Articles in PresS. J Neurophysiol (November 30, 2005). doi:10.1152/jn.00781.2005

Which visual pathways cause fixation-related inhibition?

Petroc Sumner, Parashkev Nachev, Sarah Castor-Perry, Heather Isenman,

and Christopher Kennard

Department of Visual Neuroscience, Division of Neuroscience, Faculty of Medicine, Imperial College London, St Dunstan's Road, London W6 8RP, UK

Running head: Visual pathways for fixation-related inhibition

Address correspondence to:
Petroc Sumner, p.sumner@imperial.ac.uk.
Dept Visual Neuroscience (room 10L15a)
Division of Neuroscience
Faculty of Medicine, Imperial College London
St Dunstan's Road, London W6 8RP
+44 20 8383 0584 (office)
+44 20 8846 1670 (shared fax)
+44 7855 813753 (mobile)

Abstract

Visual stimuli can inhibit as well as activate motor mechanisms. In one well known example, the latency of saccadic eye movements is prolonged in the presence of a fixation stimulus, relative to the case in which the fixation stimulus disappears before the target appears. This automatic sensory-motor effect, known as the gap effect or fixation offset effect, has been associated with inhibitory connections within the superior colliculus (SC). Visual information is provided to the SC and other oculomotor areas, such as the frontal eye fields (FEF), mainly by the magnocellular geniculostriate pathway, and also by the retinotectal pathway. We tested whether signals in these pathways are necessary to create fixation-related inhibition, by employing stimuli invisible to them. We found that such stimuli, visible only to short wave sensitive cones (S cones), do produce fixation-related inhibition (including when warning effects were equated). We also demonstrate that this fixation-related inhibition cannot be explained by residual activation of luminance pathways, and must be caused by a route separate from that of luminance fixation signals. Thus there are at least two routes that cause fixation-related inhibition, and direct sensory input to the SC or FEF via the magnocellular or retinotectal pathways is not required. We discuss the implications that there may be both cortical and collicular mechanisms.

Introduction

Behaviour depends upon complex interactions between initiation and restraint, even for relatively simple saccadic eye movements towards visual stimuli. While non-foveal visual events cause automatic elicitation of orienting activity (Hess et al. 1946), foveal stimuli inhibit eye movements. Such fixation-related inhibition has been popularly indexed by a simple paradigm: Participants make saccades to peripheral stimuli while a fixation stimulus either stays on ("overlap condition") or disappears just before the saccade target appears ("gap condition"). Saccadic latency is reduced in the gap condition, and this is known as the gap effect or fixation offset effect (Reuter-Lorenz et al. 1991; Saslow 1967). If, in contrast, the fixation stimulus becomes brighter or larger just before a saccade, latency is increased (e.g. Pratt et al. 2000).

The gap effect has become associated with inhibitory connections in the superior colliculus (SC), a midbrain centre that makes the major input into the brainstem saccadic generator (e.g. Dorris et al. 1997; Isa 2002; Munoz et al. 2000; Munoz and Istvan 1998; Sparks 2002). "Fixation cells", located in the rostral pole of the SC, are active in response to foveal stimuli, and are thought to inhibit "saccade cells" located caudally in the intermediate layers (e.g. Dorris et al. 1997; Munoz and Fecteau 2002; Munoz and Istvan 1998; Munoz and Wurtz 1992). Alternatively or additionally, the SC fixation cells may suppress saccadic initiation via omnipause neurons in the pontine reticular formation (Takahashi et al. 2005).

Cortical areas such as the frontal eye fields (FEF) also seem to play a role. Some FEF cells are active during fixation (e.g. Hanes et al. 1998), while other cells show a correlate of disengagement from fixation (Dias and Bruce 1994). The FEF makes a large projection to the intermediate and deep layers of the SC, both directly and via the basal ganglia, and is thought to exert an important regulatory influence on the SC (e.g. Everling and Munoz 2000; Hikosaka and Wurtz 1989; Krauzlis 2005; Schall 1997; Segraves and Goldberg 1987). The FEF also makes direct projections to brainstem nuclei (e.g. Izawa et al. 2005). Similarly, the lateral intraparietal area (LIP in monkey, possibly corresponding to the human parietal eye field) makes considerable projections both to the SC and to other oculomotor nuclei in the brainstem (e.g. Krauzlis 2005; Pare and Wurtz 1997). Thus cortical areas have the potential both to modulate collicular mechanisms, and to mediate fixation-related inhibition independently or upstream of the SC.

While the gap paradigm has been used widely in the context of motor production, little attention has focussed on the neural pathways that may supply the *visual* information to the saccade system. One possibility is that fixation-related inhibition is caused by visual signals reaching the SC directly (and the contribution of cortical areas may be to modulate this collicular mechanism). Alternatively, the gap effect may be caused by visual information reaching cortical oculomotor mechanisms, and the

observed patterns of collicular activation may occur downstream. Thirdly, various visual pathways may supply input to two or more inhibitory mechanisms, which each produce fixation-related inhibition in their own right.

There are several ways in which visual information can reach the SC without involving the cortical eye fields. The most direct way is via the retinotectal pathway, which projects directly from the retina to the superficial layers of the SC. The role of this pathway remains debated, with suggestions including eye movements, attention and even fear perception (Morris et al. 1999; Rafal et al. 1991; Rafal et al. 1990). There are also projections from primary visual cortex to the SC superficial layers (e.g. Sparks 1986). These sensory superficial layers are arranged in a spatial map in which cells responding to foveal stimuli are aligned with the fixation cells in the intermediate layers (Schiller and Stryker 1972), whose activity is thought to cause fixation-related inhibition (e.g. Dorris et al. 1997; Munoz and Istvan 1998). However, it is not yet clear how strong the interlaminar connections are between the sensory cells and the fixation cells (e.g. Isa 2002). The intermediate layers themselves receive projections from extrastriate areas of visual cortex, and also from parietal, frontal and temporal areas (e.g. Sparks 1986). To take one example, middle temporal and medial superior temporal areas (MT/MST), which are associated with motion perception, make strong collicular projections that are important for pursuit eye movements (e.g. Krauzlis 2005). Since fixating a stationary stimulus and fixating a moving one may share neural mechanisms, this extrastriate projection may contribute to fixation-related inhibition.

The visual signals travelling to the SC via any of the cortico-collicular pathways seem to rely on activity in the magnocellular geniculostriate pathway. Schiller et al. (1979) found that inactivating the magnocellular laminae of the LGN reduced or eliminated visually driven activity in all collicular cells except those in the superficial layers driven directly by the retinotectal pathway. Inactivating the parvocellular laminae had no effect (Schiller et al. 1979), and converging evidence has shown that the initial sensory activity in SC cells does not distinguish colours (Marrocco and Li 1977; Ottes et al. 1987). Colour-specific activity develops later if colour-defined stimuli are targets for saccades, presumably following target selection in cortical areas (Ottes et al. 1987). In this sense, colour pathways seem to influence the SC only via some intervening oculomotor processing that selects saccade targets.

Likewise, the initial sensory activity in FEF seems to come from magnocellular signals, since it occurs with a short latency similar to the activation latency of areas MT and MST (mean 75 ms), and shorter than the mean latency in areas V2 and V4 (82 and 104 ms) (Schmolesky et al. 1998). More importantly, sensory cells in the FEF have not been found to show colour or form sensitivity (e.g. Stuphorn and Schall 2002; Thompson and Bichot 2005), despite the known projections to FEF from temporal cortex, for example. This suggests that, similar to the case of the SC, if chromatic signals are

to influence FEF processing, they must pass through a process that abstracts colour information into signals about targets for oculomotor plans. Fixation related-inhibition may occur as part of this target selection process that turns chromatic visual information into oculomotor information *before* it reaches the FEF or SC.

