Effect of Microstimulation of the Superior Colliculus on Visual Space Attention

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Abstract

■ We investigated the effect of microstimulation of the superficial layers of the superior colliculus (SC) on the performance of animals in a peripheral detection paradigm while maintaining fixation. In a matching-to-sample paradigm, a sample stimulus was presented at one location followed by a brief test stimulus at that (relevant) location and a distractor at another (irrelevant) location. While maintaining fixation, the monkey indicated whether the sample and the test stimulus matched, ignoring the distractor. The relevant and irrelevant locations were switched from trial to trial. Cells in the superficial layers of SC gave enhanced responses when the attended test stimulus was inside the receptive field compared with when the (physically identical) distractor was inside the field. These effects were found only in an "automatic" attentional cueing paradigm, in which a peripheral stimulus explicitly cued the animal as to the relevant location in the receptive field. No attentional effects were found with block of trials. The transient enhancement to the attended stimulus was observed at the onset and not at the offset of the stimulus. Electrical stimulation at the site corresponding to the irrelevant distractor location in the SC causes it to gain control over attention, causing impaired performance of the task at the relevant location. Stimulation at unattended sites without the presence of a distractor stimulus causes little or no impairment in performance. The effect of stimulation decays with successive stimulations. The animals learn to ignore the stimulation unless the parameters of the task are varied. ■

INTRODUCTION

The superior colliculus (SC) of the macaque has long been known to play an important role in the generation of saccadic eye movements (Schiller, True, & Conway, 1980; Goldberg & Wurtz, 1972a, 1972b; Wurtz & Goldberg, 1972a, 1972b; Schiller & Koerner, 1971). Cells in the intermediate and deep layers of the SC discharge before eye movements, and cells in the superficial layers give enhanced responses to visual stimuli that are the targets of eye movements (Mohler & Wurtz, 1976). Lesions or chemical deactivation of the SC lead to a transient impairment in the ability to move the eyes into the contralesional field, and microstimulation of the SC causes eye movements to the visuotopic locus of the stimulation site in the SC (Munoz & Wurtz, 1993a, 1993b; Ma, Graybiel, & Wurtz, 1991; Hikosaka & Wurtz, 1986).

Electrophysiological recording and lesion experiments have increasingly implicated eye-movement planning structures in the control of covert spatial attention. The evidences suggest that the SC also contributes to the spatial attention, in the absence of eye movements. We recorded the responses of cells in the superficial layers of the SC in monkey performing a visual discrimination task on target stimuli at one location in the visual field, with distractor stimuli presented at another location.

We found that responses to attended targets were larger than to physically identical, but ignored, distractor stimuli. The larger responses to attended targets appeared to be because of a transient elevation of the cells' baseline activity when attention was directed to the receptive field as well as a transient enhancement of the response to the target stimuli (Gattass & Desimone, 1996). Other electrophysiological recording studies (Ignashchenkova, Dicke, Haarmeier, & Their, 2004; Kustov & Robinson, 1996) provided evidence to the role of the SC in the control of attention.

Single-unit recordings have detected additional attentional effects in other eye movement-related areas of the brain, including the pulvinar, the inferior parietal cortex (Bisley, 2011; Bisley & Goldberg, 2003; Robinson, Petersen, & Keys, 1986; Bushnell, Goldberg, & Robinson, 1981; Yin & Mountcastle, 1977), and the FEFs (Thompson & Schall, 2000; Kastner, Pinsk, De Weerd, Desimone, & Ungerleider, 1999; Kodaka, Mikami, & Kubota, 1997). Electrophysiological evidence, however, is necessarily correlative and cannot demonstrate that neural activity causes behavior (Desimone, Wessinger, Thomas, & Schneider, 1990).

The superficial layers of the SC receive direct retinotopically organized projections from the K and M ganglion cells in the retina, which are restricted to the upper half of the stratum griseum superficiale (Graham, 1982; Ogren & Hendrickson, 1976; Hendrickson, Wilson, & Toyne, 1970). Whereas the projections from V1 to the SC are similarly

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restricted to the upper half of the stratum griseum super-ficiale (Ungerleider, Desimone, Galkin, & Mishkin, 1984), those from extrastriate areas V2, V4, middle temporal, and temporal occipital extend through this stratum to include the stratum opticum as well (Gattass, Galkin, Desimone, & Ungerleider, 2013; Webster, Bachevalier, & Ungerleider, 1993; Ungerleider et al., 1984). For both striate and extra-striate areas, projections to the colliculus are in register with the visuotopic organization of the structure (Cynader & Berman, 1972). According to Cynader and Berman (1972), the fovea is represented anteriorly; the peripheral visual field, posteriorly; the lower visual field, laterally; and the upper visual field, medially. Inasmuch as visuotopic inputs to the colliculus are superimposed on an oculomotor map (Tabareau, Bennequin, Berthoz, Slotine, & Girard, 2007; Skaliora, Doubell, Holmes, Nodal, & King, 2004; Wallace, McHaffie, & Stein, 1997; Baleydier & Mauguiere, 1978), it may be that projections from V4 provide visual feature information, which could trigger orienting oculomotor re-actions to spatially localized regions based on unexpected form, color, or texture (Zénon & Krauzlis, 2012). These authors (Zénon & Krauzlis, 2012) found that, although in-activation of the SC led to attention-like deficits, it did not diminish the attention-related modulation within extrastri-ate visual cortex. This observation demonstrates that the SC is not the only key player in driving attentional selec-tion. The independency of the SC mechanism to that of the cortex was also suggested at the study of the effect of attention on the activity of SC superficial cells. The larger responses to attended targets that appeared when atten-tion was directed to the receptive field in an unblocked paradigm did not appear with the blocked or cognitive paradigm (Gattass & Desimone, 1996).

Albano, Mishkin, Westbrook, and Wurtz (1982) have reported that lesions of the SC impair monkey's ability to detect the dimming of a peripheral stimulus. Rafal and Posner (1987) reported a similar impairment in patients with supranuclear palsy, which is thought to affect the SC. They argue that the SC is involved in the ability to "move" attention from one location to another. Finally, Desimone, Wessinger, Thomas, and Schneider (1989) find that focal deactivation of SC impairs a monkey's ability to discriminate a stimulus at the visuotopic locus of the de-activated zone if there is a distractor stimulus at another location in the visual field. They argue that, within the attentional control system, each location in the visual field is competing with every other location for attention (Katyal, Zughni, Greene, & Ress, 2010). The SC forms one component of this control system, but it works in parallel with other structures. Dysfunction (through lesions or deactivation) of a portion of visuotopic map in the SC throws the competition out of balance, giving an advantage to stimuli outside the dysfunctional zone (Desimone et al., 1990). Thus, both the lesion and recording data suggest that the SC, particularly the superficial layers, does play some role in spatial attention in addition to its role in the generation of eye movements.

