Dichoptic Visual Masking Reveals that Early Binocular Neurons Exhibit Weak Interocular Suppression: Implications for Binocular Vision and Visual Awareness

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Abstract

■ Visual masking effects are illusions in which a target is rendered invisible by a mask, which can either overlap or not overlap the target spatially and/or temporally. These illusions provide a powerful tool to study visibility and consciousness, object grouping, brightness perception, and much more. As such, the physiological mechanisms underlying the perception of masking are critically important to our understanding of visibility. Several models that require cortical circuits have been proposed previously to explain the mysterious spatial and timing effects associated with visual masking. Here we describe single-unit physiological experiments from the awake monkey that show that visual masking occurs in at least two separate and independent circuits, one that is binocular and one that is monocular (possibly even subcortical), without feedback from higher-level visual brain areas. These and other results together fail to support models of masking that require circuits found only in the cortex, but support our proposed model that suggests that simple ubiquitous lateral inhibition may itself be the fundamental mechanism that explains visual masking across multiple levels in the brain. We also show that area V1 neurons are dichoptic in terms of excitation, but monoptic in terms of inhibition. That is, responses within area V1 binocular neurons reveal that excitation to monocular targets is inhibited strongly only by masks presented to the same eye, and not by masks presented to the opposite eye. These results lead us to redefine the model for the first stage of binocular processing in the visual system, and may be crucial to interpreting the effects of other similar binocular and dichoptic stimulation paradigms, such as the binocular rivalry family of illusions. ■

INTRODUCTION

The anatomical location in which dichoptic masking first begins is critical to understanding the relevance of most models of masking, and it is also important to our understanding of the functional relationship between neurons in the LGN and the subcortical and cortical structures that feedback onto the LGN. We address this issue here by conducting single-unit physiology of LGN and area V1 neurons while presenting monoptic and dichoptic stimuli to awake rhesus monkeys. To our knowledge, these are the first dichoptic masking experiments to be conducted physiologically. Our results show that monoptic masking effects occur in all neurons of the early visual system, whereas dichoptic masking effects occur solely cortically in a subset of binocular neurons. We also find that, in the first binocular neurons in the visual system, excitatory responses to targets presented monocularly are inhibited strongly only by inhibitory stimuli presented to the same eye, whereas interocular inhibition is strikingly weak.

The undignified birth of "visual masking" was as an artifact in one of Exner's (1868) studies of consciousness. He had been trying to determine the shortest flash duration necessary for a target (a bar of light) to be visible. As a control condition, he presented two identical targets in different places of the visual field and at different times, expecting that they would be perceived as identical in appearance. It was a real surprise when this was not necessarily so. In fact, under certain specific timing conditions, the first target was rendered invisible by the presentation of the second target! Stigler (1926) later called this illusion "metacontrast" (what we now call *backward masking*). It was subsequently discovered that, under other timing conditions, the first target could also mask the second target: Stigler called this phenomenon "paracontrast" (what we now call forward masking).

In our own previous perceptual and physiological studies of visual masking in the human and primate, we found that the mysterious timing characteristics of both forward and backward masking could be accounted for by a simple lateral inhibition circuit model: The onset-responses and after-discharges that correlated with the presentation of the mask seemed to laterally inhibit the onset-responses and after-discharges that correlated with the presentation of the target, thereby causing the signals representing the target to

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be suppressed and the target to therefore become less visible (Macknik, Martinez-Conde, & Haglund, 2000; Macknik & Livingstone, 1998). In contradiction to various theoretical predictions of different models of visual masking (Enns, 2002; Enns & Di Lollo, 2000; Lamme, Super, Landman, Roelfsema, & Spekreijse, 2000; Purushothaman, Ogmen, & Bedell, 2000; Thompson & Schall, 1999; Francis, 1997; Breitmeyer & Ganz, 1976; Matin, 1975; Weisstein, Ozog, & Szoc, 1975; Kahneman, 1968; Weisstein, 1968), physiological recordings within the lateral geniculate nucleus of the thalamus (LGN) showed that responses to targets are inhibited by masks in both forward masking (Macknik et al., 2000; Bridgeman, 1975; Coenen & Eijkman, 1972; Schiller, 1968, 1969) and backward masking (Macknik et al., 2000) conditions. However, these LGN physiology experiments did not rule out the possibility that the circuits mediating visual masking were primarily cortical, and that subcortical neurons were then modulated in their response through feedback mechanisms (Enns, 2002).

One of the main reasons that models of visual masking often propose cortical circuits is that "dichoptic" visual masking exists. To be clear about the jargon: "Monocular" means "with respect to a single eye," and "monoptic" means either "monocular" or, "not different between the two eyes." "Binocular" means "with respect to both eyes" and "dichoptic" means "different in the two eyes." Thus, in dichoptic visual masking, the target is presented to one eye and the mask to the other eye and the target is nevertheless suppressed. Despite the robustness of some dichoptic masking illusions, reports in the literature have not always agreed that dichoptic masking effects exist (Kolers & Rosner, 1960; Alpern, 1952, 1953), and Schiller (1969) has reported that dichoptic masking is strong under some circumstances, but not others. Our first experiment therefore compared systematically the perception of monoptic to dichoptic visual masking in humans over a wide range of timing conditions never before tested. We found that dichoptic masking was as robust as monoptic masking, and dichoptic masking exhibited the same timing characteristics previously discovered in humans for monoptic masking (Macknik et al, 2000; Macknik & Livingstone, 1998; Crawford, 1947).

