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Superior Colliculus and Visual Spatial Attention

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Abstract

The superior colliculus (SC) has long been known to be part of the network of brain areas involved in spatial attention, but recent findings have dramatically refined our understanding of its functional role. The SC both implements the motor consequences of attention and plays a crucial role in the process of target selection that precedes movement. Moreover, even in the absence of overt orienting movements, SC activity is related to shifts of covert attention and is necessary for the normal control of spatial attention during perceptual judgments. The neuronal circuits that link the SC to spatial attention may include attention-related areas of the cerebral cortex, but recent results show that the SC's contribution involves mechanisms that operate independently of the established signatures of attention in visual cortex. These findings raise new issues and suggest novel possibilities for understanding the brain mechanisms that enable spatial attention.

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INTRODUCTION

Visual spatial attention allows animals to base decisions on relevant environmental stimuli and suppress irrelevant signals. It is associated with a variety of changes in neural processing and is controlled by a network of cortical brain areas, especially the parietal, prefrontal, and extrastriate visual cortices. The importance of this cortical network has been established using a range of techniques, including lesions, electrophysiology, and fMRI, and this work has been thoroughly summarized in several reviews (Desimone & Duncan 1995, Petersen & Posner 2012, Reynolds & Chelazzi 2004).

Investigators have long recognized that, beyond these cortical areas, the superior colliculus

(SC), an evolutionarily conserved structure located on the roof of the vertebrate midbrain, also plays a central role in visual spatial attention (Goldberg & Wurtz 1972). A key aspect of this role is controlling orienting movements of the eyes and head that are tightly linked to shifts of spatial attention; this motor function of the SC has been reviewed elsewhere (Gandhi & Katnani 2011, Sparks 1999, Wurtz & Albano 1980). However, several lines of evidence indicate that the SC does more than simply implement the motor consequences of attention shifts prescribed by the cerebral cortex. In this article, we first review evidence that the SC is necessary for the normal control of spatial attention. We then consider several candidate circuits that could mediate this role, illustrating that key components of the brain mechanisms of attention may lie outside the scope of current models.

BASIC FEATURES OF THE SC

We first very briefly review some of the basic features of the primate SC; a more comprehensive review can be found elsewhere (May 2006).

The SC is a laminar structure delineated by alternating strata of fibers and soma. In primates, these are usually divided broadly into superficial, intermediate, and deep layers. The superficial layers receive direct projections from both retinal ganglion cells and striate cortex and contain neurons that exhibit a variety of responses to salient visual stimuli. Neurons in the intermediate and deep layers receive input from the extrastriate cortex and also respond to visual stimuli; however, consistent with the diverse anatomical connections of these layers, these neurons also respond to stimulus modalities in addition to vision, and most exhibit activity patterns related to the planning and execution of orienting movements. This diversity belies the view of the SC as simply a node in a descending motor pathway; instead, it contains multiple classes of neurons that provide points of interconnection between many circuits serving a range of sensory, motor, and cognitive functions.



In addition to their diverse features and properties, SC neurons are organized in a topographic map of visual space. The SC on each side of the brain contains a representation of the contralateral visual field, with an enlarged representation of the central visual field. In the superficial layers, this is a map of stimulus position. In the intermediate and deep layers, a corresponding map organizes activity related to orienting movements and selecting visual stimuli. These maps provide the anatomical basis for the role of the SC in visual spatial attention.

EVIDENCE FOR A ROLE IN SPATIAL ATTENTION

The Sprague Effect

As first described by Sprague (1966), lesions of the SC in cats can lead to an unexpected recovery from deficits in spatial orienting caused by damage to other parts of the attention network. After the occipital or parietal cortex is lesioned on one side of the brain, cats exhibit visual neglect—the tendency to ignore visual objects presented in the affected part of the visual field. When activity in the SC on the opposite side of the brain is then suppressed, the symptoms of visual neglect are typically relieved. In a remarkable clinical case, the symptoms of visual neglect experienced after damage to the frontal cortex were relieved by additional subsequent damage to the contralateral SC, suggesting that the Sprague effect also extends to humans (Weddell 2004).

The Sprague effect was initially thought to be a recovery from cortical blindness, in which the transmission of visual information from the superficial layers of the SC to the cortex (via pulvinar) was disinhibited by ablating the SC on the other side (Diamond & Hall 1969, Robson & Hall 1977, Trojanowski & Jacobson 1975). Subsequent work found that the effect is not caused by interactions between the two sides of the SC but instead depends on inhibitory input from the substantia nigra pars reticulata or pedunculo pontine region (Ciaramitaro et al. 1997; Durmer & Rosenquist 2001; Wallace

et al. 1989, 1990). The anatomy of these connections implicates the intermediate and deeper SC layers, rather than the superficial layers, in these manipulations of spatial orienting.

Selecting Visual Targets

In addition to the SC's function in the motor implementation of orienting movements, multiple lines of evidence indicate that the SC plays a central role in the process of selecting which stimuli will guide behavior.

Neuronal activity in the intermediate and deeper layers of the SC is related to evaluating possible saccade targets. SC neurons show elevated activity for visual stimuli that will be selected as the end point of saccades, relative to those that are ignored (Glimcher & Sparks 1992, Krauzlis & Dill 2002, McPeck & Keller 2002), and this activity is proportional to the probability that a saccade will be made into their response fields (Basso & Wurtz 1998, Dorris & Munoz 1998, Horwitz & Newsome 2001). For many neurons this modulation predicts the upcoming saccade, but for others it is related to the selected visual stimulus rather than to the movement itself (Horwitz et al. 2004, Horwitz & Newsome 1999, McPeck & Keller 2002).

Some aspect of SC activity is necessary for saccade target selection because chemically blocking activity disrupts saccade choices: When the target is placed in the affected part of the visual field, saccades tend to be erroneously directed to distracter stimuli located elsewhere (McPeck & Keller 2004, Nummela & Krauzlis 2010). Conversely, when SC activity is artificially raised by electrical microstimulation, saccade selection favors the stimulus location matching the activated SC site (Carello & Krauzlis 2004, Dorris et al. 2007).

