

*Annual Review of Vision Science*

# Role of the Superior Colliculus in Guiding Movements Not Made by the Eyes

Bonnie Cooper and Robert M. McPeck

Graduate Center for Vision Research, SUNY College of Optometry, New York,  
New York 10036, USA; email: [bcooper@sunyopt.edu](mailto:bcooper@sunyopt.edu), [rmcpeek@sunyopt.edu](mailto:rmcpeek@sunyopt.edu)

Annu. Rev. Vis. Sci. 2021. 7:279–300

First published as a Review in Advance on  
June 8, 2021

The *Annual Review of Vision Science* is online at  
[vision.annualreviews.org](http://vision.annualreviews.org)

<https://doi.org/10.1146/annurev-vision-012521-102314>

Copyright © 2021 by Annual Reviews.  
All rights reserved

ANNUAL  
REVIEWS **CONNECT**

[www.annualreviews.org](http://www.annualreviews.org)

- Download figures
- Navigate cited references
- Keyword search
- Explore related articles
- Share via email or social media

## Keywords

superior colliculus, optic tectum, visual behavior, reaching movements

## Abstract

The superior colliculus (SC) has long been associated with the neural control of eye movements. Over seventy years ago, the orderly topography of saccade vectors and corresponding visual field locations were discovered in the cat SC. Since then, numerous high-impact studies have investigated and manipulated the relationship between visuotopic space and saccade vector across this topography to better understand the physiological underpinnings of the sensorimotor signal transformation. However, less attention has been paid to the other motor responses that may be associated with SC activity, ranging in complexity from concerted movements of skeletomotor muscle groups, such as arm-reaching movements, to behaviors that involve whole-body movement sequences, such as fight-or-flight responses in murine models. This review surveys these more complex movements associated with SC (optic tectum in nonmammalian species) activity and, where possible, provides phylogenetic and ethological perspective.

## 1. INTRODUCTION

In mammals, the superior colliculi (SCs) are a pair of small structures on the roof of the midbrain underneath the thalamus. The midbrain is thought to have evolved to give sensory inputs from the forebrain influence over fixed action pattern generators to guide behaviors such as locomotion, grasping, and orienting (Schneider 2014). The earliest observed motor responses produced by stimulation of the SC were orienting saccadic eye movements, evoked using electrical microstimulation in cat (Adamuk 1870). Importantly, Apter (1946) demonstrated that the saccade generated by a particular site in the SC corresponds to the visual receptive field location of cells at that site. From this work followed a series of influential physiology papers in macaques delineating the properties of visual and movement fields in the SC (e.g., Goldberg & Wurtz 1972), their orderly retinotopic mapping (e.g., Robinson 1972, Wurtz & Goldberg 1971), and their correspondence in visual space (e.g., Schiller & Stryker 1972). The SC's topography allows the spatial relations and behavioral contexts of stimuli to be manipulated with relative ease to better understand the neural representations of stimuli, the decision processes that govern responses, and the motor commands that execute responses, as well as the various effects of attention and other internal states (for a review, see Basso & May 2017). As a result of this orderly relationship of sensory inputs to saccade vectors, much of the work in the primate SC has centered around the sensorimotor transformations that guide saccades (for reviews, see, e.g., Gandhi & Katnani 2011, Sajad et al. 2020).

Despite this focus on gaze shifts, SC activity has been associated with many other, more complex responses. In a remarkable conservation of function across phylogeny (Kaas 1997, Sparks 1988), the involvement of the SC (or optic tectum in nonmammals) in orienting movements toward novel stimuli has been demonstrated in species as diverse as rats and hamsters (Goodale & Murison 1975, McHaffie & Stein 1982, Mort et al. 1980), rabbits and cats (Harris 1980, Munoz & Guitton 1989, Roucoux et al. 1980, Schaefer 1970), bats (Valentine et al. 2002), goldfish (Herrero et al. 1998), zebrafish (Bianco et al. 2011), and lower vertebrates such as lampreys (Saitoh et al. 2007).