Because excitatory binocular processing within the geniculocortical pathway occurs first in the primary visual cortex (Hubel, 1960; Le Gros Clark, & Penman, 1934; Minkowski, 1920), it has been assumed that dichoptic masking must originate from cortical circuits. However, LGN neurons have shown interocular transfer of information, especially with respect to their receptive field surrounds (Sillito, Jones, Gerstein, & West, 1994; McClurkin & Marrocco, 1984; Marrocco, McClurkin, & Young, 1982). Moreover, the LGN is connected reciprocally to other thalamic nuclei that contain binocular neurons, such as the perigeniculate nucleus (PGN) (Jones, 1985; Steriade & Deschenes, 1984), which is itself interconnected with various subcortical and cortical visual areas that contain binocular neurons (Uhlrich, Cucchiaro, & Sherman, 1988; Ungerleider, Desimone, Galkin, & Mishkin, 1984; Maunsell & Van Essen, 1983). Therefore, one of three possibilities exists: First, both monoptic and dichoptic masking are mediated by circuits in the LGN (and feedback may or may not be relevant); Second, only monoptic masking can be mediated by circuits in the LGN, but LGN responses nevertheless reflect dichoptic masking because of feedback from binocular circuits; Third, LGN cells can mediate only monoptic masking effects, and dichoptic masking effects occur only later within binocular cells. In testing these possibilities here, we discovered that this third possibility was correct, and this discovery moreover revealed novel findings concerning the role of excitation and inhibition in the first binocular circuit in the visual system.

RESULTS

All of our stimuli were presented binocularly (both eyes open), either monoptically (same stimuli in both eyes) or dichoptically (different stimuli in the two eyes). This is a semantic issue solely: The effects seen in the monoptic masking condition are perceived as qualitatively identical whether viewed through one or two eyes.

Psychophysical Measurements of Dichoptic Visual Masking

In humans, we compared directly the timing parameters and strength of dichoptic and monoptic masking effects. The subject's task, shown in Figure 1A, was to determine which one of two targets was longer, in a two-alternative forced-choice task (Macknik & Livingstone, 1998; Macknik et al., 2000). The stimulus onset asynchrony (SOA) between the onset of the 300-msec duration mask and the onset of the 10-msec duration target was varied so that target visibility was measured during forward (when the mask is presented before the target), simultaneous (when the mask and target are presented simultaneously), and backward (when the mask is presented after the target) masking conditions. Subjects were tested while wearing shutter goggles that allowed either monoptic masking (shutters over both eyes were open for both the target and the mask) or dichoptic masking (shutters directed the target to one eye and the mask to the other). To test if the shutters truly prevented transmission of the target, the shutters were sometimes shut over both eyes to block the target completely. Figure 1B shows the target length discrimination performance in seven human subjects as tested with 64 conditions (4 shutter arrangements × 16 SOAs, with 10 trials/condition), plotted as a function of SOA. These results show for the first time that dichoptic masking has the same perceptual strength and timing

