and hindbrain TMS is consistent with the connections between hindbrain and VTA. Similarly, the link between rivalry and mood disorder is strikingly supported by the dramatic, reversible mood changes that are produced by unilateral electrical stimulation of the VTA in humans being treated for Parkinson's disease (Bejjani *et al.*, 1999). Finally, the global connections of the VTA are capable of accounting for the complexity and widespread features of rivalry, which involves many brain structures in addition to the visual cortex and which seem to defy explanation by conventional hierarchical and parallel models of the visual system. The global connectivity of the VTA is well summarized in the following quote:

A review of the organization of some of these afferents in relation to the known cortical-subcortical-mesencephalic projection systems, suggests that the VTA is in a position to receive information from a massively convergent system derived ultimately from the entire archi-, paleo-, and neo-cerebral cortices. (Phillipson, 1979)

The vast literature on the motivational and mood aspects of VTA is daunting, but on the other hand this breadth may be essential if one is to account for the diverse aspects of rivalry that cannot be understood in the context of early visual processing. The conflation of emotional processing with visual processing may be disconcerting, even daunting, to psychophysicists trained in precision measurements of stimuli. Nevertheless, this line of argument is also followed by Damasio (2000), who argues that emotion and consciousness are intimately related.

COMPARISON WITH OTHER HYPOTHESES FOR THE SITE OF RIVALRY

There seem to be three positions adopted by those prepared to be explicit about the neural locus of rivalry. I have dealt in detail with the first position, adopted by the fairly large and traditional school that posits a major role for early visual processing in V1. The second position emphasises a much wider role of different cortical areas, including frontal cortex, from brain scanning studies using fMRI and MEG (Lumer *et al.*, 1998; Srinivasan *et al.*, 1999). A striking feature of these studies, particularly the MEG investigation, is the marked individual variation in the pattern of cortical activation during rivalry. This is a more satisfactory result, compared with the V1 fMRI studies, in accounting for the marked individual variations in the pattern of binocular rivalry seen with the same stimulus conditions. Finally, there is the position that I have proposed here, where widespread cortical regions are involved in rivalry, including V1, as shown in fMRI and MEG, but where the regions are coordinated, sometimes on a hemispheric basis, by a brainstem oscillator that alternates “attention” or “activation” between cortical sites, such as relatively large, homologous parts of each hemisphere. While focusing attention on the brainstem oscillator to provide an explanation for the temporal properties of rivalry, the interhemispheric switching hypothesis of rivalry also incorporates the diversity of cortical physiology in different regions, whose individual combinations could then provide a basis for the marked individual variation in binocular rivalry under the same stimulus conditions. In this way, some individuals may have a greater emphasis on connectivity related to early visual processing, with a resulting strength in visual imagery, and a fast switch that reflects this “more posterior” kind of connectivity. In contrast, less common individuals may have a greater emphasis on anterior cortical processing with resulting less concrete and more abstract visual imagery, and a slower rivalry switch because of the biased connectivity to the more frontal regions where switches are slower (Figures 3 & 4). It is worth noting that the MEG study, as well as supporting this great

inter-individual variation in the pattern of involvement of different cortical areas in rivalry, identified many examples where there was complementary interhemispheric activity between homologous cortical sites during rivalry, in keeping with the interhemispheric switching hypothesis (Srinivasan *et al.*, 1999). These effects may have cancelled because of averaging in the fMRI studies.

CORPUS CALLOSUM AND RIVALRY

Perhaps the most common question raised in the context of an interhemispheric switching basis for rivalry concerns the corpus callosum. Is the corpus callosum involved in the switching of perceptual rivalry? A number of reasons have already given why the corpus callosum is unlikely to be involved in rivalry despite its interhemispheric connections (Miller *et al.*, 2000). In the same publication it is also predicted that split-brain subjects will experience rivalry (Miller *et al.*, 2000). In view of the persistence of this issue, as well as the recent study of binocular rivalry in split-brain subjects (O'Shea and Corballis, 2000, 2001), I have devoted more detailed discussion here.