Microstimulation of the SC improves performance by focusing attention on a specific region of visual space without moving the eyes (Müller, Philiastides, & Newsome, 2005). Thus, one can test if microstimulation of extrafoveal locations of the SC contributes to the control of covert spatial attention, a process that focuses attention on a region of space different from the point of gaze. Previous studies have shown that microstimulation can bias per-ceptual choices in discrimination tasks (Bisley, Zaksas, & Pasternak, 2001; Salzman, Britten, & Newsome, 1990) or serve as a substitute for a stimulus that is not actually pre-sent (Romo, Hernandez, Zainos, & Salinas, 1998).

To complete the parallel with the SC's role in eye movements, microstimulation of the SC should cause a shift in attention to the visuotopic locus corresponding to the stimulation site. Because microstimulation of the intermediated or deep layers causes eye movements, the most likely portions of the SC for eliciting attentional shifts alone are the superficial layers. In this study, we report the results of recording and stimulating the super-ficial layers of the SC in two monkeys.

METHODS

Subjects

Two rhesus monkeys (*Macaca mulatta*) weighing 6–8 kg were used over a period of 18–25 months. These were the same monkeys used in the single-unit recording study of the SC (Gattass & Desimone, 1996). All experimental protocols were conducted following National Institutes of Health (NIH) guidelines for animal research and were ap-proved by the Committee for Animal Care and Use of NIH.

Surgical Procedures

Before the implantation of the recording chamber, the animals were placed in a plastic stereotaxic machine and scanned with magnetic resonance imaging. A head-restraint post, recording chamber, and scleral eye coil for monitoring eye position (Robinson, 1963) were implanted under aseptic conditions while the animal was anesthetized with sodium pentobarbital. Using the coordinates derived from the magnetic resonance imaging images, the record-ing chamber was oriented in the Horsley–Clark stereotaxic plane and cemented on the skull above the SC. The animals received antibiotics and analgesics postoperatively.

Recordings

We mapped the SC in each animal before the beginning of the single-unit study or before the stimulation session. Later, in each stimulation session, we mapped a multiunit receptive field before the placement of the stimulation electrode. The locations of the multiunit receptive field were used to position the test stimuli inside the receptive field and its companion distractor in a corresponding

location in the other visual hemifield. These cells were studied under 24 different conditions containing foveal, extrafoveal, and eye-movement tasks. We recorded multi-unit activity from the superficial layers of the SC using 1- to 2-MΩ-impedance tungsten microelectrodes. The electrical activity was amplified and filtered with a band-pass filter at 300–8000 Hz The receptive fields were initially localized and mapped using a hand-plot mapping procedure, using the CORTEX program (Laboratory of Neuropsychology, NIMH/NIH, Bethesda, MD) and the computer mouse to control the stimulus location.

Behavioral Task

Attentional Task with Distractor

The general behavioral design was used to measure the animal's ability to attend to a target stimulus and ignore a distractor when the visuotopic location of either the target or distractor was electrically stimulated within the SC. The stimulation site was always within the left SC, but the target and distractor locations varied. The stimuli were small colored bars, generally 0.8° × 0.8°, presented on a computer graphics display. The background luminance of the display was 0.65 cd/m, and the stimulus luminance was 13.4 cd/m.

Figure 1 shows the three types of tasks used for recording and for microstimulation. They are two extrafoveal discrimination tasks and one eye movement task. The discrimination task used to manipulate the animal's attention (Figure 1A) was a modified version of delayed match-to-sample (DMS). The animal initiated a trial by grabbing a bar. After 200 msec, a small (0.2°) fixation stimulus appeared, which the animal was required to fixate. The fixation stimulus remained on for the remainder of the trial, and trials were aborted if the animal's gaze deviated from the fixation stimulus by more than 0.5°. At 30 msec after the animal achieved fixation, a single sample stimulus appeared at a peripheral location for

120 msec. Then, after a blank delay period of 200–300 msec, test stimuli appeared at two locations. The animal was supposed to attend to the test stimulus that appeared at the same location as the sample, which we will term the "target," and to ignore the test stimulus at the other location, which we will term the "distractor." The target and distractor were on for 120 msec. On "match" trials, the target matched the sample, and the animal was required to release the bar within 750 msec for orange juice reward, which terminated the trial. On "nonmatch" trials, the target did not match the sample, and the animal was required to continue holding the bar. On these trials, the nonmatching target and the distractor were then followed by another blank delay period of 350–450 msec, followed by a third set of stimuli presented at the same two locations. In this case, the stimulus at the location of the previous sample was always a match and thus served simply as a releasing stimulus for the animal's behavioral response, which was followed by juice reward. Incorrect trials were not rewarded and were typically followed by a 2-sec time-out period. Our primary interest was to study and to stimulate at the time of the target (and distractor) presentation, as this was the time at which the animal had to make its decision to release the bar immediately (match trials) or to continue holding the bar until the releasing stimulus (nonmatch trials). Figure 2B shows a DMS task with the sample stimulus at the fovea. It is a task of foveal attention task with peripheral distractors. Figure 1C is a schematic diagram of the eye movement task used. A fixation spot appears on the screen, and the animal has to gaze on it and hold fixation. After a fixation period, a sample stimulus appears on the fovea for 250 msec and then moves to a peripheral location (location of the receptive field), and the animal has to move his eyes to that location.

In the initial stimulation sessions in the first animal tested, the distractors never match the sample and thus conveyed no useful information. On nonmatch trials, the nonmatching distractor provides consistent information with the target, whereas on match trials, it provided