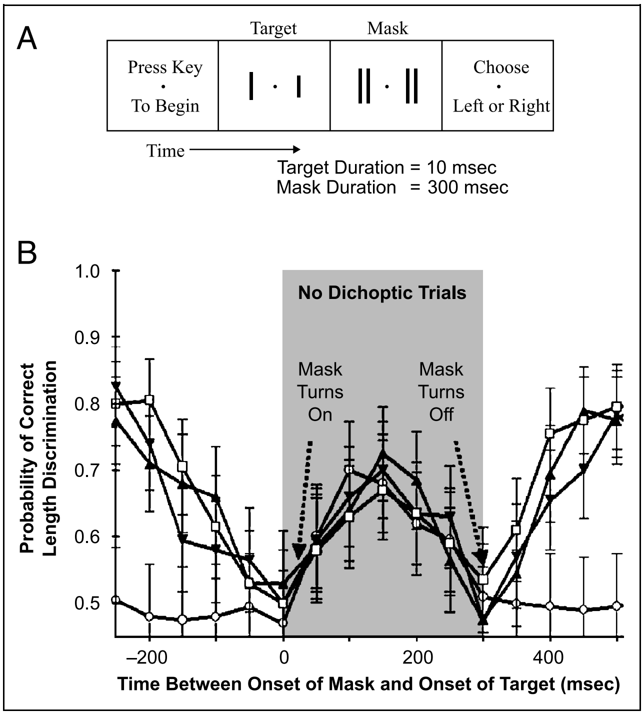

Figure 1. Psychophysical examination of dichoptic versus monoptic visual masking in humans. (A) The sequence of events during the course of a psychophysical trial. The trial started with a delay of 500 to 1500 msec. The target and the mask were then presented in sequence. Stimuli are drawn here with the target presented first, but sometimes the mask was displayed first and sometimes both stimuli were presented simultaneously. After termination of all stimuli, there was another 500 msec delay, after which the subject indicated which side had the longer target. (B) Human psychophysical measurements of visual masking when 10 msec duration target and 300 msec duration mask were presented to both eyes together (monoptic masking) and to the two eyes separately (dichoptic masking). The probability of discriminating correctly the length of two targets is diminished, in the average responses from seven subjects, when they are presented near the times of mask onset and termination. This is true regardless of whether the target and the mask are presented to both eyes (open squares), or if the target was presented to one eye only and the mask was presented to the other (target = left, mask = right: closed upright triangles; target = right, mask = left: closed upside-down triangles). Open circles signify when the target was displayed with both shutters closed, showing that the stimuli were not visible through the shutters. When the mask and the target were presented simultaneously, both eyes' shutters were necessarily open (dichoptic presentations using shutters are impossible when both stimuli are presented at the same time), and so between times 0 and 250 msec all four conditions were equivalent. Dichoptic masking is nevertheless evident when the target was presented before the mask was presented (−250 to −50 msec on the abscissa), as well as when the target was presented after the mask had been terminated (300 to 500 msec on the abscissa).

parameters previously reported for both forward and backward monoptic masking (Macknik et al., 2000; Macknik & Livingstone, 1998; Crawford, 1947).

Physiological Experiments

We recorded from 301 neurons in the LGN and area V1 from three rhesus monkeys, while presenting unmasked and masked stimuli. This procedure enabled us to ask whether neural responses correlated with perception or with the physical stimulus. Targets were 60 msec duration bars of optimal contrast, size, position, and orientation (if the neuron was an oriented cortical cell) over the receptive field of each neuron. Masks were two bars of 110 msec that flanked and abutted the targets to either side and had the same contrast and orientation as the target. When cycled, this stimulus results in a powerful masking illusion called the "Standing Wave of Invisibility," which has been previously characterized by us and others physiologically and perceptually (Enns, 2002; Macknik et al., 2000; Macknik & Haglund, 1999; Macknik & Livingstone, 1998). We tested the effect of masks on target responses when all stimuli were presented to both eyes (monoptic Standing Wave), and we also developed a new modified dichoptic version of the Standing Wave, to also measure the responses when the target was presented to one eye and the mask was presented to the opposing eye (go to http://neuralcorrelate.com for a demonstration of the monoptic and dichoptic versions of the Standing Wave of Invisibility).

Because of fixational microsaccades in the awake monkey (Martinez-Conde, Macknik, & Hubel, 2000, 2002, 2004; Leopold & Logothetis, 1998; Gur & Snodderly, 1997), targets were not solely in the center of the receptive field, and masks were not solely in the surround; both stimuli encroached at times, upon every part of the receptive field. Of the 301 cells that were initially characterized, we went on to analyze 212 cells (78 from the LGN and 134 from area V1). These cells were successfully tested with at least 50 trials per condition, and with no measurable cross-eye leakage through the eye-filter system (in all cells that appeared to be binocular, we either swapped the colored lenses between eyes and retested or alternatively we blocked one eye at a time to be sure the lenses were not leaking; when using the shutter system cross-eye leakage was tested by measuring the responses from a flickering target that was blocked by the shutters: gray lines, Figures 2A,D and 3A,D). LGN neurons had an eccentricity range of 2°–30°; area V1 neurons had a range of 4°–28°. To ensure that visual masking was an appropriate stimulus for LGN and area V1 neurons, we tested each cell with the target alone, the mask alone, and target and mask presented "together" to both eyes (i.e., the monoptic Standing Wave of Invisibility), in randomly interleaved trials. The results show that visual masking stimuli are appropriate to testing thalamocortical processing since, in Figure 2A, individually tested LGN cells exhibited target response inhibition when the target and mask were each presented monoptically to both unobstructed eyes (two-tailed t test, in all conditions $p < .01$). This effect also occurred in individually tested area V1 neurons (Figure 2D and Figure 3A,D). These results match our previous data collected with the monoptic Standing Wave in the LGN and area V1 (Macknik et al.,