Experiments using pursuit eye movements, rather than saccades, show that SC activity is not involved just in saccade selection but also in the process of target selection itself. In contrast with saccades, which rapidly redirect the line of sight, pursuit slowly rotates the eyes to follow moving targets (Krauzlis 2005, Lisberger 2010). Because pursuit depends on the motion



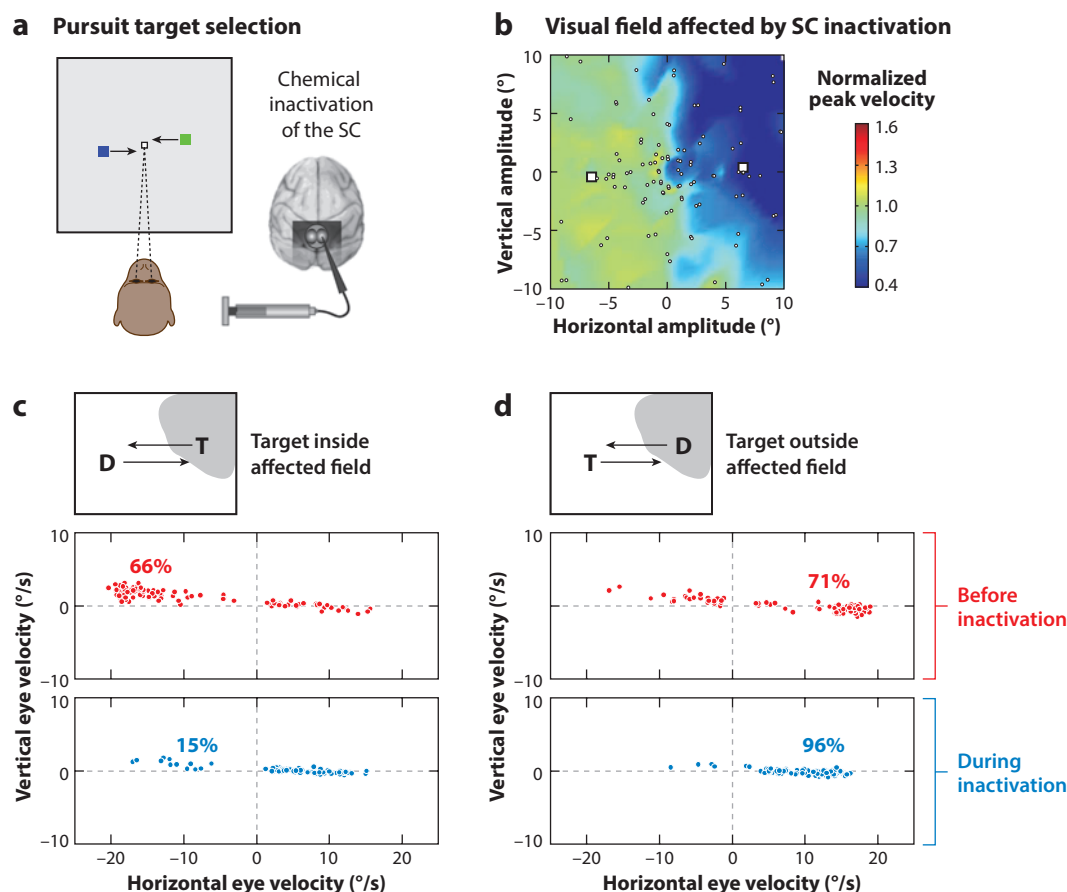


Figure 1

Effects of superior colliculus (SC) inactivation on pursuit target selection. (a) The task was to smoothly track the target defined by a precue. Performance on this two-alternative task was measured before and after SC inactivation. (b) The area affected by SC inactivation was estimated by measuring the change in peak velocity of saccades to visual targets. (c) Changes in performance when the target appeared inside the affected part of the visual field. The distributions of target choices are illustrated by plotting the mean horizontal eye velocity against mean vertical eye velocity over the first 100 ms of the pursuit eye movement response. SC inactivation reduced correct choices from 66% to 15% correct. (d) When the distracter appeared in the affected part of the visual field, correct pursuit choices improved from 71% correct to 96% correct. Overall, SC inactivation biased choices in favor of the stimulus appearing outside the affected region, even though these required movements toward the affected field. Adapted from Nummela & Krauzlis (2010).

of the target, rather than the target's location, it can dissociate target selection from movement direction; for example, if a target appears on the left and moves rightward, the subject should select the stimulus on the left even though this requires a rightward movement.

SC neurons change their activity during pursuit as expected from the retinotopic map—they increase their discharge when the image of the target falls inside their response

field (Krauzlis 2003; Krauzlis et al. 1997, 2000). When there are multiple moving stimuli, SC neurons show enhanced activity for the selected target, even if doing so requires a pursuit movement directed away from the target's starting location (Krauzlis & Dill 2002). Chemically inhibiting SC activity causes a neglect-like impairment (see **Figure 1**). Choices are strongly biased against the stimulus initially located inside the affected part of the visual field, in

favor of whichever stimulus is located outside the affected region (Nummela & Krauzlis 2010, 2011); similar pursuit impairments occur in patients with hemineglect (Rizzo & Hurtig 1992). Conversely, artificially activating the SC biases target choice in favor of the stimulus placed at the matching location in the visual field (Carello & Krauzlis 2004).

Moreover, inhibiting SC activity impairs target selection even when the eyes remain fixed and the response involves moving the hand. As in the eye movement tasks, chemical inactivation biases choices away from the stimulus placed in the affected part of the visual field. The effects are large when animals reach directly to targets on a touch screen (Song et al. 2011) and are also present when subjects press buttons on a response pad positioned outside the field of view (Nummela & Krauzlis 2010).

Overt and Covert Attention

The SC's role in target selection appears to be related to a broader role in spatial attention, including both overt shifts during saccades and covert allocation in the absence of orienting movements.

Signals related to spatial attention and saccade commands are intermingled in the primate SC. For example, the end points of saccades evoked by stimulating the SC are systematically deviated in the direction of spatial cues, suggesting that shifts of attention prompted by spatial cues automatically lead to saccade preparation (Kustov & Robinson 1996). The time course of these deviations reflects the origin of the shift: Peripheral cues cause deviations at short delays, consistent with a stimulus-driven effect, whereas central cues cause deviations at longer delays, consistent with a top-down effect.

Neuronal activity in the SC is modulated by peripheral cues in ways that parallel the behavioral effects on saccades. When a peripheral cue is flashed just before the visual target for a saccade, it reduces saccade latency and causes a larger neuronal response. These effects are larger when the cue is predictive of the target location, indicating that top-down, as well as

stimulus-driven, factors are involved (Bell et al. 2004, Fecteau et al. 2004). These results support the view that activity in the SC reflects both the stimulus-driven and top-down factors that regulate spatial attention and saccade selection (Fecteau & Munoz 2006).