Thus, while information from all visual pathways may contribute to *oculomotor* input to the SC and FEF, it seems that *visual* activity in these sites relies on the magnocellular pathway and the retinotectal pathway. If fixation-related inhibition is mediated within the SC or FEF, based on direct visual input from the fixation stimulus, one might expect such visual information to be transmitted by either the retinotectal pathway or the magnocellular pathway. The aim of our study was to test this hypothesis. We employed stimuli that were invisible to both the retinotectal pathway and the magnocellular pathway (Sumner in press; Sumner et al. 2002; Sumner et al. 2004). These stimuli were colour changes visible only to the short-wave sensitive retinal cone receptors (S cones), exploiting the fact that electrophysiological studies have consistently reported that there are no projections to the SC from S cones (de Monasterio 1978; Marrocco and Li 1977; Schiller and Malpeli 1977). The colour changes were embedded in a background of spatial and temporal luminance noise, making them additionally invisible to the magnocellular pathway from retina to cortex, as it is not colour opponent and receives little if any input from S cones (Calkins 2001; Chatterjee and Callaway 2002; Gouras 1968; Stockman et al. 1991; Yeh et al. 1995). Therefore neither the retinotectal nor the magnocellular pathway should be able to distinguish the S-cone stimuli from the background, and fixation-related inhibition mediated by these pathways should not occur.

Experiment 1

In Experiment 1, we replicated the standard gap effect for a luminance fixation stimulus and tested whether the gap effect occurs with an S-cone fixation stimulus – i.e., when the fixation stimulus is invisible to both the direct retinotectal pathway to the SC, and to the magnocellular pathway, which supplies the main projection to the SC from the visual cortex.

Materials and Methods

Participants.

8 participants were employed (4 male, 4 female, aged 18-29). All subjects had normal or corrected to normal acuity and normal colour vision.

Apparatus.

Stimulus presentation was performed by a PC-controlled Cambridge Research Systems (CRS) ViSaGe directly connected to a 21” Sony GDM-F520 Trinitron monitor. Stimulus presentation was synchronized with the screen refresh rate of 100 Hz, and timings were controlled and measured by the

CRS clock and thus not subject to the errors produced by normal PC operating systems. The ViSaGe specifies colours with a resolution of 14 bits per gun and the monitor was calibrated using a CRS ColourCal colorimeter. Eye movements were recorded using an Applied Science Laboratories (ASL) model 504 high speed remote infra-red eye-tracker with an ASL 5000 series controller, which samples eye position at 240 Hz (chin and head rest also by ASL). Both vertical and horizontal displacement were measured.

S-cone stimulus calibration.

S-cone stimuli are colour transitions that leave unchanged the signals of long-wave (L) and middle-wave (M) sensitive cones, while affecting the signal in short-wave cones. The exact colour transitions that do not affect L and M cones differ between individuals, and between retinal locations, because of variations in cone sensitivity, macular pigment, lens optical density and chromatic aberration. Therefore the S-cone stimuli were calibrated individually for each participant. A standard grey was chosen (MacLeod-Boynton colour coordinates, MB, 0.65, 0.02; luminance, 25 cdm^{-2}) and colour transitions from this grey were represented as angles in MacLeod-Boynton colour space. The theoretical S-cone angle is zero degrees for foveal stimuli (a transition from grey to lilac-blue).

The calibration procedure for each participant took 30-60 minutes and was as follows: First the luminance of the candidate range of colours was psychophysically matched to the standard grey (25 cdm^{-2}) using the minimum motion procedure introduced by Anstis and Cavanagh (1983). Second, in order to find the colour angle that would not stimulate L and M cones, these colour angles and their corresponding luminance values were used in the transient tritanopia procedure developed by Smithson et al. (2003), adapted so that the potential S-cone stimuli were only 0.4° from fixation. In this procedure, coloured patches must be detected amongst grey patches while the S-cone chromatic pathway has been made insensitive by the offset of a yellow adapting field. Thus performance is poorest for a colour that cannot be differentiated from the grey using the L-M chromatic pathway. The colour angles used ranged from -15° to +15°, first in 5° steps and then 2° steps in a MacLeod-Boynton colour space whose axes were scaled so that threshold distances in the S and L-M directions were approximately equal. The S-cone angle was selected to the nearest degree and finally the minimum motion procedure was used again to check the luminance match of the chosen colour to the standard grey.

Gap paradigm procedure.

The experimental paradigm is illustrated in Supplementary Figure S1. The task was to detect small dark grey squares appearing 8° to the left or right of fixation, and make a saccade as quickly as possible to these targets. Before each target occurred, participants were required to fixate a central square that differed from the background in colour or luminance. The background was a patchwork of grey squares (0.8° across) that created an environment of luminance noise. The luminance of each

square changed every 50 ms throughout each trial, to a value chosen at random between 24.5 and 25.5 cdm^{-2}. The luminance fixation stimulus was created by shifting the mean luminance of the central square to 30 cdm^{-2} (with random flicker range between 29.5 and 30.5 cdm^{-2}). The S-cone fixation stimulus was created by shifting the chromaticity of the central square in the direction of the S-cone colour angle calibrated as described above, creating an 80% increase in S-cone signal (with luminance flicker still occurring in the range between 24.5 and 25.5 cdm^{-2}).

The saccade target appeared on each trial at a time chosen randomly from between 500 ms and 900 ms following presentation of the background squares and fixation square. The target was the darkening to 15 cdm^{-2} of the square 8° either to the left or right of fixation. There were four types of fixation condition: luminance overlap, in which a luminance fixation stimulus remained present for the duration of the trial; luminance gap, in which the fixation stimulus disappeared (i.e. returned to randomly flickering grey between 24.5 and 25.5 cdm^{-2}) 200 ms before the onset of the target; S-cone overlap, in which an S-cone fixation stimulus remained present; and S-cone gap, in which the S-cone stimulus disappeared 200 ms before target onset.

Participants were informed that the fixation stimulus would flicker, and sometimes disappear and sometimes stay on, and were instructed to ignore this and just try to detect the target onset. The screen stopped flickering 500 ms after the target appeared, and the next trial began 1000 ms later with presentation of the fixation stimulus, at which time the patchwork of squares began flickering again. After a short period of demonstration and practice (40 trials), 480 trials were completed by each subject, with breaks every 40 trials to allow rest and free eye movements. Thus there were 120 trials of each of the four fixation conditions – with equal numbers of each associated with left and right saccade targets – presented in a random order.

Analysis

The criterion for saccade detection was a velocity of $60°s^{-1}$, and saccadic onset was defined by a velocity > $22°s^{-1}$. Eye-position traces were inspected for all trials to check that the custom Matlab routine had correctly located saccades. Saccades with latencies between 80 and 500 ms were accepted as responses to the target, and trials were discarded in which fixation was not maintained preceding target presentation. That is, trials were included in the latency analysis only if the first saccade larger than 0.5° occurred between 80 and 500 ms after target presentation, and approached the target with an accuracy of within 2°. This was achieved in over 90% of trials in all experiments. Trials were counted as errors if the first saccade following target presentation was in the opposite direction to the target, or if no response was made (<2% of trials in all experiments).

Results

The results showed that latencies for gap trials were considerably shorter than for overlap trials – the standard gap effect. There was little difference between the effect of a luminance offset at fixation or an S-cone offset at fixation (see Figure 1). This was confirmed with a 2-way ANOVA with factors of gap (gap vs overlap) and colour (luminance vs S-cone). There was a main effect of gap ($F(1,7)=35.8$, $p<0.001$) but no effect of colour, and no interaction between the gap effect and the colour of the fixation stimulus ($F(1,7)=2.1$, $p=0.19$).

The crucial result is that there was an S-cone gap effect – that the offset of a stimulus invisible to the retinotectal and magnocellular pathways still had the standard effect of reducing saccadic latency. Thus the gap effect does not require sensory signals in either the retinotectal or magnocellular pathways.