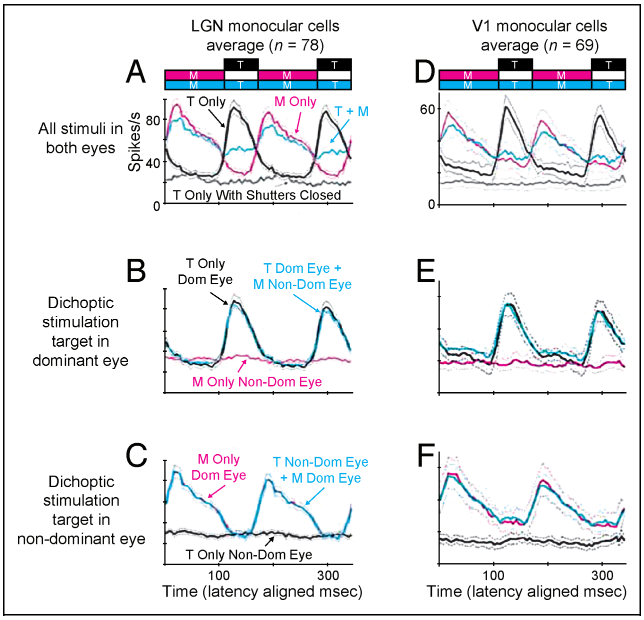

Figure 2. Physiological correlates of monoptic and dichoptic visual masking in monocular neurons of the LGN and area V1 of primates. (A) Stimulus-triggered average response from 78 LGN neurons (latency aligned to peak firing rate) to target only (black histogram), mask only (pink histogram), and target and mask together (blue line; the Standing Wave of Invisibility illusion) presented to both eyes (bin size = 5 msec). Note that during the illusion condition (blue histogram), target responses are inhibited, in correlation with our perception. The gray histogram represents the responses of the cells when a target is presented alone (with the same time course as the target used in the black histogram) while both shutters were closed (when the target turned off, the shutters opened), in the subset of cells tested with shutters. This shows that the shuttering system did not leak when shut, and did not cause large responses when opening. (B) LGN response histograms to the target presented only to the neurons' dominant eye (black line), to the mask presented only to the cells' nondominant eye (pink line), and to the target presented to the cells' dominant eye with the mask being presented to the nondominant eye (blue line; Dichoptic Standing Wave illusion condition). Note that target responses are not inhibited when the mask is presented to the opposing eye, in contrast to human perception and also with monoptic geniculate responses in A. (C) LGN responses when the target is presented only to the neurons' nondominant eye (black line), when the mask is presented only to the cells' dominant eye (pink line), and when the target is presented to the cells' nondominant eye together with the mask being presented to the dominant eye (blue line; illusion condition). The cells thus seem capable of responding to masks when they are presented to the dominant eye only. (D–F) Average responses from 69 area V1 monocular neurons. Color-coding as in A–C.

2000; Macknik & Haglund, 1999; Macknik & Livingstone, 1998). Figure 4 shows the summary statistics (black bars). Masking magnitude was calculated as the difference between the peak of the target-only response and the peak of the target's response in the monoptic masking condition at the same latency, normalized by dividing by the difference between the peak of the target response and the trough of the mask-only response. Overall masking magnitude was similar for all cell types tested (the groups along the abscissa of Figure 4). The effect of masking type (monoptic vs. dichoptic), however, was highly significant (two-way ANOVA of cell type vs. masking type, masking type: $F_{1,420} = 80.54, p < .0001$).

To test the effects of dichoptic masking, we presented a monocular target alone, a monocular mask alone to the opposite eye, and the monocular target and mask presented "separately" to each eye (i.e., the Dichoptic Standing Wave) in trials randomly interleaved with the monoptic trials (Figures 2, 3, and 4, white bars). The dichoptic responses from LGN neurons are shown in Figure 2B. When we presented the Dichoptic Standing Wave illusion so that the target was in the dominant eye and the mask was in the nondominant eye (Figure 2B), the mask did *not* suppress target responses. This result shows that there were no interocular interactions in LGN neurons when using the Dichoptic Standing Wave illusion. There were also no significant interocular interactions, on average, for monocular cells, as well as most of the binocular cells, of area V1 (Figures 2E, 3B, and 4 [the first three columns of white bars as compared to 0]). To ensure that both the mask and the target were each capable of stimulating every neuron monocularly through either eye, we swapped the target and mask to opposing eyes and retested (Figures 2C,F and 3C,F). As expected, neurons responded to the mask, which was now in the dominant eye, but they did not respond to the target, which was in the nondominant eye. Weak dichoptic masking was seen (two-tailed *t* test, $p < .01$)

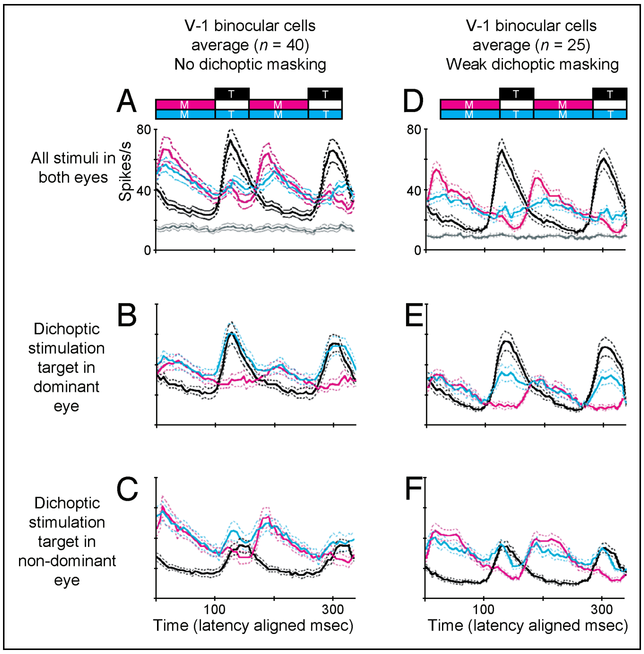

Figure 3. Physiological correlates of monoptic and dichoptic visual masking in binocular neurons of area V1. Color-coding defined in Figure 2A–C. (A–C) Average responses from 40 V1 binocular neurons that did not show target response suppression in the dichoptic conditions. (D–F) Average responses from 25 V1 binocular neurons in which the target response was somewhat inhibited in the dichoptic conditions.