Although SC activity may have been restricted to spatial attention associated with eye movements, other studies have shown that the SC may play a role in covert attention. In one study, animals discriminated the orientation of a Landolt "C," and spatial attention was manipulated using spatial and symbolic cues (Ignashchenkova et al. 2004). The pattern of effects depended on the type of neuron (see **Figure 2**). "Visual" neurons (with visual activity but lacking saccade-related activity) had larger responses to the appearance of the "C" when the location was cued, for both spatial and symbolic cues. In contrast, "visual-motor" neurons (with both visual and saccade-related activity) showed a similar effect, but only for spatial cues and not for symbolic cues. These neurons also showed higher activity during the delay period after the spatial cue was presented but before the appearance of the "C" stimulus, suggesting that visual-motor SC neurons may be especially important for stimulus-driven shifts of attention.

Some studies have applied subthreshold microstimulation (too weak to evoke saccades directly) to test whether SC activity plays a causal role in spatial attention. One study (Cavanaugh et al. 2006, Cavanaugh & Wurtz 2004) tested spatial attention using change-blindness, the inability to detect changes in a visual scene when those changes are accompanied by a full-field transient such as a blank screen (Rensink 2002). Animals were shown three patches of random-dot motion and were required to detect if any patch changed its motion direction after the blank. On some trials, the animal was given a spatial cue to indicate which motion patch might change, and on other trials the SC was microstimulated at a location matching one of the three patches. SC microstimulation caused effects nearly identical to those obtained with spatial cues: Detection performance improved and reaction times decreased. These effects



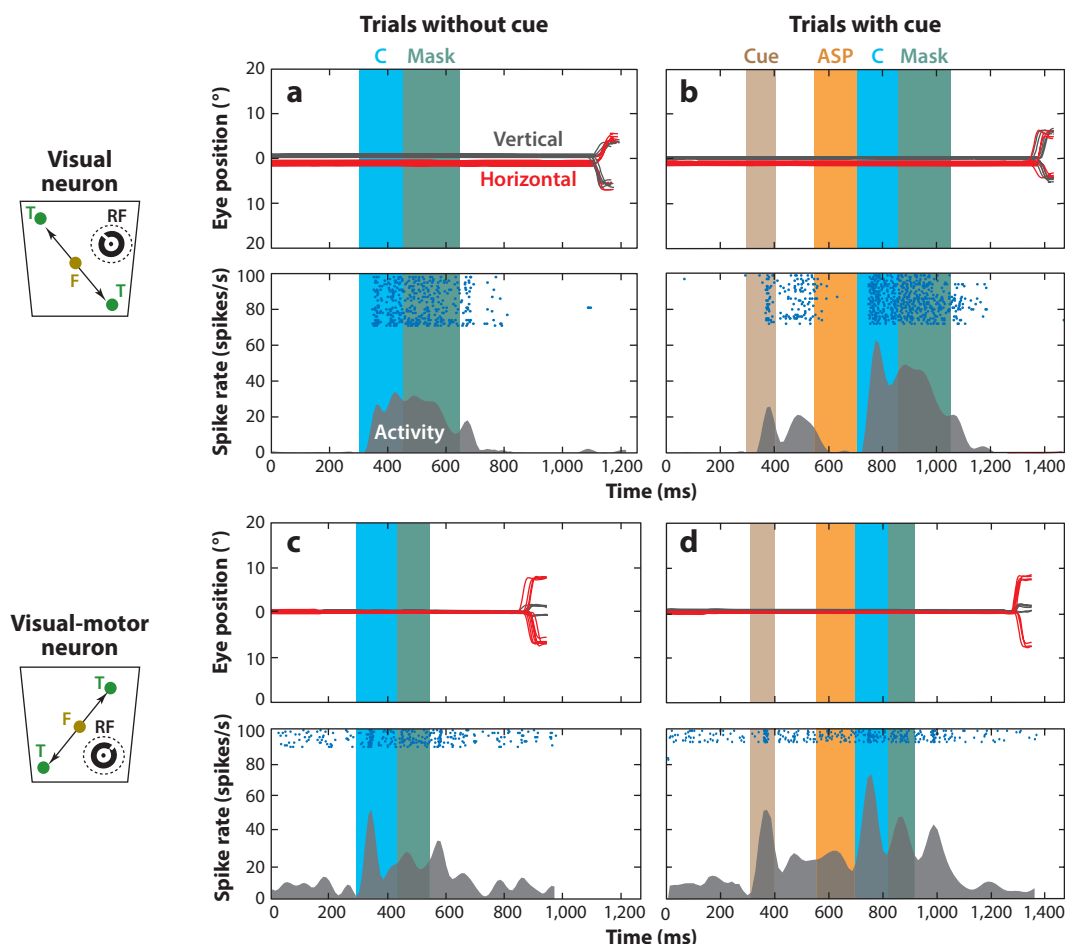


Figure 2

Changes in superior colliculus (SC) activity during covert shifts of spatial attention. The sample visual neuron showed enhanced activity (*shaded area*) when the animal was shown a spatially precise cue (*b*) compared to when the animal was shown no cue (*a*). (*c–d*) Sample visual-motor neuron under the same task conditions. Both the visual and visual-motor neurons responded to the presentation of the “C” (*pink*), but this activity was higher when the location of the “C” (*blue*) was cued than when it was not cued. Also, the visual-motor neuron showed activity during the time epoch before the presentation of the “C” [attention shift period (ASP), *orange*], but the visual neuron did not. Abbreviations: F, fixation spot; RF, receptive field of neuron; T, choice target. Adapted from Ignashchenkova et al. (2004).

cannot be explained by a response bias because the animals were not simply more likely to report a change but rather became better at detecting when changes occurred.

In another study, SC microstimulation was applied as animals judged the direction of motion in a random-dot motion patch, which was made more challenging by including irrelevant flickering dots elsewhere in the display (Müller et al. 2005). The performance of the an-

imal was summarized with psychometric curves showing how the percentage of correct answers increased with signal strength. Microstimulation in the intermediate SC improved discrimination performance; the psychometric curves shifted leftward, meaning that less visual motion was needed to achieve a particular level of performance. This improvement in performance was observed only if the SC site and motion patch were at spatially coincident locations.