Figure 1. Behavioral tasks (for details, see text).
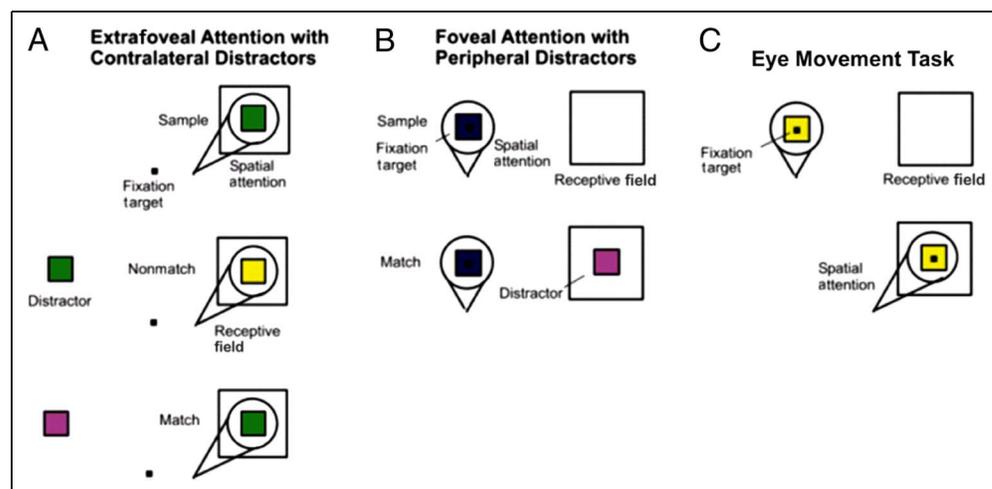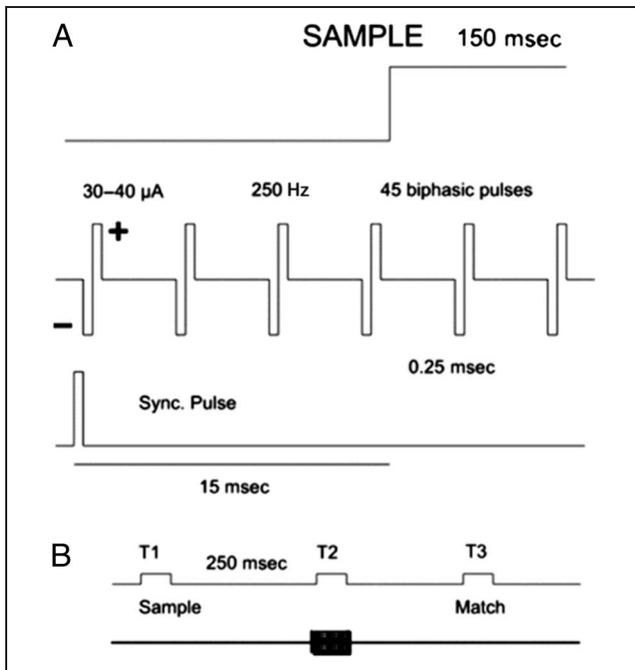
Figure 2. Parameters of stimulation. A train of biphasic negative/positive pulses of 200–250 Hz with pulse duration of 0.2 msec and amplitude of 30–40 μA were used during the presentation of the sensory stimulus. To minimize the damage caused by the microstimulation, we shortened the presentation of the test stimuli to 150 msec and increased the ISI accordingly.

contradictory information to the target. If the animal tried to perform the matching task on the sample and distractor, its performance would necessarily be 50% correct. In later sessions with both animals, we added trials in which the distractor matched the sample. In both the initial and later sessions, the distractor provided information consistent with the target on half of the trials and inconsistent with the target on the other half.

The sample stimulus served as an explicit spatial cue, which indicated to the animal which of the subsequent two test stimuli it should attend to to perform the task. In addition to the explicit spatial cue in this design, there was also an implicit, nonspatial cue for the attended spatial location. We presented the trials in blocks, with the sample at one location for 40–80 trials and at the other location for an equal number of trials, in alternation. Thus, after the first trial in a block, the animal could anticipate which location would contain the sample stimulus and the target for the remainder of the trials (Figure 1A). One reason for using this blocking design was that Mohler and Wurtz (1976) reported that the saccadic enhancement of colliculus cells was much larger when trials using a particular location were run in blocks, so that the animal made eye movements to the same location for trial after trial.

One of the two locations tested in the visual field was always at the site of the stimulating electrode in the SC, which was typically at 4°–5° eccentricities in the upper or lower visual field. For most of the stimulation studies, the

other location was across the midline in a symmetrical position; however, we also tested the effects of stimulating the foveal representation with a distractor in the periphery or vice versa.

To test whether any behavioral impairment required that a distractor be present at the site of stimulation, we included blocks of trials in each session in which we stimulated at the same unattended sites, but the distractor was not presented.

Stimulation Techniques

Before stimulation, we first mapped the receptive fields of cells in the superficial layers of the SC at the stimulation site. Cells were recorded, and sites were stimulated using 1- to 2-MΩ tungsten microelectrodes. Following penetration of the dura mater with a guide tube, the electrode was advanced in the vertical plane down to the surface of the SC, and the depth of the first activity was recorded. We then advanced the electrode and mapped the multiunit receptive field while the animal fixated a small target. Two stimulus locations were then selected, one inside and another outside the receptive field, typically in a symmetrical location in the opposite visual hemifield. Then, the electrode was advanced through the SC to a depth of 500–700 μm, and the stimulation was initiated. Electrical stimulation (200 Hz, 30–40 μA, biphasic current pulses, 200–250 μs per phase; see Figure 2) was applied in the superficial layers of the SC, at the same topographic site as either the relevant or irrelevant stimuli. The biphasic stimulation, with 300-msec duration, began 50 msec before the stimulus presentation (Figures 2 and 3). Trials with and without electrical stimulation were randomly interleaved. Figure 3 shows a DMS task with stimulation (concentric rings) at the location of the distractor at the time (T2) the animal has to make a decision.

RESULTS

We describe the effect of microstimulation of foveal (14) and extrafoveal (26 sessions) regions (ranging from 2.5° to 7° eccentricity) of the SC, while the animal is performing a DMS discrimination task.

Performing on Distractor Trials across Sessions

The two animals were initially studied with the target and distractor located on opposite sides of the vertical meridian, at an eccentricity of approximately 4°. Comparing trials with stimulation with those without, the performance of both animals was impaired when we stimulated the SC at the site of the distractor. However, this impairment gradually diminished over successive daily sessions. Because we had not anticipated this change in performance, the two animals were tested in somewhat different ways. Figure 4A shows the performance of the first animal (Case 1), on trials in which the distractor location
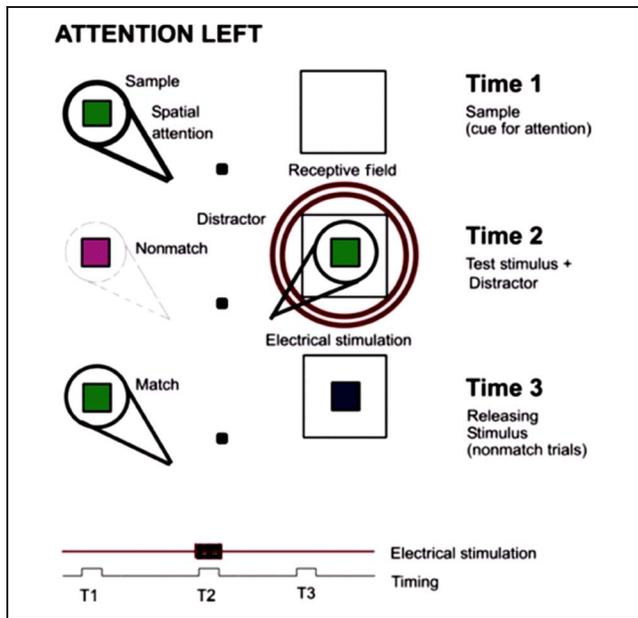
Figure 3. The paradigm we used in the microstimulation experiment involves competition between the spatial attention induced by the behavioral task and a modulation induced by the microstimulation burst. We stimulate the superficial layers of the SC while the animal was performing a visual discrimination, on a DMS task. After recording a multiunit receptive field in the superficial layers of the SC, we position the test stimuli so that it would be presented at that location. The two concentric thick lines represent the microstimulation. In this trial, a sample is presented in the ipsilateral visual field and immediately engages the spatial attention to that location. In time T2, a burst of biphasic pulses is delivered in the superficial layers, typically 400–500 μm below the collicular surface. The stimulation burst lasts throughout the presentation of a distractor in the receptive field. We assumed that the electric stimulation would capture the monkey's visual attention, competing with the engaged spatial attention. Because time T2 is the time of decision in this task, the stimulation during the presentation of the test stimulus would collide with the sensory stimulus, and the monkey would misinterpret the trails and release the bar.