In many early electrical microstimulation studies, an increase in SC stimulation intensity or duration elicited increasingly complex movements, including in rodents (Dean et al. 1989) and cats (Harris 1980). Moreover, SC stimulation in primates can also yield complex behaviors such as combined eye–head gaze shifts (e.g., Cowie & Robinson 1994, Freedman et al. 1996), reaching movements (Philipp & Hoffmann 2014), and even defensive behaviors (DesJardin et al. 2013). This review discusses some of the nongaze movement-related behaviors associated with SC activity across a selection of animals to bring both behavioral and phylogenetic context to our larger understanding of the functional role of the SC.

## 2. BASIC SUPERIOR COLLICULUS BLUEPRINT IN HIGHER MAMMALS

Understanding the architecture of the SC lends insight to understanding its function. The SC is a multilayered structure with unique anatomical, morphological, and functional distinctions among the layers (e.g., May 2006, White & Munoz 2011). In primates, the superficial layers of the SC receive visual input from the contralateral visual field, directly from retinal ganglion cells, from the visual cortex, and from other cortical areas (May 2006). This visual information projects to the SC according to an orderly retinotopic mapping, and this pattern is conserved across vertebrate species (Schneider 2014, Stein 1981).

The intermediate and deep layers of the SC receive inputs that are comparatively more diverse. In many mammals, including cats and primates, numerous sensory inputs combine with projections from the prefrontal cortex, the parietal cortex, and subcortical structures (e.g., Schneider

2014, White & Munoz 2011). The sensory input to the intermediate and deep layers includes visual, auditory, and somatosensory modalities, which combine with visual input from the superficial layers (e.g., Meredith & Stein 1986). Thus, in the intermediate and deep layers, the superficial layers' representation of visual space is integrated with a corresponding map of auditory and somatosensory signals, along with visual information from cortical visual areas, to create a topographic map to guide behavioral responses (Drager & Hubel 1975, King 2004, Meredith & Stein 1986). This multimodal sensory representation supports multisensory facilitation, where synchronous spatial and temporal stimuli from disparate sensory modalities combine to enhance detection (Welch et al. 1986). Indeed, multisensory facilitation has been demonstrated in the SC response properties of several mammals, including cats and primates (Wallace et al. 1996). Lesions to the SC in cats preferentially disrupt the ability to perform a multisensory orientation task (Burnett et al. 2004). Thus, the SC's merging of sensory modalities allows optimization of orienting responses to complex, multimodal environmental stimuli.

In addition to processing sensory information, the intermediate and deep layers of the colliculus are densely interconnected with a network of cortical areas that guide orienting movements such as saccades. In primates, this includes but is not limited to the frontal eye field and supplementary eye field in the prefrontal cortex, the lateral intraparietal area in the parietal cortex, the cingulate cortex, and the substantia nigra pars reticulata in the basal ganglia (May 2006). Within this network, the SC is distinguished by its proximity and strong connectivity to the downstream nuclei that issue oculomotor commands that ultimately result in eye movements. In addition to this, the SC projects to the reticular formation and the cervical spinal cord, allowing it to exert influence over skeletomotor movements (May 2006).

Overall, the intermediate and deep layers of the primate SC receive a diverse confluence of inputs from as many as 40 different cortical and subcortical projections (Edwards et al. 1979, Huerta & Harting 1984), enabling a flexible set of response properties. Yet most investigations of SC function have, understandably, focused on gaze control. In this review, we hope to bring renewed attention and investigation to other aspects of SC function in the control and modulation of behavior. We first consider recent work in the optic tectum (the direct progenitor of the SC) in a much older species, the lamprey, where GABAergic interneurons mediate a switch to generate opposing orienting or evasion behaviors (Saitoh et al. 2007, Suzuki et al. 2019).