These microstimulation studies show that altering SC activity is sufficient to evoke attention-like changes in performance. To test whether SC activity is necessary, behavioral performance was tested before and during reversible chemical inactivation of the SC (Lovejoy & Krauzlis 2010). The task in these experiments was to discriminate the direction of motion in a random-dot motion patch that appeared at a previously cued location (see **Figure 3**). To ensure that spatial attention was necessary to perform the task, the display included an irrelevant “foil” stimulus that also contained random-dot motion but appeared at an uncued location and should therefore have been ignored.

The ability of animals to select the appropriate stimulus for basing perceptual judgments was profoundly impaired during SC inactivation. When the cued stimulus was placed in the affected part of the visual field, performance was severely impaired, but the errors were not random. They tended to be based on the irrelevant foil stimulus placed outside the affected region. This pattern of errors shows that the animal still attempted to discriminate the direction of motion after the SC was inactivated but erroneously based his choices on the stimulus at the wrong spatial location. In control experiments,

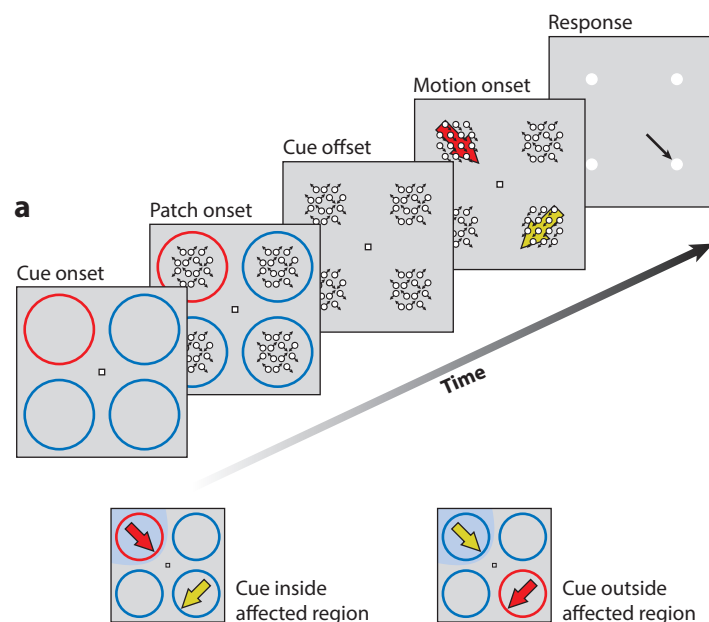
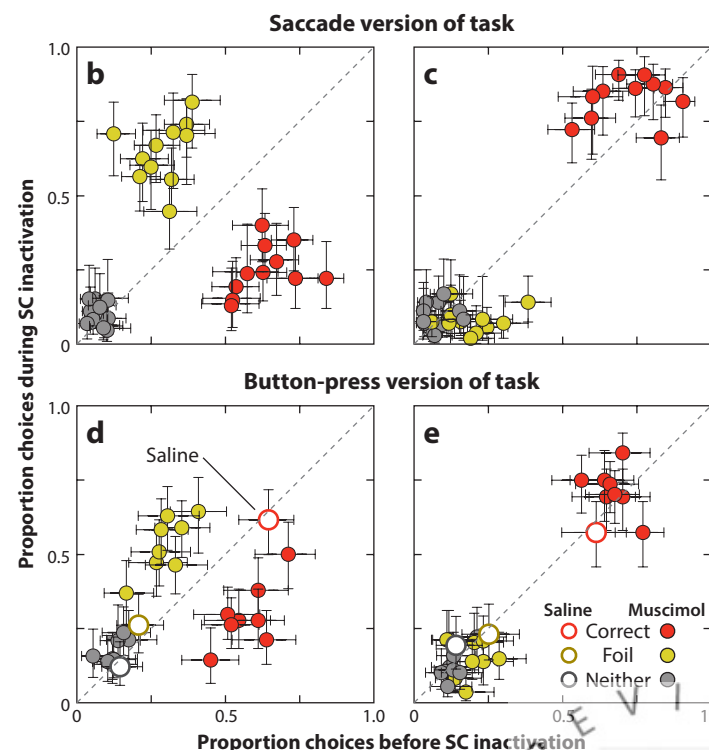


Figure 3

Impairments in covert selection of signals for perceptual judgments during superior colliculus (SC) inactivation. (a) Task design. A color cue indicated the relevant motion patch, which contained a brief pulse of motion in one of four possible directions. The animal indicated its choice either by making a saccade in the discriminated direction or by pressing a corresponding button. (b) When the cued signal was in the affected region, animals ignored this signal and instead based their choices on the foil. (c) Conversely, when the foil signal appeared in the affected region, subjects tended to ignore the foil. (d–e) Similar results were obtained in the absence of saccades during a button-press version of the task. Filled symbols show data from muscimol injection experiments; open symbols, from saline control injections. Adapted from Lovejoy & Krauzlis (2010).