was stimulated as well as on trials in which the distractor location was nonstimulated. In this animal, the impairment abruptly ceased after six sessions and did not reappear until the behavioral paradigm was changed in the twenty-third session. In the first six sessions with this animal, all trials included a distractor. Trials without a distractor were added in the seven and all remaining sessions. In addition, until the twenty-third session, the distractor never matched the sample, that is, it was nonmatching on both nonmatching and match trials. In the twenty-third session, trials were added in which the distractor matched the sample on nonmatching trials. With this change in distractor conditions, the behavioral impairment was reinstated.

The testing of the second animal (Figure 4B) included trials both with and without distractors as well as nonmatch trials in which the distractor matched the sample. Thus, the testing in this animal started off with the final testing conditions of the first animal. Figure 4B shows the behavioral performance of this animal, which was milder and diminished more gradually across sessions than in the first animal. The impairment did not disappear entirely until the twelfth session. To simplify the presentation of the remaining results, we will first summarize the behavioral effects of stimulation in Sessions 1–6 and 23–30 in the first nine sessions of the second animal, when the effects of stimulation were strongest. The numbers of correctly and incorrectly performed trials in each of the conditions are given. We will return to the issue of recovery later in the Results section.

Effects of Varying the Distractor

Figure 5A and B summarize the effects of stimulating the SC at the location of the distractor in each of the two animals. As indicated above, the data from animal A are taken from Sessions 1–6 and 23–30, and the data from animal B are from Sessions 1–9. Compared with the trials
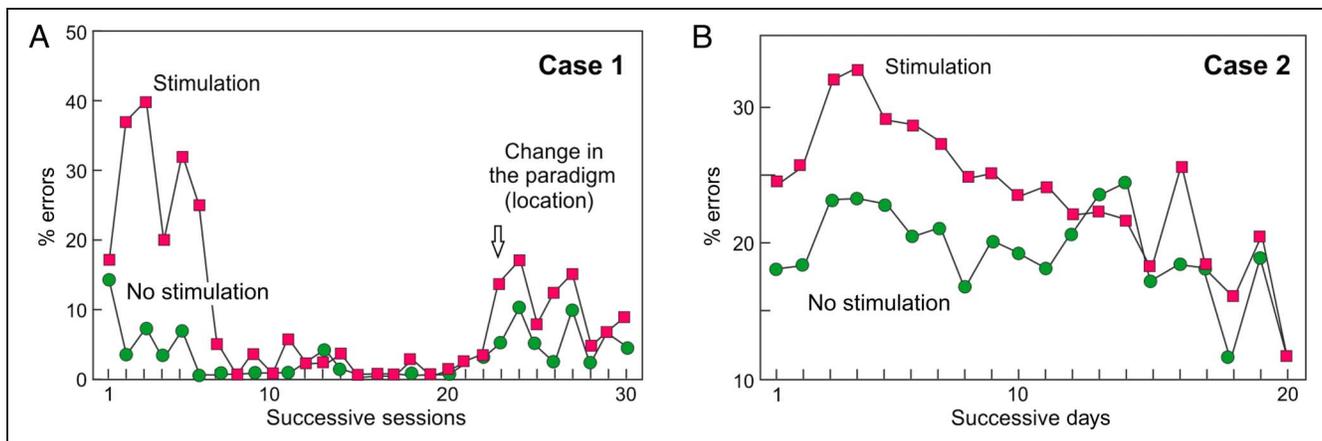
Figure 4. Decay of the effect of stimulation in Cases 1 and 2. In both animals, performance gradually improved over the course of several days of stimulation. This suggests that the animals learned to ignore the attention-diverting effects of SC stimulation. (B) Transient recovery in Case 1. When the parameters of the task were changed, the impairment was reinstated.
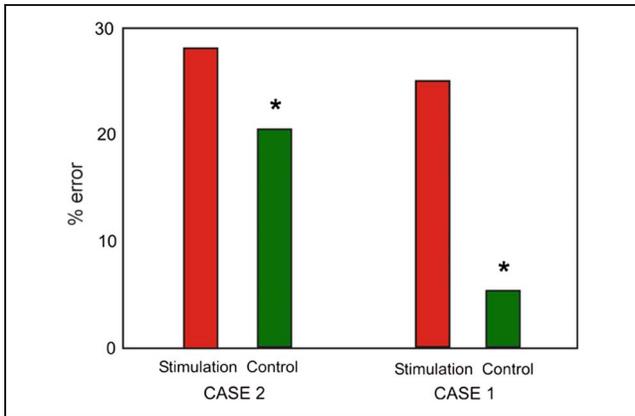
Figure 5. Effect of stimulation at the location of the distractor.

with no stimulation, both animals were significantly impaired when we stimulated at the distractor location (Case 2: $\chi^2 = 4.96$, $p = .02$; Case 1: $\chi^2 = 49.6$, $p < .001$). By comparison, when we stimulated at the location of the target, there was no significant change in perfor-

mance (Case 2: $\chi^2 = 0.038$, $p = .84$; Case 1: $\chi^2 = 0.095$, $p = .75$). Thus, stimulation at the site of the distractor appeared to make it more "distracting," presumably by shifting the animal's attention away from the target.

If stimulation at the site of the distractor shifted the animal's attention away from the target, one can imagine two possible outcomes. Either the animal could try to perform the matching task by (inappropriately) comparing the distractor color to the sample, or it could simply respond randomly or adopt a response bias. If the former, then the animals should make more errors on trials in which the distractor provides information inconsistent with the target than on trials in which the distractor and target were consistent. An "inconsistent" trial, for example, would be one in which the target matched the sample but the distractor did not, and vice versa. A consistent trial would be one in which both the target and the distractor matched or did not match the sample.