Experiment 2

The S-cone gap effect found in Experiment 1 may be explained in two ways. First, there may be true fixation-related inhibition produced by signals in the S-cone pathway. Second, the S-cone fixation offset may simply serve as a warning that a target is imminent. As might be expected, it is known that some of the simple gap effect can be attributed to warning that a stimulus is about to appear, which is sometimes referred to as a nonspecific motor preparation effect (e.g. Kingstone and Klein 1993; Klein et al. 1995; Taylor et al. 1998). However, several studies show that there is also a component related specifically to the presence or absence of a visual fixation stimulus, indexing true fixation-related inhibition. For example, while a highly predictive warning tone reduces saccadic latency, a non-predictive (temporally varied) fixation offset reduces latency further (Pratt et al. 2000; Reuter-Lorenz et al. 1995; Taylor et al. 1998). This additional effect occurs for offsets at or near fixation but not for visual offsets 2° or more from fixation (Fendrich et al. 1999; Taylor et al. 1998). An alternative to using a warning tone is to have the fixation stimulus undergo a change that supplies visual warning without an offset. For example, Pratt et al. (2000) found that abruptly reducing the fixation stimulus in size reduced latency and an increase in size prolonged latency, even though both manipulations provided visual warning. The term “fixation offset effect” is often used to refer exclusively to the non-warning component of the gap effect (e.g.Pratt et al. 2000).

In Experiment 2 we tested whether the S-cone fixation stimulus provides fixation-related inhibition over and above any warning effect. To this end, we employed a change at fixation on every trial, rather than just on gap trials (see supplementary movie 2). If the S-cone gap effect was due to warning, and any true fixation-related inhibition was restricted to retinotectal or magnocellular sensory signals, then it should not matter whether a luminance fixation stimulus disappears, or whether it changes into

an S-cone stimulus (i.e. one that differs from the background only in the S-cone colour direction). Neither the retinotectal pathway nor the magnocellular pathway should differentiate between these two conditions, as they would not signal the difference between the S-cone stimulus and the flickering background squares. Both the luminance decrement and warning element is the same in each condition. If, on the other hand, S-cone stimuli cause true fixation-related inhibition, we predict that latencies should be longer when a luminance fixation offset is accompanied by an S-cone fixation stimulus onset, compared to when the luminance fixation stimulus simply disappears. All aspects of the apparatus, calibration, procedure, and analysis were identical to Experiment 1, except where specified below.

Materials and Methods

Participants.

8 participants were employed (3 male, 5 female, aged 18-26). All subjects had normal or corrected to normal acuity and normal colour vision, and none had participated in Experiment 1.

Procedure

The overlap conditions in Experiment 1 were replaced with "fixation change" conditions, in which the fixation square changed from a luminance stimulus to an S-cone stimulus or vice versa, 200 ms before target onset. Thus there were four conditions: luminance offset, as in Experiment 1; S-cone offset, as in Experiment 1; luminance-to-S-cone change; and S-cone-to-luminance change (see Supplementary Figure S2). Again, participants were informed that the fixation square would flicker and change, but to try to ignore this and simply detect the target and move their eyes to it as quickly as possible.

Results

Since there was a change at fixation 200 ms before every target, the warning effect in all conditions should be equivalent. The only exception might be the S-cone offset condition – the S-cone pathway is known to be slower than luminance pathways (Smithson and Mollon 2004) and to have lower temporal resolution (Brindley et al. 1966), potentially leading to a weaker warning effect and longer latencies. Thus the warning explanation predicts equal latencies for all conditions containing a luminance change at fixation (i.e. the two change conditions and the luminance offset condition). Figure 2 shows that this was not the case.

The crucial comparison is between the luminance gap condition and the luminance-to-S-cone change condition. These are equated in both warning effect and in the luminance decrement visible to the retinotectal and magnocellular pathways. However, latency for the luminance-to-S-cone condition was significantly prolonged compared to the luminance gap condition ($t = 3.5$, $df = 7$, $p < 0.01$). Therefore S-cone stimuli must cause fixation-related inhibition.

It is also interesting to compare the two change conditions. If the luminance and S-cone stimuli produced equal fixation-related inhibition then latencies should be equivalent whether the change in fixation was from luminance to S-cone or vice-versa. In fact the S-cone-to-luminance change produced significantly longer latency than the luminance-to-S-cone change ($t = 3.8$, $df = 7$, $p < 0.01$). Thus the S-cone stimulus produced less fixation-related inhibition than did the luminance stimulus, consistent with the idea that signals reaching the SC directly might cause a greater effect.

Experiment 3A

Experiment 2 showed that S-cone stimuli do produce true fixation-related inhibition, and that the S-cone gap effect could not be explained only by a warning effect. In addition, Experiment 2 showed that the S-cone stimuli had a lesser effect than the luminance stimuli on saccadic latency. The next question is whether the S-cone stimuli have their effect via a distinct route from the luminance stimuli, or whether the S-cone stimuli are in fact behaving like luminance stimuli of lower contrast. Our S-cone stimuli were designed to be visible only to the S-cone colour opponent channel, which projects to layers 3B and 4A of the primary visual cortex, via small and large bistratified ganglion cells in the retina, and koniocellular layers of the lateral geniculate nucleus (LGN) (Chatterjee and Callaway 2003; Dacey et al. 2003). The exact projections of this colour pathway become less clear in extrastriate cortex, but it is assumed to project to V4 and thence to temporal cortex. However, S cones may make some contribution to the magnocellular pathway (Calkins 2001; Chatterjee and Callaway 2002; Stockman et al. 1991), and although this signal should be masked by luminance noise, it remains possible that the luminance noise in our paradigm was insufficient. It also remains possible that there are unknown S cone projections in the retinotectal pathway. Third, the luminance levels used in these experiments would not prevent all rod activity, which might allow the S cone stimuli to activate the magnocellular and retinotectal channels (although any contribution of rod activity to "S-cone" stimuli should have been minimised by having a psychophysical, rather than computational, calibration procedure, and rod-intrusion should also be masked by the luminance noise).

Thus it remains possible that the S-cone stimuli may cause fixation-related inhibition via the same route as luminance stimuli. If this is the case, the S-cone stimuli should simply behave in the same way as luminance stimuli of low (but unknown) contrast. The key to the logic of Experiment 3 is that this "equivalent-luminance-contrast" of the S-cone stimuli should be fixed if the S-cone fixation stimuli cause their inhibitory effect in the same way as the luminance fixation stimuli. If, however, the S-cone stimuli cause their effect via a distinct route, their relationship to the luminance stimuli need not be fixed, because luminance and colour pathways are known to be non-linear in different ways (e.g. Kaplan and Shapley 1986) and adaptation to luminance contrast and colour contrast can occur independently in post-receptoral pathways (e.g. Pugh and Mollon 1979; Webster and Mollon 1993).

Rather than exhaustively measure the exact "equivalent-luminance-contrast" of fixation-related inhibition caused by S-cone stimuli in different situations, the aim of Experiment 3 was to take advantage of the likely non-linearity in the luminance pathways (e.g. Kaplan and Shapley 1986) to show that the relative "strength" of an S-cone stimulus and a given luminance stimulus can reverse from one simple condition to another. This would prove that the S-cone stimuli do not have a consistent "equivalent-luminance-contrast", and must therefore be transmitted by a different pathway.

Experiment 3A measured the relative inhibitory effects of the S-cone and low luminance stimuli compared to a high luminance stimulus. In two of the conditions in Experiment 3A we employed fixation changes from low to high luminance, or vice versa. It was expected that the high luminance stimulus would cause the most fixation related inhibition, and thus saccade latencies would be greater following a low-to-high-luminance change at fixation compared to the high-to-low condition. The difference in mean latency between these conditions would be the measure of the relative difference in fixation-related inhibition caused by the two stimuli. We also employed fixation changes from the S-cone stimulus to the high luminance stimulus, or vice versa. It was again expected that the high luminance stimulus would cause the most fixation related inhibition, and thus following the S-to-high-luminance change at fixation, saccadic latencies would be longer than in the high-to-S condition. The key question was whether the difference in fixation-related inhibition between the high luminance and S-cone stimuli was greater or smaller than the inhibition difference between the high and low luminance stimuli. If it was smaller, then the S-cone stimulus would seem to create more fixation related inhibition than the low luminance stimulus (Figure 3Ai). If it was larger, the S-cone stimulus would seem to create less inhibition than the low luminance stimulus (Figure 3Aii).