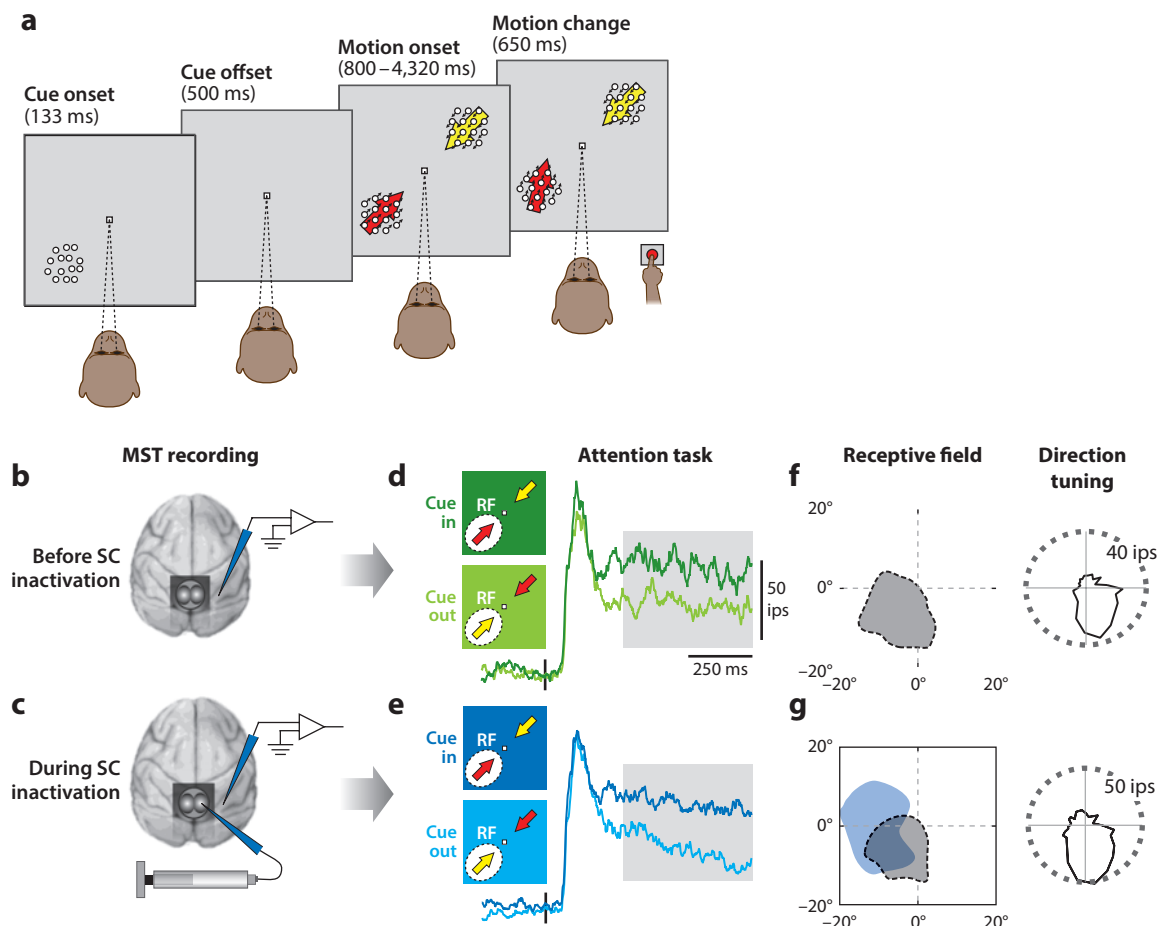


Figure 4

Neuronal correlates of spatial attention remain intact in visual cortex during superior colliculus (SC) inactivation despite behavioral deficits in attention. (a) Task design. A color cue indicated the relevant motion patch, and later either this cued patch or the foil patch changed its direction. If the cued patch changed, the animals reported this detection by pressing a button. (b–c) Neuronal activity was recorded in the medial superior temporal area (MST) before (b) and during (c) SC inactivation. (d–e) Activity of a sample neuron during the attention task before (d) and during (e) SC inactivation. Despite large deficits in task performance caused by SC inactivation, the modulation of neuronal activity by spatial cues remained intact. (f–g) Receptive field and tuning properties before (f) and during (g) SC inactivation. The blue shading shows the affected region. Abbreviations: RF, receptive field. Adapted from Zénon & Krauzlis (2012).

when investigators presented only a single motion patch in the affected part of the visual field, the animal exhibited only a minor impairment in performance, showing that the impairment in the attention task cannot be explained by a deficit in visual-motion processing. This study demonstrates that the SC is not just linked to the neuronal circuit for spatial attention but in fact is necessary for its normal operation.

Interaction with the Visual Cortex

Researchers have generally assumed that if the SC plays a role in the control of spatial attention, it uses the same mechanisms responsible for the well-known effects of spatial attention in the visual cortex (Desimone & Duncan 1995, Petersen & Posner 2012, Reynolds & Chelazzi 2004). However, recent direct tests cast doubt on this assumption (see **Figure 4**). In these

experiments (Zénon & Krauzlis 2012), activity in the SC was chemically inactivated during a motion-change detection task while neuronal activity was simultaneously recorded in two cortical visual areas well known to be modulated by spatial attention: the middle temporal area (MT) and the medial superior temporal area (MST). As in earlier work (Lovejoy & Krauzlis 2010), SC inactivation caused large and spatially specific deficits in spatial attention—the animals' ability to detect changes in the cued stimulus was markedly impaired when it was placed in the affected part of the visual field. These effects cannot be explained by a motor deficit because the operant response was a single-button press that was unimpaired when the attended stimulus was placed outside the affected part of the visual field. If these behavioral deficits were caused by changes in activity ascending from the SC to the visual cortex, then inactivating the SC should also change attention-related effects in the visual cortex. Contrary to this prediction, the attention-related effects in visual cortex—including each of the major signatures of spatial attention—did not change during SC inactivation. Moreover, the ability of neurons to detect the stimulus change, overall firing rates, and other aspects of their activity also did not change, despite the behavioral deficit.

These results are strong evidence against the idea that SC activity contributes to spatial attention through the same mechanisms responsible for the well-known correlates of attention in the visual cortex. The crucial changes may have taken place in other cortical areas—for example, the frontal eye fields (FEF)—but in that case one would still have expected to detect neuronal changes because of the feedback from the FEF to the visual cortex (Moore & Armstrong 2003, Moore & Fallah 2001). Instead, these results demonstrate that the SC's control of spatial attention depends on additional processes that operate independently of the known modulations of activity in the visual cortex.

POSSIBLE NEURONAL CIRCUITS

Although the SC has now been demonstrated to be a key part of the mechanisms for spatial

attention, the neuronal circuits involved are unknown. In addition to establishing well-known connections with motor structures in the brain stem and cerebellum, which is important for the control of orienting movements, the SC also forms circuits with many other brain regions that could serve nonmotoric functions, including spatial attention.

Pathways to the Cortex: Inferior Pulvinar

A circuit from the SC through the inferior pulvinar might explain the possible changes in sensory processing with spatial attention (Figure 5). The properties of this circuit are poorly understood in primates, but in birds it plays a striking role in gating the transmission of visual signals. The superficial layers of the bird optic tectum (homologous to the primate SC) contain a distinctive class of neurons called tectal ganglion cells, which respond to visual motion across large parts of the visual field and contribute to the even larger receptive fields of neurons in the thalamic nucleus rotundus (homologous to the primate pulvinar). Cholinergic inputs to the superficial SC modulate the efficacy of retinal inputs onto these tectal ganglion cells and are involved in resolving competition among multiple stimuli (Lai et al. 2011, Marín et al. 2005, Wang et al. 2006). When this cholinergic input is locally blocked, neurons in the nucleus rotundus no longer respond to visual stimulation in the affected subregion of the visual field (Marín et al. 2007).