In a previous study of local SC deactivation, we found that the animal's ability to attend to a target at the deactivation site was impaired only if there was a distractor
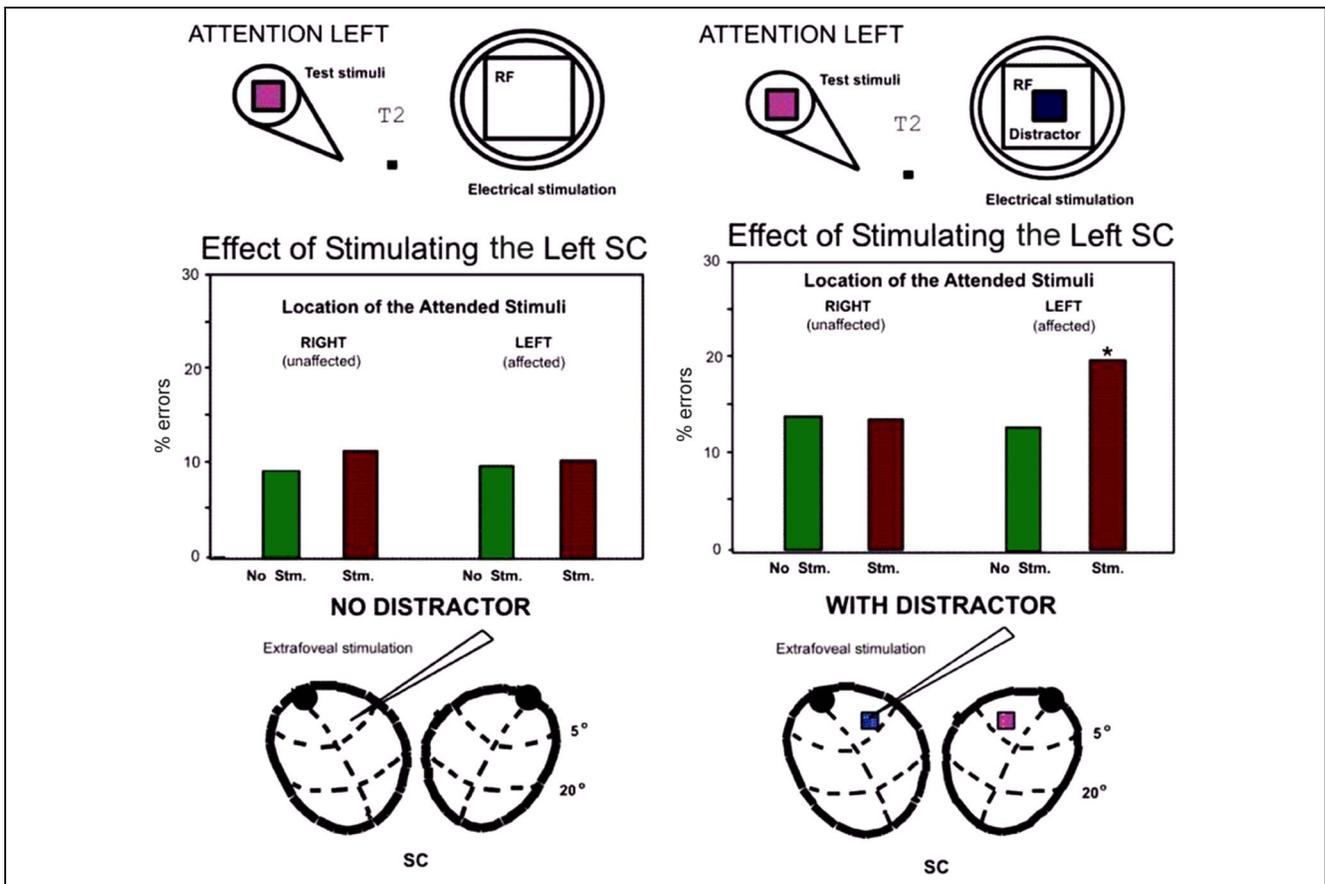
Figure 6. Ineffective and effective shifts of attention in Case 2. (A) Stimulation of unattended sites without a distractor causes little or no impairment. Stimulation at unattended sites at the time of the sample stimulus (no distractor present) also causes little or no impairment. (A) Stimulation of the SC at the site of an irrelevant distractor impairs performance. Changes of the focus of spatial attention (cone) by electrical stimulation (concentric rings) at time T2, the time in which the animal makes the match/nonmatch decision. Performance is impaired when the site of the distractor is stimulated.
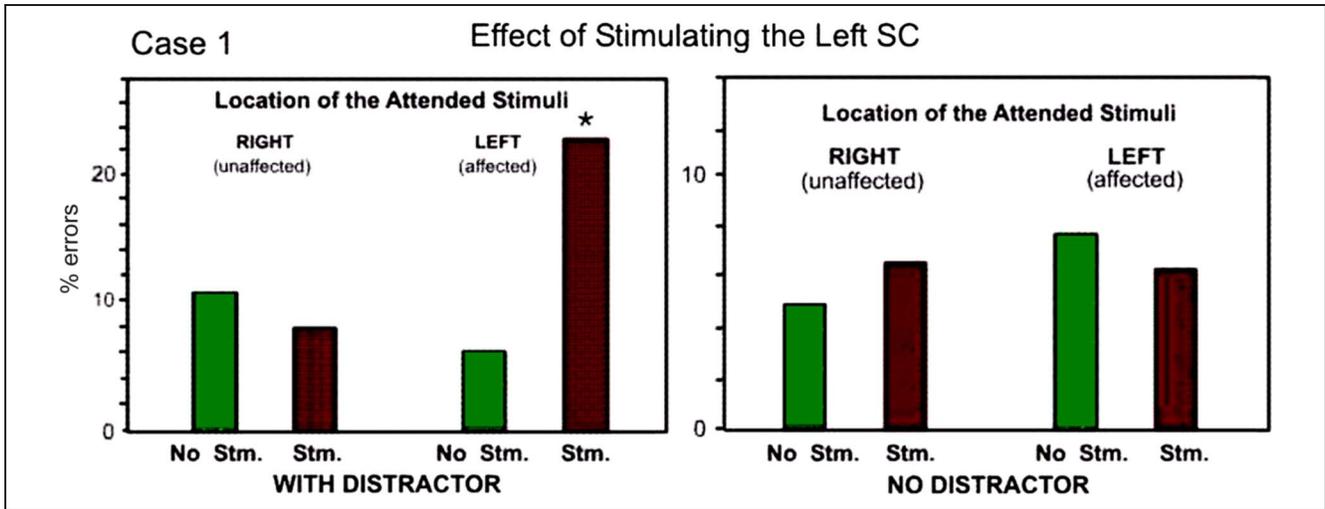
Figure 7. Ineffective and effective shifts of attention in Case 1. (A) Stimulation of unattended sites without a distractor causes little or no impairment. Stimulation at unattended sites at the time of the sample stimulus (no distractor present) also causes little or no impairment. (A) Stimulation of the SC at the site of an irrelevant distractor impairs performance. Changes of the focus of spatial attention (cone) by electrical stimulation (concentric rings) at time T2, the time in which the animal makes the match/nonmatch decision. Performance is impaired when the site of the distractor is stimulated.

elsewhere in the visual field. We therefore expected that the behavioral effects of stimulation would be more severe with a distractor present than if the stimulated site was blank. Figure 6 shows that this was the case.