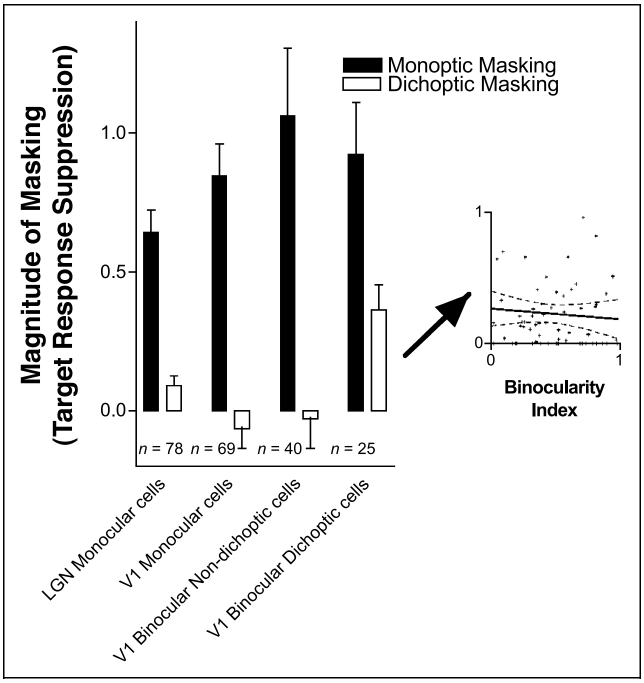

Figure 4. Summary statistics of monoptic vs. dichoptic masking responses in the LGN and area V1. Monoptic (black bars) and dichoptic (white bars) masking magnitude as a function of cell type: LGN, V1 monocular, V1 binocular (nondichoptic masking responsive), and V1 binocular (dichoptic masking responsive) cells. Masking magnitude index calculated as described in the Results section. Inset shows the linear regression of the dichoptic masking magnitude seen in V1 binocular neurons (dichoptic masking responsive) as a function of their degree of binocularity (all neurons displayed here were significantly binocular as measured by their relative response to monocularly presented target stimuli to the two eyes sequentially): BI of 0 would indicate that the cells were monocular, while a BI of 1 means both eyes were equally dominant.

in only one subset of cells comprising less than half of the binocular neurons in area V1 (Figure 3E and Figure 4 [fourth column white bar as compared to 0]). Even in this dichoptic-responsive subset of binocular cells, dichoptic masking was weaker than monoptic masking in every cell; on average, dichoptic masking was only 42% as strong as monoptic masking in the same neurons (matched t test, $p < .01$). This suggests that binocular cells in area V1 are binocular in that they have "excitatory" input from the two eyes, but interocular and intracortical "inhibitory" inputs from each of the two eyes are not as strong.

The Effect of Binocularity on Dichoptic Masking Strength

One might have expected that dichoptic masking effects would be strongest in cells that are most binocular; however, the inset of Figure 4 shows that the linear regression between the binocularity index (BI) of cells and the strength of dichoptic masking seen had a slope of 0 ($r^2 = .007$; taken from dichoptic-responsive cells). BI was determined by first measuring the peak response size to a monocular target in the dominant eye (T_{d}, in our sample there was always at least a small dominance of one eye over the other), and normalizing it to a value of 1, where 0 was the minimal response size during the target condition. The response size of a monocular target in the nondominant eye (T_{n}, assayed at the same latency as T_{d}) was then calculated using the normalization parameters from the dominant eye so that they were at the same scale, BI = $T_{\mathrm{n}}/T_{\mathrm{d}}$. If they were exactly equal (they never were in our sample), BI = 1, whereas if the cells were completely monocular, BI = 0 (in the binocular cells, obviously, this never happened either). Binocular neurons were said to be those neurons with BI > 0.

DISCUSSION

We found that responses to the target in LGN neurons and in most area V1 neurons (both monocular and binocular cells) were suppressed during monoptic masking conditions, but not during dichoptic masking conditions. These results suggest that the monocular neurons of the early visual pathway (LGN and area V1) correlate with "monoptic" masking effects without the benefit of feedback from those binocular neurons that produce "dichoptic" masking effects. If visual masking in these monocular cells had been the product of feedback from the circuits responsible for dichoptic masking effects, then we would have expected the monocular cells' responses to reflect target suppression during dichoptic masking as well. One might suppose that the LGN monocular cells may have received feedback from the monocular cells of area V1, however, we have shown that the monocular cells of V1 (and most binocular cells of V1) do not produce dichoptic masking effects and so do not themselves receive significant feedback from the circuits responsible for dichoptic visual masking. Therefore, the circuits responsible for monoptic and dichoptic masking must exist in at least two places independently, one in monocular circuits and one in binocular circuits. As we know of no extant theories of visual masking that propose that monoptic and dichoptic masking are generated by two different circuits, one that lies in binocular cells and the other that lies solely (and specifically) within the monocular cells of V1 (and not the LGN or retina), we believe that our results support the most parsimonious conclusion: that the circuit underlying visual masking is simple lateral inhibition, which lies in all known circuits of the visual system. We expect that, although the specific timing parameters that underlie the actions of this circuit may vary from tissue to tissue, its fundamental action may be the same everywhere. Moreover, the known presence of lateral inhibition in different brain areas may explain the existence of the various and disparate types of visual masking that are known to exist. If lateral inhibition is the basis of the many different modes of masking, it may also be the basis for many nonvisual masking (and other cognitive masking-like) effects.