Whether a similar functional circuit operates in the primate is not clear, but the inferior pulvinar receives efferents from the superficial layers of the SC and projects to areas in the extrastriate cortex that are specialized for processing visual motion. Investigators identified this pathway using transsynaptic anatomical tracers (Lyon et al. 2010), and they also used electrical stimulation to identify neurons that both project to the cortex and receive inputs from the SC (Berman & Wurtz 2010). Because it provides a direct route to motion-processing areas in the cortex, this pathway has been implicated

FEF: frontal eye fields



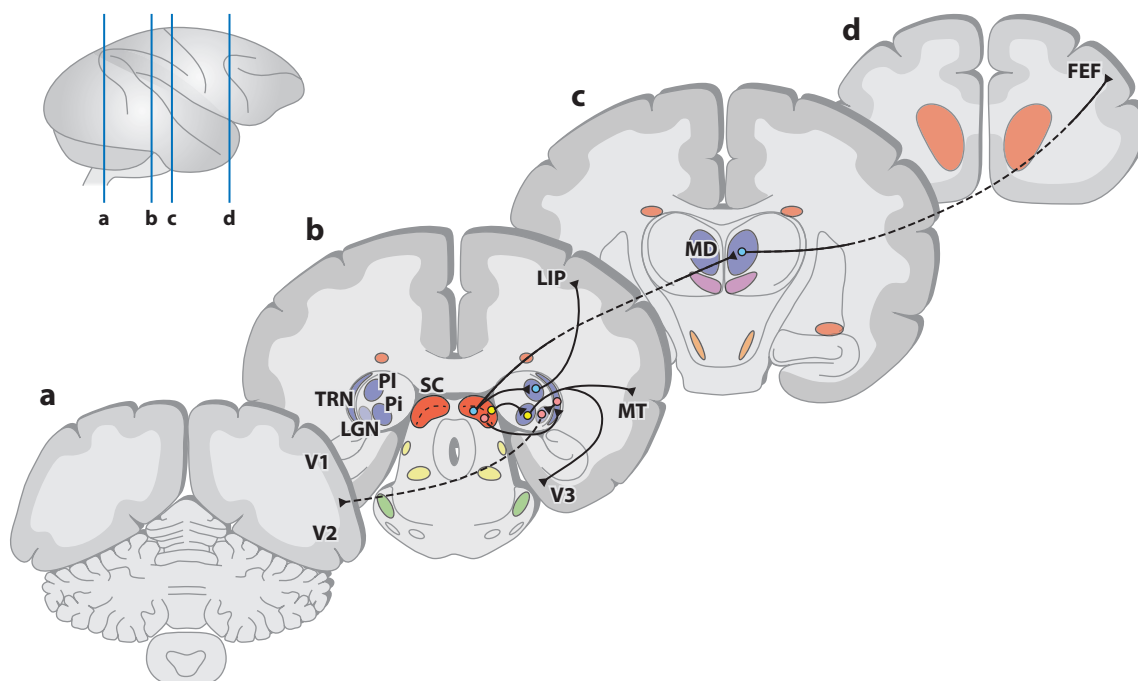


Figure 5

Possible ascending neuronal circuits accounting for the superior colliculus (SC) role in spatial attention. Three circuits are outlined in these schematic sections of the monkey brain. One pathway (*yellow*) passes through the inferior pulvinar (Pi) to the middle temporal area (MT). A second pathway (*pink*) involves the thalamic reticular nucleus (TRN), which connects to the lateral geniculate nucleus (LGN), which, in turn, projects to the visual cortex (V1 and V2). A third pathway (*light blue*) passes through the lateral pulvinar (PI) to the lateral intraparietal area (LIP) and through the mediodorsal thalamus (MD) to the frontal eye fields (FEF).

in the changes in performance on visual-motion tasks caused by SC stimulation (Cavanaugh & Wurtz 2004, Müller et al. 2005).

However, because this circuit links the SC to the visual cortex, its role in the control of attention is not compatible with the observation that the disruption of attention following SC inactivation leaves visual cortical activity unchanged. Moreover, this putative explanation is complicated by the fact that it relies on a circuit involving the superficial layers of the SC. The strongest evidence for a role of the SC in attention implicates the intermediate layers, and the functional role of connections between the intermediate and superficial layers of the primate SC remains an unresolved issue. Therefore, we do not know if such a circuit would be sufficient to explain the role of the SC in the control of attention. Instead, recent evidence suggests

that it may suppress the transmission of self-induced visual signals during saccades (Berman & Wurtz 2011).

Pathways to the Cortex: Thalamic Reticular Nucleus

Another possible circuit involves the thalamic reticular nucleus (TRN). As fibers from other thalamic nuclei pass through the TRN en route to the sensory cortex, they give off collateral branches that contact inhibitory neurons in the TRN that project back to sensory thalamic nuclei (Figure 5). This thalamic feedback loop through the TRN could provide a gating mechanism that regulates signal transmission to the cortex, and the topographic ordering of the connections in the TRN provides a possible anatomical correlate of the putative searchlight

of attention (Crick 1984, Guillery et al. 1998). Consistent with this hypothesis, neuronal activity in the visual TRN is modulated during attention tasks, and these changes precede complementary changes in the lateral geniculate nucleus, the primary visual thalamic nucleus (McAlonan et al. 2006, 2008). Because the intermediate and deep layers of the SC project to the TRN, SC activity may help determine how the TRN gates the transmission of visual signals to the cortex.

Although this putative circuit places the intermediate SC in a central role, it still depends on the notion that the SC contributes to spatial attention by changing sensory processing, which is not consistent with the finding that attention-related changes in the visual cortex remain intact during SC inactivation (Zénon & Krauzlis 2012).