The relative amount of fixation-related inhibition elicited by the S-cone stimuli will be compared across Experiments 3A and 3B. If the S-cone stimuli cause fixation-related inhibition in the same manner as luminance stimuli, then the relative fixation-related inhibition elicited by the S-cone stimuli should not differ between Experiments 3A and 3B (as indicated in Figure 3). Therefore, in Experiment 3A we rank the Low luminance and S-cone stimuli in terms of their inhibitory effect, and in Experiment 3B we test whether this rank remains consistent in other conditions.

Materials and Methods

Participants.

8 participants were employed (3 male, 5 female, aged 22-24). All subjects had normal or corrected to normal acuity and normal colour vision, and none had served in Experiments 1 or 2.

Procedure

All aspects of the apparatus, calibration, procedure, and analysis were identical to Experiments 1 and 2, except where specified below. In all trials there was a change in the fixation stimulus 200 ms before

the onset of the saccade target. There were two types of block: in luminance blocks, the fixation stimulus changed from high luminance (mean 35 cdm^{-2}, randomly flickering over a range of 1.0 cdm^{-2}; see Methods of Experiment 1) to low luminance (mean 28 cdm^{-2}) or vice versa; in S-cone blocks, the fixation stimulus changed from high luminance (mean 35 cdm^{-2}) to an S-cone stimulus (mean 25 cdm^{-2}), or vice versa. As before, the S-cone stimuli were individually calibrated for each participant to differ from the flickering grey background squares only in the S-cone colour direction, creating an 80% increase in S-cone signal. Participants performed 120 trials per block, and three blocks of each type. Again, participants were informed that the fixation square would flicker and change, but were instructed to ignore this and simply detect the target and move their eyes to it as quickly as possible.

Results

Figure 4A shows the results for Experiment 3A. As expected, fixation changes from low to high luminance caused longer saccadic latency than changes from high to low luminance – the difference was 29 ms. Also as expected, fixation changes from S-cone to high luminance stimuli caused longer saccadic latency than changes from high luminance to S-cone stimuli. But crucially the difference, 16 ms, was smaller than the difference produced by low and high luminance stimuli (ANOVA interaction: $F(1,7)=6.5$, $p<0.05$). This indicates that the S-cone stimuli caused more fixation-related inhibition than the low luminance stimuli. That is, the "equivalent-luminance-contrast" of the S cone stimuli was greater than that of the low luminance stimuli.

Experiment 3B

If the S-cone stimuli cause more fixation-related inhibition than do the low luminance stimuli, this predicts that changes at fixation from the low luminance to the S-cone stimuli should cause longer saccadic latencies than changes from S-cone to low luminance (see Figure 3Bi). Experiment 3B tested this prediction using the same subjects and procedure as Experiment 3A (except where detailed below). The prediction ought to be met if the S-cone stimuli cause fixation related inhibition in the same way as the luminance stimuli. In this case it ought to be possible to consistently rank fixation stimuli according to their "equivalent-luminance-contrast" (i.e. the relative effect they have on saccadic latency, see Figure 3). If, however, the S-cone stimuli cause fixation-related inhibition by a different pathway from luminance stimuli, there may be no such consistent ranking, because of differences in adaptation and non-linearity of response. In this case, just because the S-cone stimulus had greater "equivalent-luminance-contrast" than the low luminance stimulus in Experiment 3A, it does not necessarily follow that the S-cone stimulus must always create more fixation-related inhibition than the low luminance stimulus.

Materials and Methods

Participants.

The same 8 participants were employed as in Experiment 3A.

Procedure

All aspects of the apparatus, calibration, procedure, and analysis were identical to Experiment 3A, except that the fixation stimulus changed from low luminance (mean 28 cdm^{-2}) to the S-cone stimulus, or vice versa. Participants performed three blocks of 120 trials each. Again, participants were informed that the fixation square would flicker and change, but to try to ignore this and simply detect the target and move their eyes to it as quickly as possible.

Results

Figure 4B shows the results for Experiment 3B, which are opposite to those predicted by the results of Experiment 3A (see Figures 3A,B and 4A). Fixation changes from S-cone stimuli to low luminance stimuli produced 13 ms longer saccadic latencies than changes from low luminance to S-cone ($t = 3.1$, $df = 7$, $p<0.05$). In other words, the low luminance stimuli created more fixation related-inhibition than did the S-cone stimuli, despite the fact that in Experiment 3A, the S-cone stimuli appeared to be more similar to the high luminance stimuli than did the low luminance stimuli. This result is inconsistent with the idea that the S-cone stimuli achieve their inhibitory effect by the same route as the luminance stimuli. If this was the case there should be a consistent relationship between the effects of each stimulus.

Discussion

Fixation-related inhibition is a fundamental component of gaze control, and has been strongly associated with automatic inhibitory connections in the superior colliculus. We set out to test whether such inhibition relies on visual input to the colliculus either directly from the retinotectal pathway or from the magnocellular pathway via the various cortico-collicular projections. We examined the standard behavioural index of fixation-related inhibition – the gap effect or fixation offset effect – employing both luminance stimuli and stimuli visible only to S cones, which are invisible to both the retinotectal and magnocellular pathways. In Experiment 1 we found a similar gap effect for luminance fixation stimuli and S-cone stimuli. In Experiment 2 we found that this could not be explained by a warning effect, since the presence of an S-cone fixation stimulus prolonged saccadic latency when warning was equated across several conditions. Thus the results of Experiments 1 and 2 showed that fixation-related inhibition can be driven by S-cone stimuli embedded in luminance noise, which should be visible only to the S-cone colour opponent channel (Chatterjee and Callaway 2003; Dacey et al. 2003) and invisible to the retinotectal and magnocellular sensory pathways.

To be sure that the S-cone stimuli cause fixation-related inhibition via a route that is really distinct from the route by which luminance stimuli cause fixation-related inhibition, we conducted Experiment 3. We found that S-cone stimuli do not have a consistent "equivalent-luminance-contrast" – that is, they do not consistently behave like any luminance stimulus of a fixed, though unknown, luminance contrast. S-cone stimuli cannot be ranked in efficacy alongside luminance stimuli, because the S-cone stimulus may in one condition appear to produce more fixation-related inhibition than a certain luminance stimulus (Experiment 3A), but in another condition produce less inhibition (Experiment 3B). These apparently paradoxical results can be explained if the luminance and S-cone signals cause inhibition by separate pathways, and the luminance pathway is highly non-linear. The non-linearity means that relatively small luminance changes can have nearly as much effect as larger luminance changes, and thus the signal from the luminance pathway may be quite similar in all three of our conditions containing luminance increments or onsets: the low-high luminance condition, S-cone-to-high luminance condition, and the S-cone-to-low luminance condition. Any large difference in effect between these conditions must then be explained by signals in another pathway. In this case offset signals in the S-cone pathway oppose the effect of the luminance onset in two of the conditions, but not for the low-high luminance change which had the greatest effect. Thus to explain the results there must be at least two pathways at play with different response properties.

We suggest that many pathways and more than one mechanism may be involved in fixation-related inhibition. Since many studies have linked fixation-related inhibition to inhibitory connections in the superior colliculus (see Munoz et al. 2000, for a review), it seems likely that the direct retinotectal pathway would contribute. The magnocellular pathway is also known to be essential for collicular function (Schiller et al. 1979), and is likely to contribute both through direct collicular projections from primary visual cortex, and through projections via MT/MST and the cortical eye fields (see Krauzlis 2005, for a review). In addition the S-cone stimuli contribute via a different cortical route, which may perhaps be via V4 and the posterior part of the inferotemporal cortex (area TEO), and thence to the frontal eye fields (Schall et al. 1995).