### 3. OPTIC TECTUM OF A LIVING FOSSIL

Lampreys and related jawless fish have long been considered living fossils and the direct ancestors of other modern vertebrates (Xu et al. 2016). Lamprey anatomy has remained relatively unchanged for hundreds of millions of years (Gess et al. 2006), and therefore, lampreys have been used as a model organism to study vertebrate evolution and development (Green & Bronner 2014, McCauley et al. 2015, Nikitina et al. 2009, Xu et al. 2016). Lampreys are thought to have diverged from other vertebrates as many as 550 million years ago (Kumar & Hedges 1998), yet the lamprey optic tectum shares many anatomical and physiological similarities with the SC of modern mammals, making lampreys an attractive model system to investigate midbrain sensorimotor transformations (Xu et al. 2016).

As in other vertebrates, the superficial layer of the lamprey optic tectum receives afferent visual input from the retina (Kennedy & Rubinson 1977, Kosareva 1980). These retinotectal projections follow two main pathways: The axial optic tract carries afferents from the central visual field to the pretectum and has been implicated in visual escape behaviors, while the lateral optic tract projects a retinotopic mapping of the lateral retina to the optic tectum and has been associated with either escape or goal-orienting behaviors (Cornide-Petronio et al. 2011, Jones et al. 2009).

Retinotopic visual signals in the superficial layer are further shaped by GABAergic lateral connections (Kardamakis et al. 2015), which suppress extraneous activity to reduce competition once a target has been detected. Therefore, while significant differences exist between lampreys and other species, the superficial optic tectum of the lamprey receives a retinotopic mapping of salience across visual space, similar to other vertebrates. As in higher vertebrates, the intermediate and deep layers of the tectum receive inputs of increasing complexity. For example, the intermediate tectum receives electrosensory input from the octavolateral tract (Bodznick & Northcutt 1981, Kardamakis et al. 2016). This combines with the visual signals from the superficial layer to build a multimodal representation of the environment, enhancing event detection (Kardamakis et al. 2016).

The deep layer of the lamprey optic tectum integrates information from the overlying layers onto two classes of output neurons that either descend ipsilaterally (iBP neurons) or decussate, crossing to the contralateral side (coBP neurons) of the brainstem. Stimulation of the optic tectum produces an orderly topographic output of various eye–body motor responses.

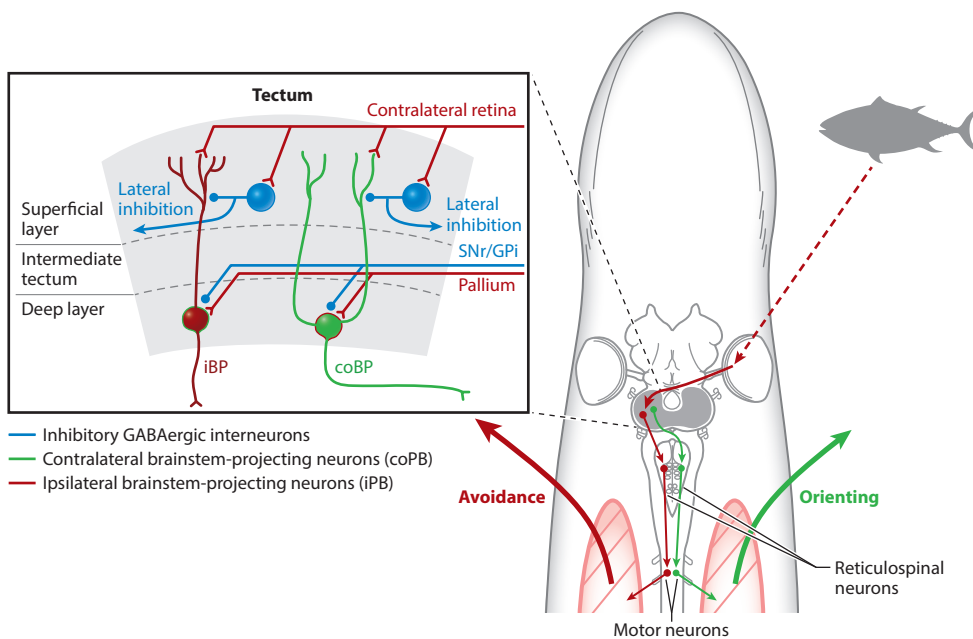
The work of Grillner and collaborators (e.g., Grillner et al. 2008) describes how the neural circuit of the optic tectum integrates sensory information and acts as a switch to guide behavior via the two distinct descending pathways for either evasive escape behaviors (iBP) or orienting behaviors (coBP), given the appropriate sensory input (Suzuki et al. 2019) (**Figure 1**). By modulating the properties of looming stimuli, Grillner and colleagues demonstrated that local inhibitory neurons in the superficial optic tectum are responsible for selecting downstream motor commands via distinct classes of neurons in deep layers of the tectum.