For the first animal (Case 1), the data are shown for distractor and no distractor conditions in those sessions in which both types of trials were used (Sessions 7 and 23). For the second animal, the performance on the distractor trials was shown previously in Figure 7. In one animal, there was a small significant effect of stimulation without a distractor at the stimulation site (Case 1: $\chi^2 = 0.144$, $p = .705$; Case 2: $\chi^2 = 0.029$, $p = .866$). As a comparison, we also tested the effects of stimulating the unattended site at the time of the sample stimulus, when no distractor was present in the visual field (not shown). In neither animal was the effect of stimulation significant, compared with the nonstimulated condition (Case 1: $\chi^2 = 6.87$, $p = .009$; Case 2: $\chi^2 = 4.06$, $p = .04$). Thus, it appears that stimulation must be combined with a visual stimulus to "grab" the animal's attention.

Effects of Stimulation with Foveal and Extrafoveal Stimuli

In one animal (Case 1), we tested the effects of stimulation when the attended stimulus was at the fovea and the unattended site was at an eccentricity of 4° in the field contralateral to the stimulating electrode in SC. These tests were conducted in sessions that were "interleaved" with Sessions 7–22 in the studies described earlier in the Results with the attended and unattended locations across the midline. Figure 8 shows that the animal was significantly impaired when we stimulated the site of distractor in the contralateral field while the animal was
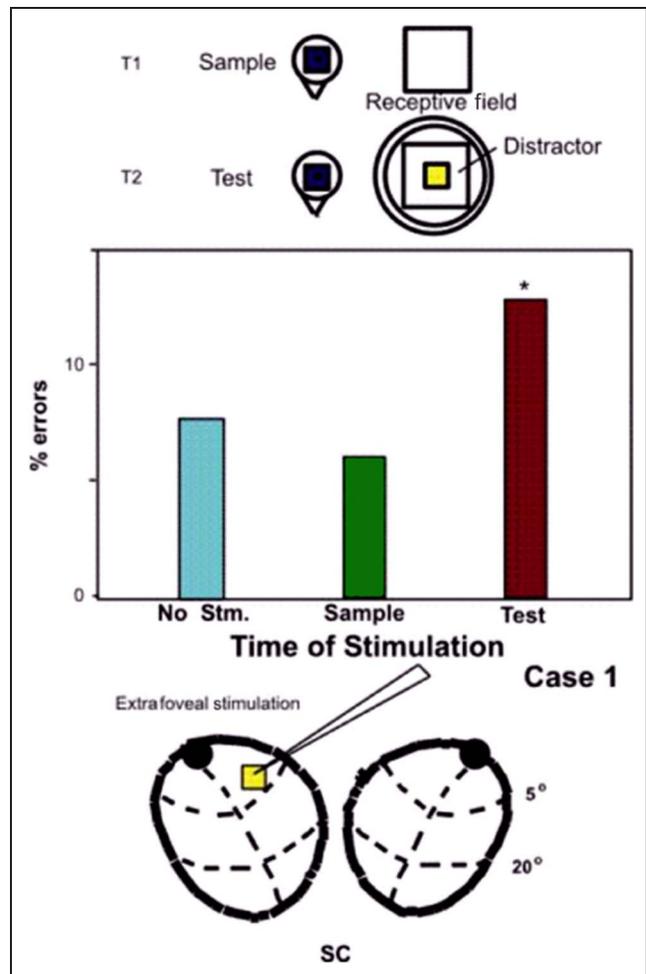
Figure 8. Extrafoveal stimulation during the test stimuli (in T2) in trials with distractor led to significantly more errors than the same trials in the absence of a distractor.

performing the task with stimuli at the fovea ($\chi^2 = 7.38$, $p = .007$). The figure also shows that stimulating the unattended site at the time of the sample stimulus (when no distractor was presented in the visual field) had no significant effect on performance ($\chi^2 = 1.37$, $p = .24$), which is consistent with the results without a distractor described earlier. Interestingly, when we stimulated at the site of the target presented on the fovea, with the distractor in the periphery, performance was actually improved with stimulation compared with the unstimulated condition ($\chi^2 = 3.96$, $p = .04$). Thus, stimulating at the site of the attended stimulus on the fovea apparently made the extrafoveal distractor less "distracting."

Effects of Stimulation on Eye Movements

In the same animal (Case 1) in which we studied the effects of foveal stimulation on attention, we also examined the effects of foveal stimulation on saccadic eye movements to extrafoveal targets. In this task, the animal was rewarded for making an eye movement to a target that appeared in the field ipsilateral or contralateral to the stimulating electrode, at an eccentricity of 4°–5°. Figure 9 shows the results of stimulating the foveal representation on eye movements into the ipsilateral or contralateral visual field. Compared with the unstimulated condition, the animal was impaired in making eye movements into the field ipsilateral to the stimulating electrode ($\chi^2 = 4.25$, $p = .039$).

When the animal was performing the task with the relevant stimuli presented at the fovea and a distractor in the periphery, stimulation at the fovea caused an improvement in performance. Performance is however impaired after the stimulation at the location of a distractor when the animal was performing a foveal task.

In summary, foveal and extrafoveal stimulation during the test stimuli (in T2) in trials with distractor led to significantly more errors than the same trials in the absence of a distractor. Stimulation of the foveal region leads to qualitatively different results from those of stimulation of the extrafoveal region; stimulation during the presentation of the test stimuli at the representation of the location of a distractor induces the animal to make more errors. Stimulation during the presentation of the sample (in the absence of a distractor) had no effect in all conditions.