One possibility is that all fixation-related inhibition still occurs in the superior colliculus, and that the S-cone signal is simply delivered to the SC via a less direct cortical pathway than the luminance signal. However, if this were the case, we would expect there to be chromatic sensory responses in the SC, which have not been found. The initial sensory activity in SC cells does not distinguish colours, and differential activity develops only if colour-defined stimuli are relevant for saccades (Marrocco and Li 1977; Ottes et al. 1987). It seems that when eye movement targets are defined by properties to which the SC is not directly sensitive, spatial information about these targets is conveyed to the SC only after some target selection has occurred elsewhere.

Oculomotor target selection processes are likely to involve the frontal eye fields (FEF), which contain both visually driven cells and oculomotor cells, and have inhibitory connections between cells with response fields in different parts of the visual field (e.g. Hanes et al. 1998; Schall 1997; Schiller and Tehovnik 2003; Schlag-Rey et al. 1992; Thompson and Bichot 2005). In general, patients with lesions encompassing the FEF seem to have difficulty inhibiting saccades to inappropriate stimuli (Braun et al. 1992; Guitton et al. 1985; Machado and Rafal 2004a). More specifically for fixation-related inhibition, such patients can show abnormally small fixation offset effects on their contralesional side (Machado and Rafal 2004b). Stimulation in the FEF can suppress saccades (e.g. Izawa et al. 2005) and some cells show fixation related activity (e.g. Hanes et al. 1998), while activity in other cells correlates with disengagement from fixation (Dias and Bruce 1994). Thus the FEF may mediate the gap effect upstream or independently of the SC. Alternatively, rather than being responsible for *creating* automatic fixation-related inhibition, the FEF has been suggested to provide goal-directed modulation of a collicular mechanism. For example, Machado and Rafal (2004b) found that informatively pre-cueing target location modulated the gap effect in healthy participants but not in FEF lesion patients. Thus FEF involvement in fixation-related inhibition seems likely, although its exact role remains uncertain.

However, the sensory cells in FEF, like those in SC, also seem not to be selective for colour or form (e.g. Stuphorn and Schall 2002; Thompson and Bichot 2005), so target selection must involve additional areas that are selective for these properties. We suggest that S-cone fixation stimuli create inhibition in a cortical target selection process incorporating areas such as TEO as well as the cortical eye fields. Thus overall, while it is well established that inhibitory connections in the SC are likely to cause fixation-related inhibition, and that the FEF may play an important role, our results imply that there is also be a further cortical inhibitory mechanism. In order for this mechanism to produce S-cone fixation-related inhibition when warning effects are equated (e.g. Experiment 2), this mechanism must be specifically related to fixation stimuli rather than generalised warning and motor readiness.

The wider implications of this are that low level effects thought to represent collicular function may also represent cortical function, and furthermore, phenomena interpreted as cortical control over colliculus, may instead represent interactions within cortex. For example, manipulating the strategic set of saccade expectancy, using warning tones, or by cueing the target location or increasing the proportion of trials requiring saccades, can reduce the fixation offset effect (Machado and Rafal 2000a; Machado and Rafal 2000b; Rafal et al. 2000; Taylor et al. 1998), and this effect can be disrupted in patients with frontal lesions that include the FEF (Machado and Rafal 2004b). This has been interpreted as an example of how FEF can exert strategic control over the SC, with the lesions disrupting such control. However, this assumes that the fixation offset effect represents collicular function. If there is also a cortical source, the strategic control and the effect of the lesions may both reflect intra-cortical interactions rather than cortico-collicular modulation. Likewise, we would not

need to assume any *collicular* imbalance to explain asymmetrical fixation offset effects in patients with unilateral *cortical* damage (e.g. Machado and Rafal 2004a, b).

One further point for discussion is whether the fixation offset effect is caused by the absence of a fixation stimulus during saccade preparation, as is often implied by descriptions of the effect, or whether it is caused by the occurrence of the offset itself, as might be expected from sensory pathways with non-linear and transient response properties. In other words, is it the nature of the fixation stimulus *present* during saccade preparation that is important, or is it the nature of the previous stimulus *change* that is important? Pratt et al. (2000) found that a 20-pixel reduction in fixation size had markedly different effect depending on whether any fixation stimulus remained or not: removing a 20-pixel fixation stimulus produced much shorter latencies than reducing a 40-pixel fixation stimulus to 20 pixels, and the latter had almost no effect when paired with a warning tone, while the former still had a large effect. This may be taken to suggest that the presence or absence of a remaining fixation stimulus is the crucial factor rather than the size of the visual change. However, in this example it was absolute change that was equated, whereas *relative* change may be more relevant. Our results in Experiment 3 imply that the nature of the stimulus change at fixation is important in addition to the nature of the stimulus present when a saccade is required. For example, compare the High-to-Low luminance condition with the S-cone-to-Low luminance condition. In both conditions the same fixation stimulus was present by the time the saccade target appeared, but latency was greater in the latter condition than the former, presumably because the latter condition contained a signal increment at fixation rather than a decrement.

In conclusion, the sensory-motor phenomenon of fixation-related inhibition has been widely studied in the context of motor control, but the pathways that supply the sensory information have not previously been explicitly tested. Although fixation-related inhibition has been strongly associated with the SC, our data show that it does not rely on signals in either of the sensory pathways on which visual input to the SC is thought to depend. Further, we suggest that S-cone fixation-related inhibition is generated in a cortical mechanism that is not simply within the FEF. These results may necessitate some re-assessment of previous data interpreted in the context of cortico-collicular modulation.

Acknowledgements

We would like to thank Tom Sterling for help with Experiment 3, Elaine Anderson and Andy Parton for comments and all the participants for their time.

Grants

The research was supported by the Hammersmith Hospitals Trust Research Committee, the University of London Central Research Fund, the Wellcome Trust and the BBSRC.

References

Anstis SM and Cavanagh P. A minimum motion technique for judging equiluminance. In: *Colour Vision: Physiology and Psychophysics*, edited by Mollon JD and Sharpe LT. London: Academic Press, 1983, p. 155-166.

Braun D, Weber H, Mergner T, and Schultemonting J. Saccadic Reaction-Times in Patients with Frontal and Parietal Lesions. *Brain* 115: 1359-1386, 1992.

Brindley GS, Du Croz JJ, and Rushton WAH. The flicker fusion frequency of the blue-sensitive mechanism of colour vision. *J Physiol* 183: 497-500, 1966.

Calkins DJ. Seeing with S cones. *Progress in Retinal Eye Research* 20: 255-287, 2001.

Chatterjee S and Callaway EM. Parallel colour-opponent pathways to primary visual cortex. *Nature* 426: 668-671, 2003.

Chatterjee S and Callaway EM. S cone contributions to the magnocellular visual pathway in macaque monkey. *Neuron* 35: 1135-1146, 2002.

Dacey DM, Peterson BB, Robinson FR, and Gamlin PD. Fireworks in the primate retina: in vitro photodynamics reveals diverse LGN-projecting ganglion cell types. *Neuron* 37: 15-27, 2003.

de Monasterio FM. Properties of ganglion cells with atypical receptive-field organisation in the retina of macaques. *J Neurophysiol* 41: 1435-1449, 1978.

Dias EC and Bruce CJ. Physiological correlate of fixation disengagement in the primate's frontal eye field. *J Neurophysiol* 72: 2532-2537, 1994.

Dorris MC, Pare M, and Munoz DP. Neuronal activity in monkey superior colliculus related to the initiation of saccadic eye movements. *J Neurosci* 17: 8566-8579, 1997.