Specifically, fast-moving dots or bars that simulate the approach of a predator preferentially activate iBP neurons, resulting in escape or evasion behaviors mediated by ipsilateral pathways. In comparison, slow looming dots preferentially activate the coBP neurons to guide orienting behaviors via contralateral projections to the brainstem. coBP neurons are activated by relatively weaker stimuli than are iBP, possibly owing to stronger effects of lateral inhibition for slower looming stimuli. Additionally, coBP and iBP neurons select for stimuli by mapping the optic tectum surface differently: iBP neurons tile it with a relatively even mosaic, while coBP neurons are concentrated in the anterior tectum, representing the anterior visual field.

As a result of the uneven tiling of coBP neurons being superimposed on the relatively orderly mosaic of iBP neurons, anterior visual stimuli may activate both coBP neurons effecting decisions to execute orienting behaviors and iBP neurons mediating escape responses. This allows the tectum to switch between orienting and escape responses to anterior visual stimuli. In contrast, posterior visual stimuli that elicit responses in areas of the tectal topography lacking coBP neurons are more likely to evoke escape behaviors. These findings are significant because they highlight the role of the optic tectum in visuomotor decision making in vertebrates as primitive as the lamprey and set a precedent for similar mechanisms in the mammalian SC.

#### 4. EMERGENCE OF EYE MOVEMENTS AND THE OPTIC TECTUM

The optic tectum of teleost fishes marks an advancement toward the SC of mammals in part because it includes the emergence of a more sophisticated topography of eye movements (Land 2015). In contrast to the lamprey, teleost fishes have more developed ocular musculature and are therefore capable of increasingly complex eye movements (Graf & Meyer 1978, Northmore 2011, Torres et al. 1992), an advancement that is reflected in the eye-movement topography of the goldfish optic tectum (Salas et al. 1997). Electrical stimulation of the goldfish optic tectum yields a detailed topographic mapping of saccade vectors. Other functional zones subdividing the tectum are also observed: For example, the medial tectal zone reorients gaze to an area of the visual field



**Figure 1**

Optic tectal circuitry that guides visual behavior in the lamprey. In the superficial layer, direct visual input from the contralateral retina distributes across inhibitory GABAergic interneurons (*blue*), as well as distinct classes of contralateral and ipsilateral brainstem-projecting neurons (coBP and iBP; *green* and *red*, respectively), which traverse the intermediate tectum and have cell bodies primarily located in the deep layer. coBP and iBP neurons receive excitatory glutamatergic input from the pallium, as well as GABAergic inhibition from the substantia nigra pars reticulata (SNr) and globus pallidus interna (GPi) in the basal ganglia. Ultimately, coBP and iBP neurons project to reticulospinal neurons of the brainstem to elicit either orienting (coBP) or evasive (iBP) behaviors via spinal motor neurons. Figure adapted with permission from Suzuki et al. (2019).