Pathways to the Cortex: Lateral Pulvinar and Mediodorsal Thalamus

The SC is also a member of circuits that could act at stages downstream of sensory processing. Signals from the intermediate and deeper layers of the SC reach areas of the prefrontal and parietal cortex through several thalamic nuclei (**Figure 5**), including the lateral pulvinar and mediodorsal nucleus (Harting et al. 1980, Robinson & Petersen 1992). The ascending input from the SC through the lateral pulvinar reaches cortical areas involved in spatial attention, most notably, the lateral intraparietal area (LIP) in the parietal lobe (Romanski et al. 1997). Area LIP contains a salience map that can guide visual attention as well as saccadic eye movements (Bisley & Goldberg 2010). The functional circuits through the lateral pulvinar are poorly understood; however, neuronal activity in the pulvinar is modulated by manipulations of spatial attention (Benevento & Port 1995, Petersen et al. 1985), and lesions of the pulvinar cause deficits in visual attention tasks (Desimone et al. 1990). Pulvinar lesions tend to produce neglect-like deficits similar to those found during SC inactivation (Lovejoy & Krauzlis 2010)—performance is especially impaired in the presence of distracters.

SPATIAL INDEXING?

The SC contains maps of spatial locations but not stimulus features. Consequently, signals in the SC cannot directly determine the content of spatial attention but must interact with signals from other brain areas that process and represent the qualities of the attended object. One possibility is that the SC is part of a spatial indexing system that identifies which signals elsewhere in the brain should be pooled or otherwise put together to determine the content of perception. In this view, when SC activity is suppressed, signals from the affected part of space can no longer be properly retrieved or shared by other brain regions, resulting in deficits in spatial attention and visual neglect.

Another major component of the ascending input to the cortex from the SC passes through the mediodorsal thalamic nucleus to the prefrontal cortex, including the FEF. One functional role of this pathway is to convey corollary discharge signals about saccadic eye movements (Sommer & Wurtz 2008). In addition to transmitting motor signals about saccades, this pathway also transmits visual and other signals from the SC (Sommer & Wurtz 2004) that may be related to the role of the FEF in the control of attention. In particular, signals from the FEF can cause attention-like changes in the processing of visual signals in the extrastriate cortex (Moore & Armstrong 2003, Moore & Fallah 2001). By modifying signal processing in FEF, the input from the SC could regulate this cortico-cortical feedback mechanism for spatial attention.

These putative circuits place the intermediate SC in a central role and act downstream of sensory processing. However, they still assume that the control of spatial attention occurs through modulation of signal processing in the visual cortex, albeit indirectly through LIP or FEF. This assumption is undermined by the finding that attention-related changes in the visual cortex remain intact during SC inactivation, despite the presence of large deficits in attention (Zénon & Krauzlis 2012).

TRN: thalamic reticular nucleus

LIP: lateral intraparietal area



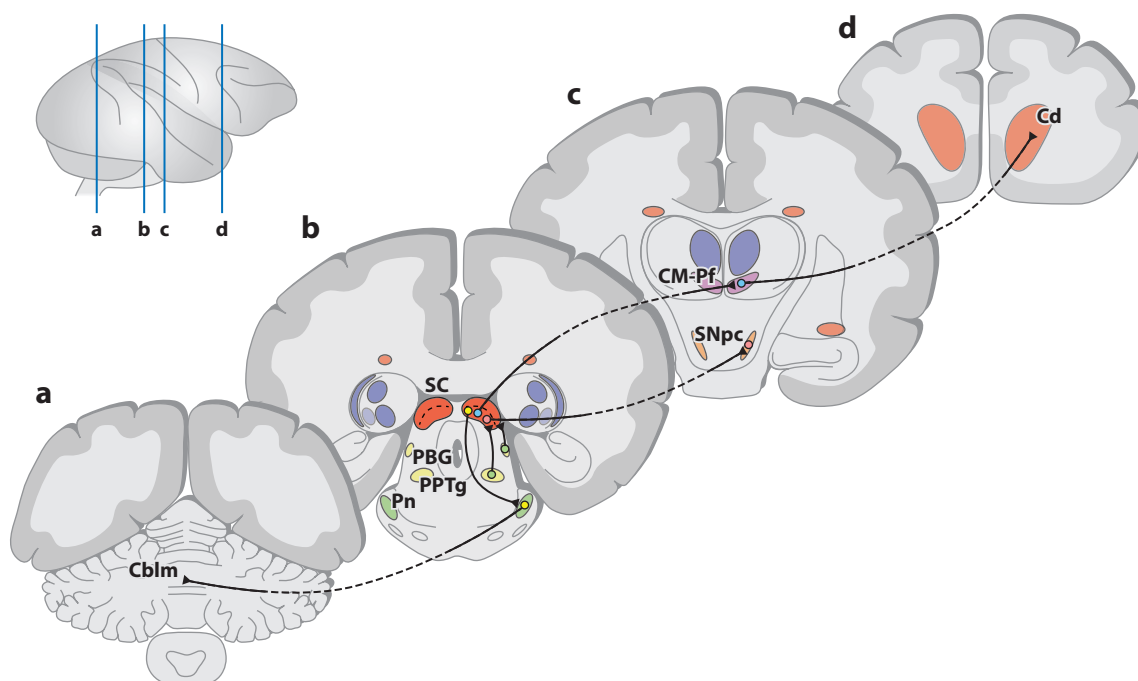


Figure 6

Possible subcortical neuronal circuits accounting for the superior colliculus (SC) role in spatial attention. One pathway (*light blue*) passes through the center median parafascicular complex (CM-Pf) to the caudate nucleus (Cd) in the basal ganglia. A second pathway (*pink*) projects to the substantia nigra pars compacta (SNpc). A third circuit (*green*) involves cholinergic inputs from the pedunculopontine tegmental nucleus (PPTg) and parabrachial nucleus (PBG). A fourth pathway (*yellow*) reaches the pontine nuclei (Pn), which relays cortical signals to the cerebellum (Cblm).

Subcortical Loops Through the Basal Ganglia

Not all the ascending circuits from the SC through the thalamus have the cortex as their primary target. Instead, some SC-thalamic projections are part of subcortical circuits linking the SC to the basal ganglia (see **Figure 6**). One such circuit involves projections to the intralaminar nuclei in the thalamus, which forms part of a loop through the caudate and putamen, to the substantia nigra pars reticulata, and back to the SC. As part of the ascending reticular activating system, the intralaminar nuclei play some role in general arousal. However, portions of the intralaminar nuclei receive inputs from the intermediate and deeper layers of the SC and appear to play a more specific role in the processing of salient events (Sadikot & Rymar 2009, Smith et al. 2004, Van der Werf et al.

2002). For example, neuronal activity in the centromedian-parafascicular (CM-Pf) complex is modulated by spatial cues during attention tasks, and chemical inactivation of the CM-Pf causes spatially specific increases in reaction times (Minamimoto & Kimura 2002). Spatially selective activity has also been found in these structures in humans during covert attention tasks (Hulme et al. 2010).