Significance for Models of Visual Masking

Lateral Inhibition

Our current and previous results support the idea that simple lateral inhibitory circuits, the very bases for receptive field structure, can explain the mysterious timing patterns of visual masking. We have shown that activity correlated to a target occurs as transient bursts of impulses in response to the onset and termination of the target (its temporal edges) within neurons that have receptive fields located at the spatial edges of the target (Macknik et al., 2000; Macknik & Haglund, 1999; Macknik & Livingstone, 1998). Spatio-temporal edges of masks also cause onset-responses and after-discharges. Visual masking occurs when the spatio-temporal responses to the mask suppress, through a lateral inhibitory connection, the spatio-temporal responses to the target; the target then has less activity with which to encode its perceptual signal and is thus degraded, becoming less visible. Previous models have proposed lateral inhibitory circuits as the basis of masking (Francis, 1997; Weisstein et al., 1975; Bridgeman, 1971; Weisstein, 1968), however, these models did not show responses that correlated with more recently discovered human psychophysical parameters showing the importance of spatio-temporal edges to the visibility, and invisibility, of both the target and the mask (Macknik et al., 2000; Macknik & Livingstone, 1998). Herzog has recently developed a new family of visual masking illusions called "shine-through" in which targets are suppressed (or not) as a function of timing and the number of bars in a mask grating (Herzog & Fahle, 2002; Herzog, Fahle, & Koch, 2001; Herzog & Koch, 2001; Herzog, Koch, & Fahle, 2001). The same group has developed a computational lateral inhibitory model of visual masking that predicts the importance of the spatio-temporal edges (Herzog & Fahle, 2003).

Dual-Channel Models of Masking

Dual-channel circuits come in several forms but all of them suggest that information about the mask, traveling through one "channel" of the early visual system, inhibits the responses to the target, traveling through a different channel of the early visual system (Purushothaman et al., 2000; Paradiso & Nakayama, 1991; Breitmeyer & Ganz, 1976). These models fail to predict recently discovered timing parameters of visual masking, however, and they moreover are described as requiring cortical circuits to operate. As the known timing parameters of visual masking are not met by these models and, moreover, the results of the present study show that visual masking circuits exist in the retina and/or LGN without feedback, we conclude that dual-channel models cannot explain visual masking.

Feedback Models

Di Lollo, Enns, and Rensink (2000, 2002), Enns and Di Lollo (1997), and the Lamme group (Lamme & Roelfsema, 2000; Lamme et al., 2000), have proposed models of visual masking that require extrastriate feedback within cortical circuits. Enns (2002) furthermore claims specifically that the Standing Wave illusion used in the present study must be explained by high-level cortical circuits. The Enns and Di Lollo groups' experimental results show that targets of a given shape are best masked by a mask of a similar shape, and that, although this type of masking only occurs when the target is not attended to, the masks do not need to be spatially near to the target (as they do with the Standing Wave of Invisibility). However, the effect of mask shape can be explained more parsimoniously by lateral inhibitory circuits in object level processing areas of the visual system: Neurons that process similar shapes are known to be clustered (Wang, Tanaka, & Tanifuji, 1996), and so one would expect that a lateral inhibitory network within IT would give rise to masking-like effects that had object-centered parameter space rather than retinotopic parameter space. The results of the Enns and Di Lollo group also show that common onset of the target and mask results in masking, and argue that this is a feature of their object substitution masking model that is unexplained by other models. However, long duration common-onset masks have been shown by our group to cause masking, and to be most parsimoniously explained by a lateral inhibition model (Macknik et al., 2000; Macknik & Livingstone, 1998). Thus, our "spatio-temporal lateral inhibition" model of masking could work in retinotopic, object, or any other space that can be represented in a neural circuit, which depends solely on the inputs to the circuit, and not on feedback. Similarly, the Lamme group's studies conclude that visual masking occurs in area V1 as the result of feedback from the extrastriate cortex.

To the contrary of these groups' predictions, our main result shows that visual masking can occur within subcortical circuits that do not receive feedback from levels of the brain that process dichoptic masking. While we therefore disagree with the conclusions of these previous studies, their experimental results do not contradict those of the present study, as their results can also be explained by one of the most prevalent circuits known to exist in the brain: lateral inhibition.