Everling S and Munoz DP. Neuronal correlates for preparatory set associated with pro-saccades and anti-saccades in the primate frontal eye field. *J Neurosci* 20: 387-400, 2000.

Fendrich R, Demirel S, and Danziger S. The oculomotor gap effect without a foveal fixation point. *Vision Res* 39: 833-841, 1999.

Gouras P. Identification of cone mechanisms in monkey ganglion cells. *J Physiol* 199: 533-547, 1968.

Guitton D, Buchtel HA, and Douglas RM. Frontal lobe lesions in man cause difficulties in suppressing reflexive glances and in generating goal-directed saccades. *Exp Brain Res* 58: 455-472, 1985.

Hanes DP, Patterson WF, and Schall JD. Role of frontal eye fields in countermanding saccades: Visual, movement, and fixation activity. *J Neurophysiol* 79: 817-834, 1998.

Hess WR, Burgi S, and Bucher V. Motor function of tectal and tegmental area. *Monatsschr Psychiatr Neurol* 112: 1-52, 1946.

Hikosaka O and Wurtz RH. The basal ganglia. In: *The neurobiology of saccadic eye movements*, edited by Wurtz RH and Goldberg ME. Amsterdam: Elsevier, 1989, p. 257–282.

Isa T. Intrinsic processing in the mammalian superior colliculus. *Curr Opin Neurobiol* 12: 668-677, 2002.

Izawa Y, Suzuki H, and Shinoda Y. Initiation and suppression of saccades by the frontal eye field in the monkey. *Ann N Y Acad Sci* 1039: 220-231, 2005.

Kaplan E and Shapley RM. The primate retina contains two types of ganglion cells, with high and low contrast sensitivity. *Proc Natl Acad Sci U S A* 83: 2755-2757, 1986.

Kingstone A and Klein RM. Visual offsets facilitate saccadic latency: does predisengagement of visuospatial attention mediate this gap effect? *J Exp Psychol Hum Percept Perform* 19: 1251-1265, 1993.

Klein RM, Taylor TL, and Kingstone A. Against a role for attentional disengagement in the gap effect: a friendly amendment to Tam and Stelmach (1993). *Percept Psychophys* 57: 573-577, 1995.

Krauzlis RJ. The control of voluntary eye movements: New perspectives. *The Neuroscientist* 11, 2005.

Machado L and Rafal R. Control of eye movement reflexes. *Exp Brain Res* 135: 73-80, 2000a.

Machado L and Rafal RD. Control of fixation and saccades during an anti-saccade task: an investigation in humans with chronic lesions of oculomotor cortex. *Exp Brain Res* 156: 55-63, 2004a.

Machado L and Rafal RD. Control of fixation and saccades in humans with chronic lesions of oculomotor cortex. *Neuropsychology* 18: 115-123, 2004b.

Machado L and Rafal RD. Strategic control over saccadic eye movements: Studies of the fixation offset effect. *Percept Psychophys* 62: 1236-1242, 2000b.

Marrocco RT and Li RH. Monkey superior colliculus: properties of single cells and their afferent inputs. *J Neurophysiol* 40: 844-860, 1977.

Morris JS, Ohman A, and Dolan RJ. A subcortical pathway to the right amygdala mediating "unseen" fear. *Proc Natl Acad Sci USA* 96: 1680-1685, 1999.

Munoz DP, Dorris MC, Pare M, and Everling S. On your mark, get set: Brainstem circuitry underlying saccadic initiation. *Can J Physiol Pharmacol* 78: 934-944, 2000.

Munoz DP and Fecteau JH. Vying for dominance: dynamic interactions control visual fixation and saccadic initiation in the superior colliculus. *Prog Brain Res* 140: 3-19, 2002.

Munoz DP and Istvan PJ. Lateral inhibitory interactions in the intermediate layers of the monkey superior colliculus. *J Neurophysiol* 79: 1193-1209, 1998.

Munoz DP and Wurtz RH. Role of the rostral superior colliculus in active visual fixation and execution of express saccades. *J Neurophysiol* 67: 1000-1002, 1992.

Ottes FP, Van Gisbergen JAM, and Eggermont JJ. Collicular involvement in a saccadic colour discrimination task. *Exp Brain Res* 66: 465-478, 1987.

Pare M and Wurtz RH. Monkey posterior parietal cortex neurons antidromically activated from superior colliculus. *J Neurophysiol* 78: 3493-3497, 1997.

Pratt J, Bekkering H, and Leung M. Estimating the components of the gap effect. *Exp Brain Res* 130: 258-263, 2000.

Pugh EN and Mollon JD. A theory of the p_1 and p_3 color mechanisms of Stiles. *Vision Res* 19: 2923-2312, 1979.

Rafal R, Machado L, Ro T, and Ingle H. Looking forward to

looking: Saccade preparation and control of the visual grasp reflex. In: *Control of cognitive processes: Attention and performance*, edited by Monsell S and Driver J. Cambridge, MA: MIT Press, 2000, p. 155-174.

Rafal RD, Henik A, and Smith J. Extrageniculate contributions to reflex visual orienting in normal humans: a temporal hemifield advantage. *J Cogn Neurosci* 3: 322-328, 1991.

Rafal RD, Smith J, Krantz J, Cohen A, and Brennan C. Extrageniculate vision in hemianopic humans: Saccade inhibition by signals in the blind field. *Science* 250: 118-121, 1990.

Reuter-Lorenz PA, Hughes HC, and Fendrich R. The reduction of saccadic latency by prior offset of the fixation point: an analysis of the gap effect. *Percept Psychophys* 49: 167-175, 1991.

Reuter-Lorenz PA, Oonk HM, Barnes LL, and Hughes HC. Effects of warning signals and fixation point offsets on the latencies of pro- versus antisaccades: implications for an interpretation of the gap effect. *Exp Brain Res* 103: 287-293, 1995.

Saslow MG. Effects of components of displacement-step stimuli upon latency for saccadic eye movements. *Journal of the Optical Society of America* 57: 1024-1029, 1967.

Schall JD. Visuomotor areas of the frontal lobe. *Cereb Cortex* 12: 527–638, 1997.

Schall JD, Morel A, King DJ, and Bullier J. Topography of Visual-Cortex Connections with Frontal Eye Field in Macaque - Convergence and Segregation of Processing Streams. *J Neurosci* 15: 4464-4487, 1995.

Schiller PH and Malpeli JG. Properties and tectal projections of Monkey retinal ganglion cells. *J Neurophysiol* 40: 428-445, 1977.

Schiller PH, Malpeli JG, and Schein SJ. Composition of geniculostriate input to superior colliculus of the rhesus monkey. *J Neurophysiol* 42: 1124-1133, 1979.

Schiller PH and Stryker M. SIngel-unit recording and stimulation in superior colliculus of the alert rhesus monkey. *J Neurophysiol* 35: 915-924, 1972.

Schiller PH and Tehovnik EJ. Cortical inhibitory circuits in eye-movement generation. *Eur J Neurosci* 18: 3127-3133, 2003.

Schlag-Rey M, Schlag J, and Dassonville P. How the frontal eye field can impose a saccade goal on superior colliculus neurons. *J Neurophysiol* 67: 1003–1005, 1992.

Schmolesky MT, Wang Y, Hanes DP, Thompson KG, Leutgeb S, Schall JD, and Leventhal AG. Signal timing across the macaque visual system. *J Neurophysiol* 79: 3272-3278, 1998.

Segraves MA and Goldberg ME. Functional properties of corticotectal neurons in the monkey's frontal eye field. *J Neurophysiol* 58: 1387-1419, 1987.

Smithson HE and Mollon JD. Is the S-opponent chromatic subsystem sluggish? *Vision Res* 44: 2919-2929, 2004.

Smithson HE, Sumner P, and Mollon JD. How to find a tritan line. In: *Normal and Defective Colour Vision*, edited by Mollon JD, Pokorny J and Knoblauch K. Oxford: OUP, 2003, p. 279-287.