The first argument against a role for the callosum in interhemispheric switching is comparative: birds and fish lack a callosum yet show the phenomenon of interhemispheric switching. In the sandlance, there is visible interhemispheric switching that does not require special apparatus to observe (Pettigrew *et al.*, 1999). Since this fish's visual pathway is completely crossed, we know that the pattern of alternation in eye movements must involve a corresponding pattern of alternation in the visual control centers, such as the midbrain optic tectum and tegmentum. In fact, it was this observation of hemispheric alternation in the sandlance, first made by Josh Wallman, that initiated my search for a switching mechanism to account for the complementary cognitive styles of the human cerebral hemispheres. I was impressed by Ramachandran's experiments that showed complementarity of the frontal lobes, with each complementary style having equal validity. Mixing the complementary styles seemed a rather pointless compromise to someone like myself who likes to call a spade a spade (see below on laughter for a more recent and less extreme viewpoint). Accordingly, it seemed that the best solution was a switch between the two complementary viewpoints, with the pattern of switching being based in a sophisticated way on both phylogenetic and ontogenetic information. Seeing an obvious pattern of interhemispheric switching in the sandlance provided an "existence proof" that galvanized me to go searching for some comparable system of switching in humans. The sandlance was also important in another way. It ensured that the framework of thinking was always comparative. Since the oculomotor-cum-attentional machinery in the brainstem is largely shared across vertebrates, but the corpus callosum is a highly derived apparatus that is not even found in marsupials and monotremes, let alone anamniotes, there has never been any serious question in my mind that this structure might play an important role in

the switching *per se*. I would be prepared to accept that the callosum plays a role in setting up some associated phenomena, such as the precision of the complementarity of the homologous representations in each hemisphere, but there are a number of reasons why it is unlikely to be the switch itself.

Temporal precision: Switching between hemispheres by means of the corpus callosum would be clumsy, in view of the limits imposed by conduction time. This is best illustrated by reference to bird song where both hemispheres play separate interdigitating roles. The high frequency note contributed by the left hemisphere can be succeeded seamlessly by the right hemisphere's contribution of the lower frequency component. This switch between hemispheres is accomplished in a millisecond or so, much faster than could be accomplished by the corpus callosum, even if the bird's brain had one! The fact that such accomplished interhemispheric switching can be achieved by the bird without a callosum strongly emphasizes my point. Not only is the callosum unnecessary for interhemispheric switching, there are other brain structures that are much better suited to this role. The example from bird song is particularly informative because the precision of interhemispheric switching during singing is so great that a subcortical bistable oscillator is the only possible explanation. Even if there were a corpus callosum in the avian brain it would not be able to provide the precision required in bird song. Reviewers were not very impressed with my argument about precision timing, given that rivalry is measured in seconds. In response I would say that any phase-shift between perceptual or behavioral states should minimize the non-functional transition time between states. A bistable oscillator of the kind I am proposing plays this role much more elegantly and cleanly than would the hemispheres, tossing timing cues at each other back and forth across the callosum.

Comparative and genetic arguments: These arguments have already been made about the switch (e.g. Miller *et al.*, 2000). The diverse but evolutionarily conserved nature of the likely brainstem structures seem more appropriate for the switch, in contrast to the simplicity and relative recency of the callosum which cannot account for the many its features.

Pacemaker neurons: In addition to the comparative and temporal precision arguments, there is no evidence for an oscillator in the callosum or callosally-projecting neurons, in contrast to the pacemaker properties of neurons in paired nuclei of the neuraxis that have the appropriate connections to mediate interhemispheric switching. These include the locus coeruleus, raphe nucleus, substantia nigra, ventral tegmental area and hypothalamus, all of which have neurons with pacemaker properties appropriate for an oscillator. All these neurons are close to the midline, especially the raphe and VTA, so could provide the precision in time at the phase-shift.

SPLIT BRAIN SUBJECTS AND PERCEPTUAL RIVALRY

If one accepts the foregoing arguments that the callosum is an unlikely candidate for the switch, one would not be surprised to find that switching is present in subjects with callosotomy. This was predicted (Miller *et al.*, 2000) and verified by the experiments of O'Shea and Corballis (2000, 2001) who have also shown that rivalry rate is slower in the left hemisphere of split brain subjects than in the right hemisphere. There are a number of reasons for considering these results in detail, particularly the fact that O'Shea and Corballis consider that their results refute the idea that the switches of perceptual rivalry are brought about by an interhemispheric mechanism.