Other Physiological Results of Masking

Thompson and Schall (1999, 2000) recorded from single units in the frontal lobes of the awake monkey and concluded that visual masking effects cannot be processed in the early visual system, but are instead processed at level of the frontal eye fields (FEFs). They suggested that the neural correlate of visual masking is the "merging" of target and mask responses, rather than the inhibition of target responses. However, as their target was almost 300 times dimmer than their mask, the target and mask responses could have merged because of the differential latencies one would expect from a dim and a bright stimulus (Gawne, Kjaer, & Richmond, 1996; Albrecht & Hamilton, 1982). This latency confound, combined with the SOAs used in this study (which approximated the latency difference one would expect from a ×300 luminance difference), made it impossible for the authors to differentiate whether the target was inhibited by the mask, or whether the mask's larger response occluded the latency-delayed contemporaneous dim-target response. (In our experiments, our stimuli were specifically designed to avoid this confound because the target and mask were of equal contrast.) Furthermore, when the authors used either very long or short SOAs, in which the target and mask responses could be differentiated in time, they found that it was the "mask's" response that was suppressed rather than the "target's"; this is the opposite of what one expects in visual masking. Finally, the monkey's task was to detect a blue target against a field of white distracter masks, and so it is possible that differential attentional effects on the target and mask responses would suppress the mask but not the target; these types of attentional effects are known to exists in the FEF and other parts of the brain when the primate is trained to direct its attention to particular colored stimuli (i.e., the target) and ignore others (i.e., the mask) (Bichot & Schall, 1999; Reynolds & Desimone, 1999). Thus, it is possible that their results are further confounded by the effects of selective attention, rather than being a function of visual masking effects.

The Role of Cortical and Intrathalamic Feedback

Cortical and intrathalamic feedback is thought to play a concerted role in gating and modifying activity in the LGN. LGN activity is moreover modulated by level of arousal (Sanchez-Vives & McCormick, 1997; McCormick, 1992; Livingstone & Hubel, 1981). Our results have no bearing on the idea that thalamocortical circuits are gated through feedback to gate ascending sensory information, such as to modulate arousal or to cause other effects unrelated to visibility.

Studying Visibility without Animal Psychophysics

As with most of the other physiological studies discussed here, our study examines the underlying mechanism of visual masking without having simultaneously measured the perception in the subject animal. Our results address the nature of the circuits, rather than the animal's state of perception. However, the perception of visual masking is known to be equivalent in monkeys and humans from previous studies (Bridgeman, 1980). Moreover, we have measured previously the retinotopic representations of the Standing Wave illusion with optical imaging techniques in the anesthetized monkey (Macknik & Haglund, 1999), and these representations also match human perception.

Although the human and primate experiments presented in this study are not intended to be directly correlated to each other, the Standing Wave illusion was the first percept that we know of to have been predicted in humans based on the physiological responses in primates, rather than the other way around. The illusion was discovered by reasoning that, because specific timing between the target and the mask can cause the suppression of the target's onset response in forward masking and the after-discharge in backward masking in primates, then it should be true that by combining these stimuli, all transient responses to a perpetually flickering and salient target would be largely suppressed in humans, resulting in a novel human illusion (the Standing Wave of Invisibility) (Macknik & Livingstone, 1998). The underlying assumption, of course, is that primate physiology in the early visual system is very similar to that of humans, which we feel is reasonable and the very cornerstone of primate visual research. Although there are many examples of direct and indirect correlation of human perception to neuronal activity in primates, we do not know of any previous novel human illusory percepts that have been "predicted" by the physiological responses found in primates.

This new method of predicting human perception as a function of monkey physiology is a potentially powerful addition to the currently applied methods used to establish the relationship between neural activity and perception by using correlation; correlations are only meaningful in their power to predict. It is further justified to assume that perceptual masking occurs in these same conditions in monkeys because the targets' correlated response in the geniculocortical system is suppressed when target masking is evident to humans, whereas target responses are not suppressed when targets are visible to humans; we see it as unlikely that responses that have been suppressed at the level of the LGN in primates could somehow be regenerated later in the visual system to produce the perception of targets.

The Relationship of These Results to Our Understanding of Visual Awareness

If the physiology of the early visual system in primates is in fact similar to that of the human visual system, then these results suggest that geniculocortical cells correlate with perception in some circumstances, but not in others, and so the activity in the LGN and area V1 cannot by itself maintain visual awareness.

Inhibitory and Excitatory Inputs to Binocular Cells

Surprisingly, we found that binocular cells in area V1 could receive strong excitatory input from both eyes (thus defining them as binocular), yet an excitatory response from a monocularly presented target was rarely suppressed (and weakly, if so) by the action of a mask presented to the other eye, even though the target responses were robustly suppressed by monoptic masks in these same binocular neurons. This suggests that interocular excitatory inputs to area V1 binocular cells are strong, whereas interocular inhibitory inputs to these cells are weak.

The monoptic masking results presented here (Figure 4) show that the strength of monoptic masking increases, as if iteratively, with each successive stage of processing in the visual system. Correspondingly, Hubel and Wiesel (1961) found that inhibitory surrounds were stronger in the LGN than in the retina. These patterns of results suggest that lateral inhibition mechanisms may gather strength iteratively in successive stages of the visual hierarchy, as a general principle. In fact, the sequential build up of lateral inhibition at each step in the visual hierarchy that bears its own lateral inhibition circuit seems to us to be a mathematical certainty, unless some heretofore undiscovered process that somehow undoes the effects of previous lateral inhibition circuits exists in the brain.

Thus, the result that we present here (Figure 4), showing that dichoptic inhibition is weak in area V1, may be a reflection of such a general principle because these area V1 binocular neurons represent the first stage where dichoptic inhibition could exist in the ascending visual system. If this is true, we would expect that subsequent binocular neurons in the visual hierarchy should show iteratively stronger dichoptic masking suppression effects. Whether these effects represent the discovery of a general principle of inhibitory iterative processing in the visual system, or not, we believe that it must be true that dichoptic masking effects become stronger downstream of V1, to account for the fact that the overall psychophysical magnitude of dichoptic visual masking is equivalent, or possibly stronger, than that of monoptic masking (as shown in Figure 1). These results are supported by psychophysical findings suggesting that stereo matching precedes dichoptic masking (Harris & Willis, 2001; McKee, Bravo, Taylor, & Legge, 1994).