DISCUSSION

Microstimulation of the SC focuses attention without moving the eyes. Stimulation of extrafoveal locations of the SC showed that it also contributes to the control of covert spatial attention, a process that focuses attention on a region of space different from the point of gaze (Müller et al., 2005). The result with single units gains support on previous data on the effect of stimulation of the SC (Gattass & Desimone, 1992). Electrical stimulation at the site of the irrelevant distractor in the SC causes it
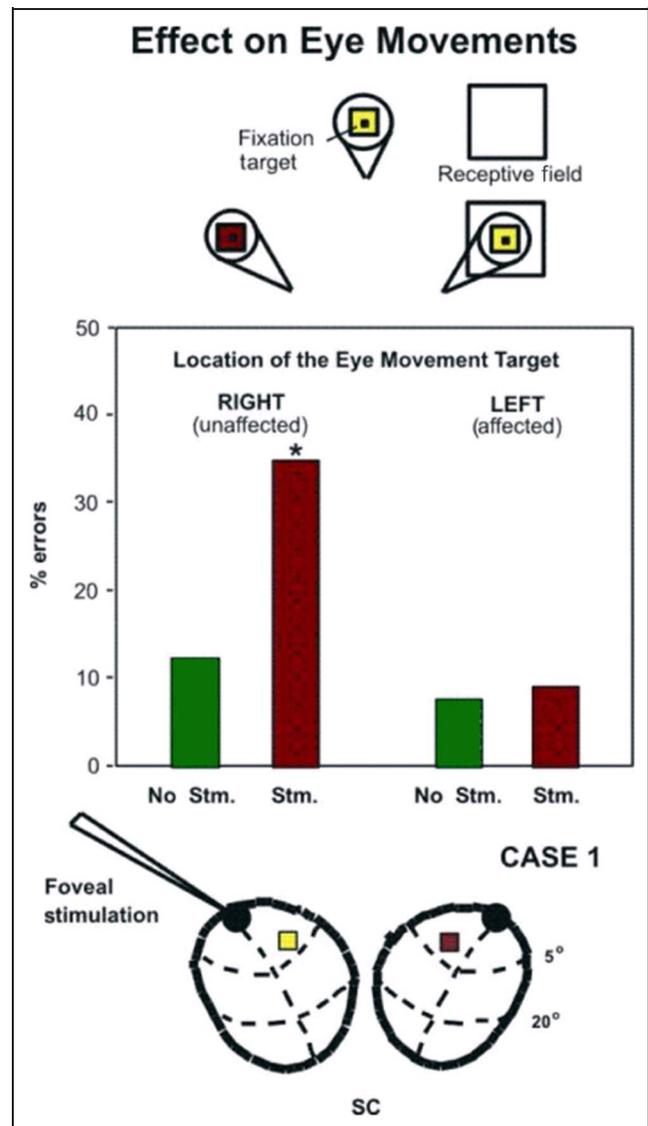
Figure 9. Effect on eye movements. Stimulation of the foveal representation in the SC disrupts or delays a saccadic eye movement when the target is located in the ipsilateral visual field.

to gain control over attention, causing impaired performance of the task at the relevant location. Stimulation at unattended sites without a distractor stimulus causes little or no impairment in performance. The effect of stimulation decays with successive stimulations. The animals learn to ignore the stimulation unless the parameters of the task are varied.

The decrease of the microstimulation effect is probably related to a learning effect related in part to the predictability of the distractor/microstimulation timing. This learning neglect is related to the locus of stimulation, inasmuch as a partial recovery of the effect is observed when we change the location of the microstimulation. The ability of the electrical stimulation to draw attention to the distractor location fades with repeated trials, as although the system were reequilibrating, or the monkeys

were somehow learning to ignore the added strength of the signal coming from that spatial location.

Using visual threshold measurements as a behavioral metric of attention, Moore and Fallah (2001, 2004) showed that electrical microstimulation of the FEF improved psychophysical performance by facilitating the deployment of attention to the location of the visual stimulus. The effect was spatially localized to the region of the visual field encoded at the stimulation site and thus could not be attributed to a general increase in arousal or vigilance. This was a landmark study first because of its implications concerning the neural substrate of visuospatial attention but more importantly because it is the only demonstration (of which we are aware) of a transient brain manipulation that actually improves perceptual performance.

Recording from single neurons has been considered an important tool for understanding the neural mechanisms of perception (Barlow, 1986; Barlow, Blackmore, & Pettigrew, 1967). In this study, we found that cells at the superficial layers of the SC contribute to the control of covert spatial attention and that electrical stimulation at the site of the irrelevant distractor in the SC causes it to gain control over attention, causing impaired performance of the task at the relevant location. We found about 18.2% of cells with clear visual responses, and these responses were enhanced when attention was focused at the receptive field location. The majority of cells showed poor visual response; nonetheless, these responses were enhanced by spatial visual attention. The paradigm used to isolate the cells was not dependent on good visual responses; thus, the sample of single unit recorded from SC was completely unbiased. The only condition to study the unit was a good signal to noise ratio (good isolation) and that the recording site where located within the first 950 μm of the surface in the superficial layers of the SC. The majority of the cells of the superficial layers of the SC of monkeys performing test requiring maintained fixation gave poor responses to the unattended distractor flashed on the receptive field. The strength of these responses contrasts with the brisk responses recorded in SC in anesthetized monkeys. We attribute the weak strength of these responses to the use of static (not moving) presentation of colored 0.7° squares and the use of a test requiring the suppression of saccadic eye movement inasmuch as the animals are required to hold fixation at a visual target throughout the trial. The population analyses showed statistically significant asymmetric distribution for all the relevant tests of automatic attention. This strong effect observed in the population analysis contrasts with the small number (16.2%) of cells with good visual response and clear attention enhancement. Figure 10 shows a summary of the single-unit attention enhancement results of the group of cells with good visual responses (Gattass & Desimone, 1991, 1996). This figure shows the distribution of the attention index from a population of 66 cells