Sparks DL. The brainstem control of sccadic eye movements. *Nat Rev Neurosci* 3: 952-964, 2002.

Sparks DL. Translation of sensory signals into commands for control of saccadic eye movements: Role of primate superior colliculus. *Physiol Rev* 66: 118-171, 1986.

Stockman AS, MacLeod DIA, and DePriest DD. The temporal properties of the human short-wave photoreceptors and their associated pathways. *Vision Res* 31: 189-208, 1991.

Stuphorn V and Schall JD. Neuronal control and monitoring of initiation of movements. *Muscle Nerve* 26: 326-339, 2002.

Sumner P. Inhibition vs attentional momentum in cortical and collicular mechanisms of IOR. *Cognitive Neuropsychology*, in press.

Sumner P, Adamjee T, and Mollon JD. Signals invisible to the collicular and magnocellular pathways can capture visual attention. *Curr Biol* 12: 1312-1316, 2002.

Sumner P, Nachev P, Vora N, Husain M, and Kennard C. Distinct cortical and collicular mechanisms of inhibition of return revealed with S cone stimuli. *Curr Biol* 14: 2259-2263, 2004.

Takahashi M, Sugiuchi Y, Izawa Y, and Shinoda Y. Synaptic inputs and their pathways from fixation and saccade zones of the superior colliculus to inhibitory burst neurons and pause neurons. *Ann N Y Acad Sci* 1039: 209-219, 2005.

Taylor TL, Kingstone A, and Klein RM. The disappearance of foveal and nonfoveal stimuli: Decomposing the gap effect. *Can J Exp Psychol-Rev Can Psychol Exp* 52: 192-200, 1998.

Thompson KG and Bichot NP. A visual salience map in the primate frontal eye field. *Prog Brain Res* 147: 251-262, 2005.

Webster MA and Mollon JD. Contrast adaptation dissociates different measures of luminous efficiency. *J Opt Soc Am A* 10: 1332-1340, 1993.

Yeh TY, Lee BB, and Kremers J. Temporal response of ganglion cells of the macaque retina to cone specific modulation. *Journal of the Optical Society of America A* 12: 456-464, 1995.

Figure Legends

Figure 1: Saccadic latency in Experiment 1. For luminance fixation stimuli, the standard gap effect was replicated, such that saccadic latency was around 50 ms longer when the fixation stimulus stayed on (overlap condition), compared to when it disappeared 200 ms before target onset (gap condition). A similar gap effect was produced by fixation stimuli visible only to S cones. Error bars are standard errors of the within subject gap effects. There were no effects in the errors (mean < 2%).

Figure 2: Saccadic latency in Experiment 2. If fixation-related inhibition requires signals in the retinotectal or magnocellular pathways, then a change of the fixation stimulus from luminance to S-cone should have the same effect as the offset of a luminance fixation stimulus. This was not the case, indicating that the S-cone stimulus itself causes some fixation-related inhibition. Error bars are standard errors of the most important within subject comparisons: the standard error of difference between the luminance offset and luminance-S change conditions is plotted on the upper bar of the former and the lower bar of the latter; the standard error of difference between the luminance-S and S-luminance change conditions is plotted on the upper bar of the former and the lower bar of the latter (the S-cone offset condition has no error bar because it is not included in these two comparisions). There were no effects in the errors (mean < 2%).

Figure 3: Predictions for Experiment 3 based on a single pathway model, in which S-cone stimuli behave like luminance stimuli of some unknown low luminance. A low luminance stimulus is chosen that may cause more or less inhibition than the S-cone stimulus, and both stimuli are tested against a luminance stimulus known to cause more than both. Fixation change trials are used, in which saccades to left or right targets are required, and 200 ms before the target appears, the fixation stimulus changes from high to low luminance or vice versa, or high luminance to S-cone, or vice versa. The difference in latency between conditions where the fixation change is reversed gives a measure of the relative salience of the two stimuli in terms of their ability to cause fixation-related inhibition (i.e. how dissimilar the two stimuli are in their activation of the inhibitory mechanism, and thus how much the input signal to that mechanism changes upon the fixation change). In **Ai** the difference between the high luminance stimulus and the S-cone stimulus is less than the difference between the high and low luminance stimuli. Thus the "equivalent-luminance-contrast" of the S-cone stimulus is greater than that of the low luminance stimulus. In other words, the signal from the S-cone stimulus to the inhibitory mechanism seems to be greater than that from the low luminance stimulus. This leads to the prediction in **Bi** that a fixation change from low luminance to S-cone should cause longer saccadic latency than a fixation change from S-cone to low luminance. In **Aii**, the situation from Ai is reversed, such that the relative signal strength from the low luminance stimulus is less different from high luminance than is the S-cone stimulus, and thus the S-cone stimulus appears weaker than the low

luminance stimulus. This leads to the prediction in **Bii**, that a fixation change from low luminance to S-cone should cause shorter saccadic latency than a fixation change from S-cone to low luminance.

Figure 4: Saccadic latency in Experiment 3. A: The pattern of results for Experiment 3A conforms to Figure 3Ai, predicting a pattern like 3Bi for Experiment 3B if the S-cone and luminance stimuli cause fixation-related inhibition by the same pathway. Error bars are standard errors of the within subject differences depicted in Figure 3A. B: The pattern of results is opposite to that in Figure 3Bi, and thus cannot be explained by a single pathway model of fixation-related inhibition. There were no effects in the errors (mean < 2%).