The anatomical loops formed by these thalamic nuclei with the SC and basal ganglia may act independently of, or competitively with, similar loops originating from the cerebral cortex. The exact role of these loops remains controversial, but one compelling theory is that they implement value-based selection mechanisms at different stages of sensorimotor and cognitive processing (McHaffie et al. 2005; Redgrave et al. 1999, 2010). By providing access to these

selection mechanisms in the basal ganglia, these circuits provide a plausible explanation for how SC inactivation could cause deficits in spatial attention without altering visual cortical responses.

Substantia Nigra Pars Compacta

In addition to a pathway through the thalamus to the basal ganglia, a direct projection from the intermediate and deeper layers of the SC to the substantia nigra pars compacta (SNpc) has been demonstrated in several species, including primates (Figure 6; Comoli et al. 2003, May et al. 2009, McHaffie et al. 2006). The SNpc contains dopamine neurons that play a prominent role in reinforcement learning by providing a prediction error signal (Niv & Schoenbaum 2008, Schultz 2010). However, SNpc neurons also respond to unexpected and salient sensory events (Redgrave et al. 2008, Schultz & Romo 1990), which could be driven at least in part by inputs from the SC and linked to shifts of spatial attention.

Modulatory Inputs from the Brain Stem

As described earlier, the SC receives cholinergic inputs from tegmental cholinergic nuclei that can modulate the transmission of visual signals to the thalamus (Figure 6). The parabrachial nucleus [nucleus isthmi pars parvocellularis in birds (PBG/Ipc)] provides cholinergic inputs mostly to the superficial layer (Wang et al. 2006), whereas the intermediate and deep layers receive cholinergic inputs bilaterally from the pedunculopontine tegmental nuclei (Harting & Van Lieshout 1991).

The PBG/Ipc is part of a circuit involving another tegmental structure, the periparabrachial tegmental nucleus [nucleus isthmi pars magnocellularis in birds (PPBN/Imc)], which sends inhibitory inputs to the intermediate and deep layers of the SC. The interaction between the facilitatory influence of PBG/Ipc cholinergic connections and the global inhibitory effects of the γ -aminobutyric

acid (GABA)ergic PPBN/Imc inputs in the SC could mediate selection between competing visual stimuli (Lai et al. 2011, Mysore et al. 2010, Wang et al. 2004) and generate the switch-like behavior of some neurons in the bird SC that seem to respond only to the most salient stimulus (Mysore & Knudsen 2011). This mechanism has been studied prominently in birds, but if similar mechanisms operate in the primate SC, they could contribute to how SC activity selects visual targets; however, investigators would still need to define the circuits involved in relaying this target selection within the SC to structures that can influence perceptual decisions.

The other cholinergic nucleus projecting to the SC, the pedunculopontine tegmental nucleus (PPTg), is sometimes considered one of the output nuclei of the basal ganglia, exhibiting reciprocal connections with many basal ganglia structures and sending efferent projections to the SC, the thalamus, and other brain stem, medullary, and spinal nuclei (Inglis & Winn 1995). Evidence points to a role in saccade control, especially in relation to reward processing (Kobayashi et al. 2002), and this function may depend on connections with the SC. Indeed, injections of cholinergic agonists in the intermediate layers of the SC, which receive cholinergic inputs from the PPTg, affect saccadic control (Aizawa et al. 1999, Watanabe et al. 2005). However, the specific role of PPTg in spatial attention has not yet been directly investigated.

Pontine Nuclei

The pontine nuclei generally act as a relay that takes signals from the cerebral cortex and provides mossy fiber inputs to the cerebellum. The portions of the pontine nuclei receiving inputs from dorsal visual areas have received special attention for their role in providing visual signals for guiding pursuit and saccadic eye movements (Thier & Möck 2006). In addition to receiving cortical inputs, the pontine nuclei also receive inputs from multiple layers of the SC, and these terminate in dorsolateral regions overlapping with inputs from the visual cortex (Glickstein et al. 1990, Harting 1977). This overlap

suggests that SC activity could modify the visual signals transmitted through the pontine nuclei (**Figure 6**). This circuit mechanism may seem unlikely because researchers do not typically consider the cerebellum to be a central player in spatial attention, and studies of this question have produced mixed results (Ignashchenkova et al. 2009, Townsend et al. 1999).

In summary, there are several possible neuronal circuits for the SC's role in attention. Some of these circuits act through established cortical mechanisms, whereas others are subcortical and could operate largely independently of the known mechanisms of attention involving modulation of visual processing in the cerebral cortex. Clarifying the functional role of these circuits is a necessary step toward understanding the complete network of brain regions that control spatial attention.

CONCLUSIONS AND SPECULATIONS

In addition to its well-established role in orienting movements of the eyes and head, the primate SC also plays a crucial role in spatial attention. Part of this role is to mediate the effects of attention during orienting movements, but SC activity is also necessary for the normal operation of spatial attention during perceptual tasks even in the absence of orienting movements. Surprisingly, the SC's role in covert spatial attention involves mechanisms that appear to operate independently of the established signatures of attention in the visual cortex, raising new questions about the organization of the neuronal circuits that underlie spatial attention.

Our working hypothesis is that the control of attention involves at least two dissociable functional modules. First, the SC is a central node in an evolutionarily older circuit with the basal ganglia; these brain areas operate together to represent the location of important objects in space. This idea contrasts with the view of attention as a unified system: the SC is usually grouped together functionally with other cortical brain regions involved in both overt and covert orienting, such as the FEF or area LIP. Unlike those cortical areas, the SC is a highly conserved component of the vertebrate brain that plays an important role in spatial orienting, even in animals that lack a well-developed neocortex; the finding that blocking SC activity causes attention deficits without altering visual cortical activity suggests that it acts downstream.

We speculate that the second module is a younger system of cortical circuits that refines the operation of the SC–basal ganglia system and that the capabilities of the mature attention system in primates are acquired through learning. Indeed, in a visually cluttered environment, developing robust stimulus-response associations is impossible without first selecting the appropriate stimulus object to associate with the reinforced action. With the expansion of the neocortex, the number of stimulus features available for classifying objects and assigning meaning has expanded far beyond the capacity of a retinotopic map of visual space; however, when it comes to selecting the content of action or perception, the central components of this evolutionarily ancient selection mechanism remain intact.

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