from the superficial layers of the SC studied with the unblocked trial paradigm shown in the top of the figure and a master histogram of 36 cells to the attended and unattended stimulus shown on the bottom. Gattass and Desimone (1996) calculated the attention index as a ratio of the response to a small colored square inside the receptive field as an attended test (nonmatch) stimulus to that of the same stimulus presented as a distractor. The distribution of the attention index shows that the number of cells with attention index higher than 1.1 is significantly higher than the number of cells with attention index smaller than 0.9 (attention bias). On average, the attended stimulus caused a response 1.2–2.2 times bigger than the response to the unattended stimulus. The master histogram (Figure 10, bottom) shows the averaged responses to a small colored square inside the receptive field as an attended test (nonmatch) stimulus and as a distractor. With a paradigm similar to the one used in this study, Gattass and Desimone (1996) showed that the response to the sample is the strongest, followed by the response to the attended test stimulus and then to the distractor. At the beginning of the trial, the sample is a unique stimulus and indicates to the
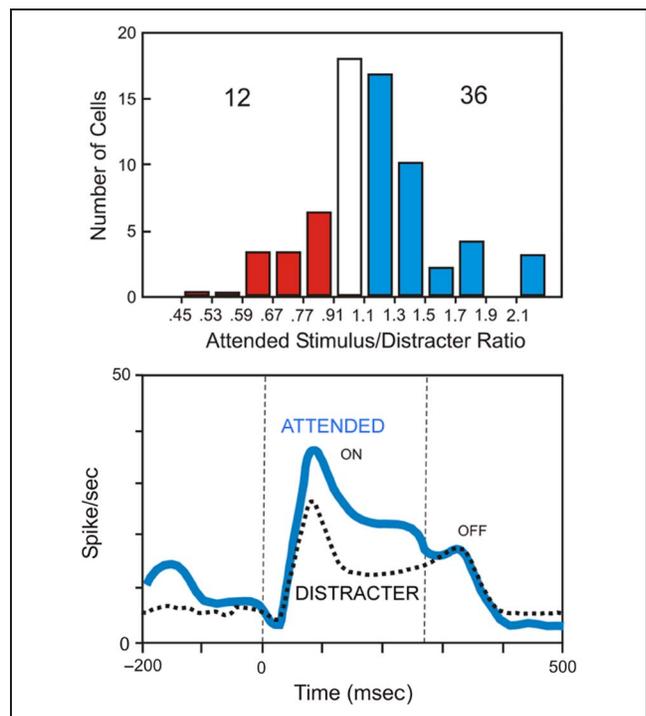
Figure 10. Attention enhancement. Distribution of the attention index from a population of 66 cells from the superficial layers of the SC studied with unblocked trial paradigm (top) and master histogram of 36 cells to the attended and unattended stimulus (bottom). The number of cells with attention index higher than 1.1 (attention bias) is significantly higher than the number of cells with attention index smaller than 0.9. The averaged response to a small colored square inside the receptive field as an attended test (nonmatch) stimulus is higher than that when the same stimulus is a distractor (modified from Gattass & Desimone, 1996).

animal to which side he has to focus his attention. In spite of the number of the effective neurons in the sample, the single-unit results support the behavioral stimulation results described here. It is also consistent with the existence of attention signals at the superficial layers of the SC that automatically propagates downwards to the deep layers and engages spatial visual attention.

Phosphenes or Direct Attentional Shift

Cavanaugh and Wurtz (2004) developed a change blindness paradigm for visual motion and then showed that presenting an attentional cue diminished the blindness in both humans and old world monkeys. When they replaced the visual cue with weak electrical stimulation of the SC to see if its activation contributes to the attentional shift that counters change blindness, they found that the monkeys more easily detected changes and had shorter RTs, both characteristics of a shift of attention. Cavanaugh, Alvarez, and Wurtz (2006) also tested the phosphene hypothesis in the SC by comparing the effect of interchanging real visual stimuli and electrical stimulation. The evidence shown by these authors (Cavanaugh et al., 2006) favors that SC stimulation produces a direct shift of attention rather than generates an internal visual cue, as a phosphene. The rejection of the phosphene hypothesis certainly applies to the SC stimulation experiments of Müller et al. (2005), suggesting that their results as well are not because of a phosphene, as they concluded from their analysis, but rather favor the concept that SC stimulation directly produces a shift of attention. Cavanaugh et al.'s (2006) arguments might apply to the experiments of Moore and Fallah (2001) that stimulated FEF, an area where the neurons also exhibit visual- and saccade-related activity. However, one would expect that stimulation of human FEF with TMS would reveal phosphenes if they were present, but no such perceptual artifact has been reported (Ruff et al., 2006). Despite the possible pathways by which these signals enhance visual processing, the main evidence points to the conclusion that attention does not follow an internal visual flash but rather shifts directly in response to SC stimulation (Cavanaugh et al., 2006). These data are consistent with a key role of the SC in the premotor theory of attention. Although we did not address this issue directly with the behavioral paradigms used, we have no evidence for the "distracting" effects of SC microstimulation because of the introduction of phosphenes at the site of the distractor, with such low currents.

Desimone and Moran (1985) proposed a mechanism on which competing processes within extrastriate areas, such as V4, would favor processing of receptive field in a specific location of the visual field allowing the information in this region to prevail over the noise (Moran & Desimone, 1985). We propose that the attentional process is composed by a series of mechanisms, which involves different subcortical structures and various corti-

cal areas. The visual topography of the cortical areas (Neuenschwander, Gattass, Sousa, & Piñon, 1994; Fiorani, Gattass, Rosa, & Sousa, 1989; Gattass, Souza, & Gross, 1988; Rosa, Souza, & Gattass, 1988; Gattass, Souza, & Rosa, 1987; Gattass, Souza, & Covey, 1985; Gattass & Gross, 1981; Gattass, Gross, & Sandel, 1981), of the pulvinar (Bender, 1981; Gattass, Oswaldo-Cruz, & Souza, 1978, 1979; Gattass, Sousa, & Oswaldo-Cruz, 1978; Allman, Kaas, Lane, & Miezin, 1972), and of the SC provide the topographical framework for spatial visual attention. The present data support a scheme that distinguishes at least two attentional mechanisms: one automatic, mediated by the FEF and SC; and another central or cognitive one, not related to the SC but rather to visual area V4.

Lovejoy and Krauzlis (2010) showed that inactivation of primate SC impairs covert selection of signals for perceptual judgments. More recently, Zénon and Krauzlis (2012) tested the hypothesis that SC, which has a crucial role in visual attention, acts through the visual cortex. They transiently inactivated the SC during a motion-change-detection task and measure responses in two visual cortical areas, middle temporal and medial superior temporal. They found that, despite large deficits in visual attention, the enhanced responses of neurons in the visual cortex to attended stimuli were unchanged. On the basis of these results, they proposed that the SC contributes to visual attention through mechanisms that are independent of the classic effects in the visual cortex, as proposed here.

Conclusions

1. The SC makes contributions jointly to both oculomotor control and covert spatial attention.

2. The spatial visual attention enhancement is limited to the unset of the response to the target stimulus. It does not modify the response to the offset of the stimulus.

3. Microstimulation of the SC focuses covert attention to an extrafoveal stimulus without moving the eyes.

4. Electrical stimulation at the site of the irrelevant distractor will cause it to gain control over attention, causing impaired performance of the task at the relevant location.

5. Stimulation at unattended sites without a distractor stimulus causes little or no impairment in performance.

6. The effect of stimulation decays with successive stimulations. The animals learn to ignore the stimulation unless the parameters of the task are varied.

7. Stimulation of the SC tips the attentional balance of the competition to the stimulus at the site of stimulation.

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