Figure 1

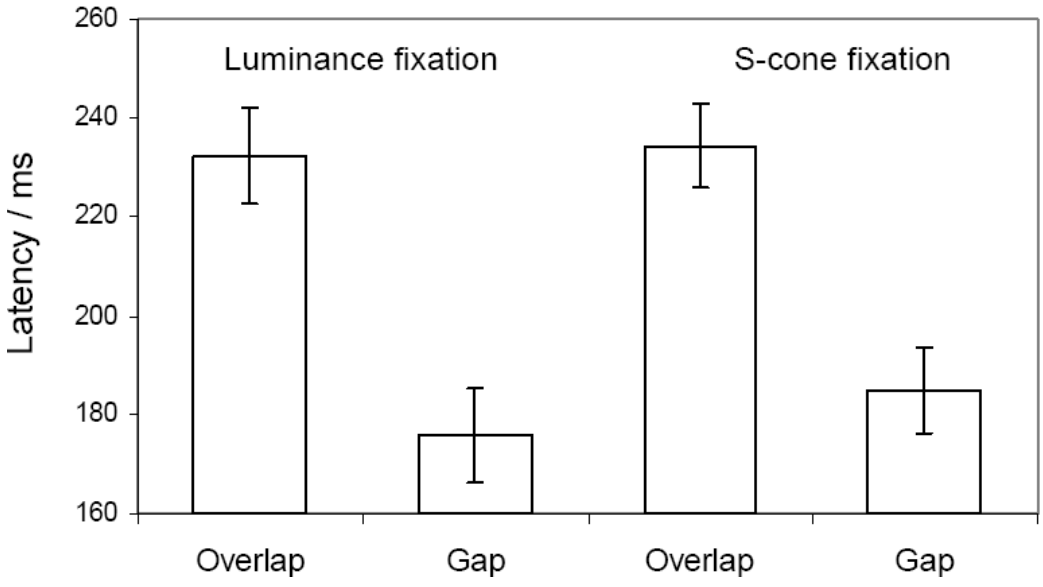


Figure 2

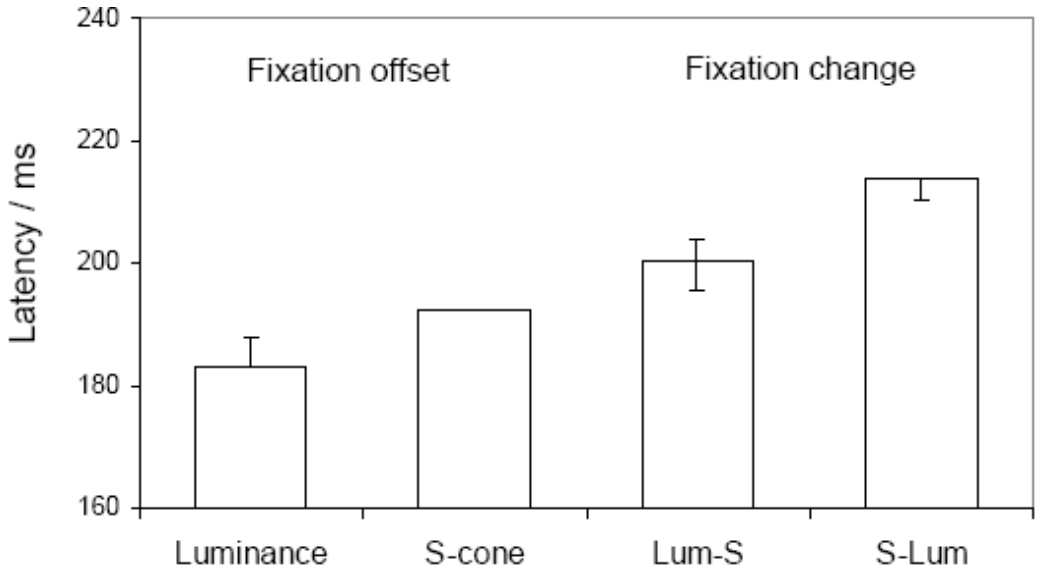


Figure 3

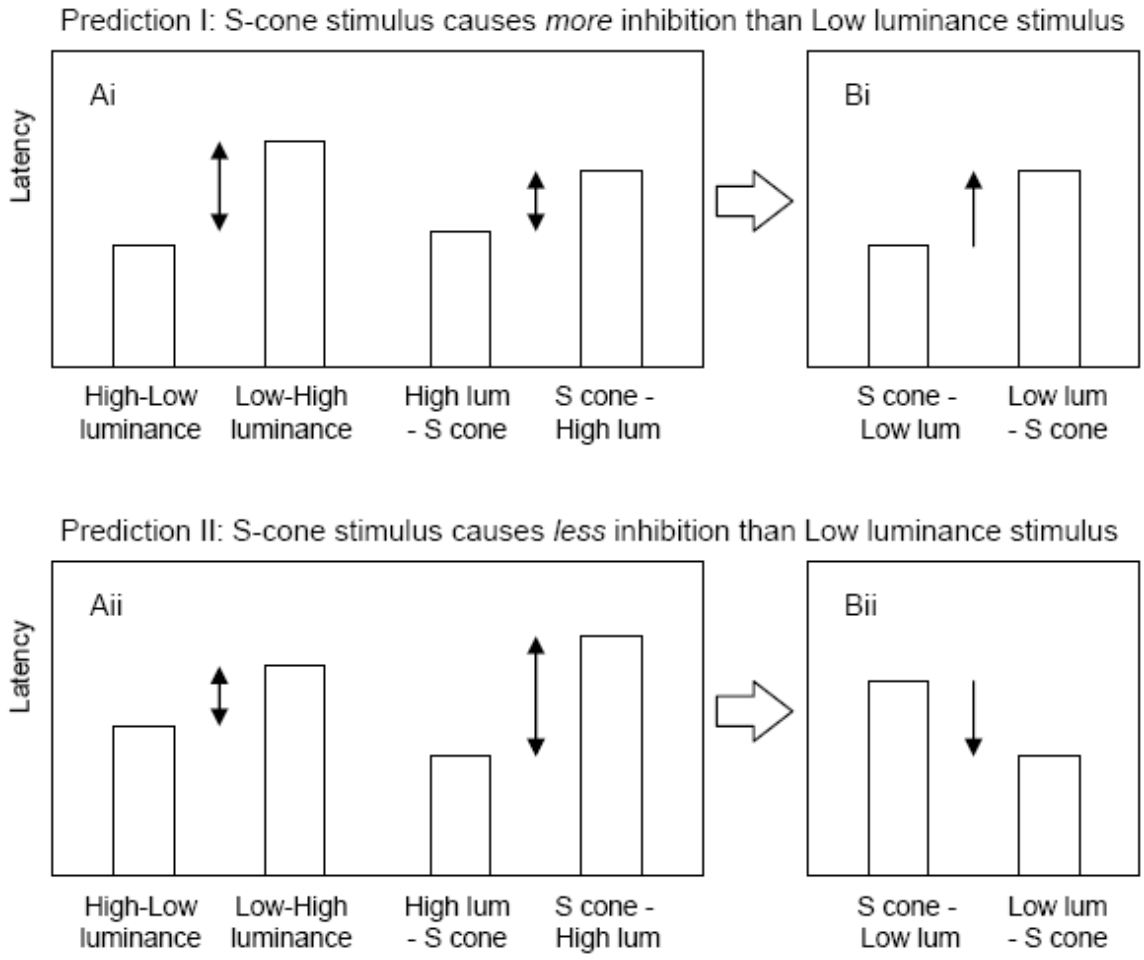
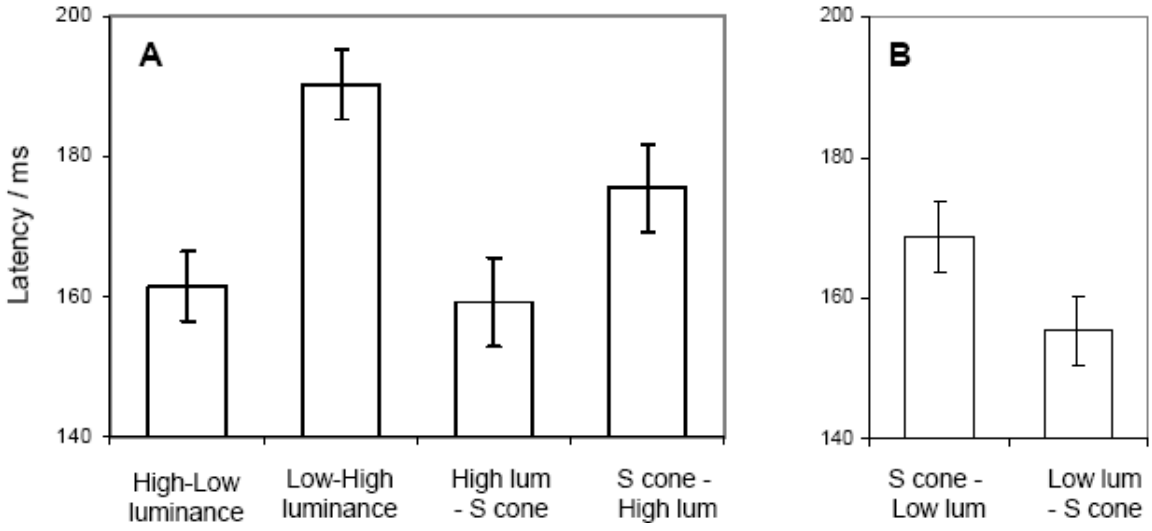

Prediction I: S-cone stimulus causes *more* inhibition than Low luminance stimulus
Ai
Bi
Latency
High-Low luminance
Low-High luminance
High lum - S cone
S cone - High lum
S cone - Low lum
Low lum - S cone
Prediction II: S-cone stimulus causes *less* inhibition than Low luminance stimulus
Aii
Bii
Latency
High-Low luminance
Low-High luminance
High lum - S cone
S cone - High lum
S cone - Low lum
Low lum - S cone

Figure 4


A
B
Latency / ms
200
180
160
140
High-Low luminance
Low-High luminance
High lum - S cone
S cone - High lum
S cone - Low lum
Low lum - S cone