The key issue is the philosophical one concerning the likely locus or loci of consciousness. If one regards consciousness as confined to either one of the single hemispheres as a result of the callosotomy, then one interpretation of their results would be that both alternate percepts of rivalry have their representations within a single hemisphere, at least the left hemisphere since it is more difficult to ascertain what is being experienced by the right hemisphere. This interpretation is not in keeping with the predictions of the interhemispheric switching model, which posits that the complementary representations will be in separate hemispheres. On the other hand, it is worth noting that these split brain subjects have had over 20 years experience of callosotomy, with well-developed compensatory mechanisms such as cross-cuing, so it might not be surprising to find some form of compensation for rivalry.

On the other hand, if one moves away from the modern preoccupation that the human cerebral cortex does everything and instead entertains a role in consciousness for the neuraxis, the results seem to fit expectations. The limitations placed upon the subject's inputs (by means of the hemifield presentation and callosotomy) and outputs (e.g. key tapping with the finger contralateral to the hemisphere being studied) would not constrain the midbrain, for example, where there would be free access to information to and from both hemispheres. This scenario was first raised in split brain subjects by the Mackays, who arranged for a game to be played between the two hemispheres that should not have been possible in terms of the conventional cortical separation of information but which was consistent with integration of the hemispheres at the brainstem level (Mackay and Mackay, 1982).

It is ironic that perceptual rivalry is often studied as a route to further understanding of consciousness (e.g. Logothetis, 1999) when the switch between alternative percepts itself is unconscious in most subjects, usually occurring unpredictably and without any significant involvement of will. In this sense, rivalry might be unlike Mackay's game, since the results of the interhemispheric exchange would be conscious in my formulation of rivalry, but not the mechanism of the timing of the exchange itself. The rivalry + split brain experiments might therefore facilitate current debates on the nature and site of consciousness in a way that neither perceptual rivalry, nor split brain studies, alone have managed to do.

TELEOLOGY OF RIVALRY

Sperry's demonstration of the functional subdivision between hemispheres captured the popular imagination and was carried so far into popular culture that it is now difficult for many academics to maintain balance when hemispheric function is discussed. Similarly, the growing evidence for a hemispheric role in mood causes awkwardness in many academic quarters, perhaps because this idea is so easily and beneficially incorporated into lay thinking (see Schiffer, 2001). With all those points in mind, it is easy to see that rivalry and hemispheres and "woolly" phenomena like mood and motivation might be linked only with difficulty by those used to the fine parametrization of binocular rivalry that has been inherent in an approach assuming V1 as its basis.

I would like to pursue the case that rivalry is not a peculiar phenomenon that is limited to a few highly specific sets of stimulus conditions, but rather a general phenomenon of perception that arises because of ever-present ambiguity in sensory input. Dale Purves has put this case eloquently for brightness estimations and illusions, where it is not possible to disentangle the relative contributions of the incident illuminance and the intrinsic reflectance properties of the surface (Purves *et al.*, 1999; Lotto *et al.*, 1999). Purves and colleagues argue that this ambiguity is inescapable, so recourse must be made to all possible sources of empirical information that have been gained from past experience, of different objects and their defining boundaries, of sources of illumination and shadow patterns, not to mention their probabilities of occurrence. In other words, recourse must be made to the whole cortical mantle! In agreeing with this conclusion, and pointing out that the integrating properties of a subcortical structure like VTA would enable appropriate marshalling of all cortical information, I add another principle: that the decision-making apparatus involved in resolving the ambiguity should show an underlying oscillation. The oscillation would help to retain flexibility and alternative points of view when inputs tend to be balanced.

This point is brought home forcibly by the Bonneh illusion, which was not initially thought to be related in any way to rivalry, yet has an underlying oscillation that shares three properties with binocular rivalry in the same individual; rate, predominance and hemispheric switching. This suggests that oscillations may be much more common in everyday perception than is commonly realized, especially when we consider that one phase of the oscillation may involve the left hemisphere process of denial, so that consciousness may be ignorant of some of its own processes. La Gioconda's ambiguous facial expression alternates at different rates in different individuals according to their binocular rivalry switch rate (JDP, unpublished), so one might speculate that Leonardo da Vinci was aware of this oscillatory aspect of perception and placed it knowingly into his famous painting. This is a different but not mutually exclusive explanation from that of Livingston (2001), who argues for a spatial frequency explanation based on changing visibility of smile and frown contours as gaze shifts.

Rivalry may thus reflect fundamental aspects of perceptual decision-making, with significant variation between individuals. The links that we have established between perceptual rivalry and the hemispheric processes of thought and mood, particularly the concept of interhemispheric switching, considerably widen the research horizon beyond V1 for those interested in the neural substrate of these striking alternations in awareness.

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