The fact that binocular cells of V1 have stronger interocular excitatory inputs than inhibitory inputs is moreover relevant to the understanding of various studies of binocular rivalry and flash suppression in area V1 (Wilke, Logothetis, & Leopold, 2003; Tong & Engel, 2001; Tong, Nakayama, Vaughan, & Kanwisher, 1998; Sheinberg & Logothetis, 1997; Leopold & Logothetis, 1996, 1999; Logothetis, Leopold, & Sheinberg, 1996). Implicit to interpreting the results of these studies in their relevance to mechanisms underlying visual awareness is the assumption that the circuits underlying binocular neurons express interocular suppression. However, our discovery that the binocular circuits of V1 show weak or nonexistent interocular dichoptic suppression suggests that the circuits of V1 may be fundamentally unable to exhibit strong interocular inhibition. If so, then binocular rivalry or flash suppression within area V1 may not be feasible mechanistically, and thus the use of binocular rivalry or flash suppression stimuli for testing neuronal response correlations with visual awareness would be inappropriate in neurons in which the strength of interocular suppression has not been assessed directly. Unlike these other dichoptic methods, visual masking illusions avoid this confound because masking occurs both monoptically and dichoptically and so the role of interocular suppression can be directly assessed in each cell directly.

METHODS

Psychophysical Methods

To generate dichoptic stimuli, human subjects wore goggles that housed ferromagnetic liquid crystal shutters (DisplayTech Longmont, CO), which decreased light transmittance by more than 1200 times when shut (when open the shutters have 30% transmittance). These shutters opened and closed in less than 70 μsec, and were shut continually over the appropriate eye during stimulus presentations that were to be blocked (rather than shuttered in syncopation with every other monitor frame as with stereo vision goggles). Psychophysical stimuli were black on a white background, and procedures (approved by the Harvard Medical School Committee on Human Studies, docket number X062896-2) have otherwise been described previously (Macknik et al., 2000; Macknik & Livingstone, 1998).

Physiological Methods

Standard electrophysiological techniques for recording from awake behaving primates and for minimizing the monkeys' discomfort were employed (Macknik et al., 2000; Livingstone, 1998; Macknik & Livingstone, 1998; Livingstone, Freeman, & Hubel, 1996). The Harvard Medical Area Standing Committee on Animals (protocol #02078) approved all experimentation. Physiological stimuli were presented on a NEC 5FG monitor at a refresh rate of 100 Hz. The monitor subtended 59° × 40° at a viewing distance of 28 cm. The dimensions of the target (a single oriented bar) were optimized for each cell. Masks were given the same characteristics as the targets and they flanked and abutted, but did not spatially overlap, the targets.

To present targets and masks to separate eyes, we used either colored stimuli with matched red–green or red–blue anaglyph lenses (optimized for the monitor's red, green, and blue phosphors), or we used fast shutters made of ferromagnetic liquid-crystals (LCD) that could be controlled independently for each eye. LCD shutters and colored lenses have complementary weaknesses and strengths for creating dichoptic stimuli, but they both rendered identical results, so we pooled the data for the analysis.

The shutter system had the advantage that the target and the mask could be of the same color and contrast, giving the assurance that the results were not an epiphenomenon of differences in stimulus parameters between target and mask. The disadvantage of the shutter system was that we could use only white stimuli on a black background, and therefore we could test only on-center neurons in the LGN. The reason for this was that cells (whether they were on- or off-center) tended to fire to the shuttering of the goggles when the background was illuminated, as it would be with black stimuli on a white background. We moreover made the stimuli very dim (the monkeys wore an additional 2 log-unit neutral density filter over each eye) when using the shutters, so that neurons would not fire in response to shuttering in the face of phosphor persistence after stimuli had already been turned off (to which neurons in the LGN can be very sensitive). This resulted in very long latency responses (~100 msec) associated with low-contrast stimuli (Gawne et al., 1996; Albrecht & Hamilton, 1982). All stimuli, when using the shutters, were white (100% contrast without neutral density filters) against a background of black in a blackened room (CIE $x = 0.287, y = 0.333$, 0.34 cd/m^2 with the shutters open and neutral density filter in place over both eyes).

The colored filter system had the advantage that we could use bright, high-contrast stimuli and we could record from either on- or off-center neurons, while rendering latencies that were in keeping with more familiar geniculate responses (~35–50 msec) (Gawne et al., 1996; Albrecht & Hamilton, 1982). Red stimuli had a luminance of 0.93 cd/m^2 to the eye with the red filter and 0.0086 cd/m^2 to the eye with the blue filter; blue stimuli were roughly equivalent to red stimuli and had a luminance of 0.89 cd/m^2 to the eye with the blue filter and 0.0072 cd/m^2 to the eye with the red filter. Red and blue stimuli thus differed from each other in luminance by only 4% and leaked into the wrong eye by less than 1%.

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