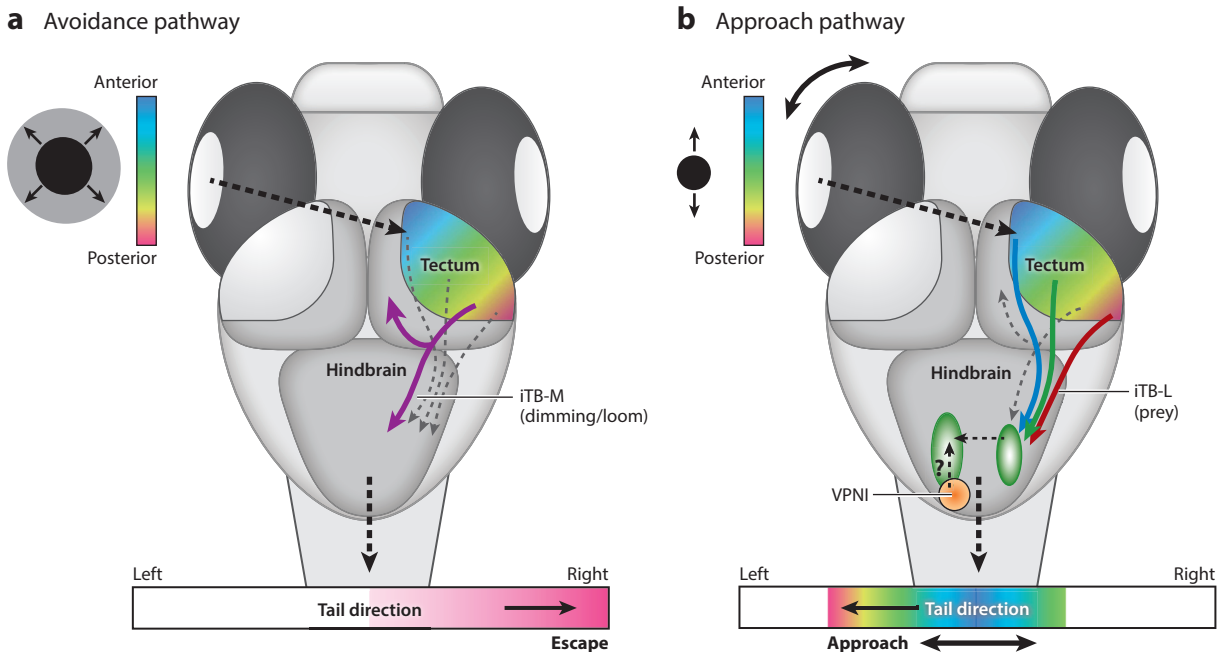
with a combination of eye and postural movements and the anterolateral zones are typified by goal-directed eye and body movements, whereas the posterior zone of the tectum elicits backing and turning movements associated with escape-like behaviors (Herrero et al. 1998, Torres et al. 2005).

Low-current stimulation to the rostral tectum typically results in movements characterized as orienting behaviors, while higher currents to the intermediate and deep layers of posterior tectal sites elicit escape behaviors. This is ethologically advantageous because, as in the lamprey, the teleost is more likely to treat a peripheral stimulus from behind (activating the posterior tectum) as a potential threat.

A similar pattern of tectal guidance for appropriate stimulus-dependent behavioral responses has been described in the zebrafish, *Danio rerio* (Bilotta & Saszik 2001, McArthur et al. 2020). In behavioral studies, zebrafish orient toward and pursue small moving stimuli, whereas large looming stimuli elicit avoidance behaviors (Bianco et al. 2011, Dunn et al. 2016, Temizer et al. 2015). Barker & Baier (2015) used calcium imaging, pharmacogenetic lesions, and optogenetic approaches to demonstrate distinct classes of tectal neurons that bias behaviors to moving visual targets (Barker & Baier 2015). GAL4 enhancer trapping methods were used to create selective ablations to the tectum (Scott et al. 2007). For instance, the *Gal4s1156t* transgenic line facilitates

selective ablations to GABAergic superficial tectal interneurons (SINs) which are critical for lateral inhibition and which, in the zebrafish, may play a role in stimulus size representation (Preuss et al. 2014). As a result, when SINs were selectively ablated, these fish demonstrated response deficits for moving stimuli that were more pronounced for large stimuli and biased SIN-ablated fish against avoidance behaviors, particularly to large stimuli. In comparison, ablations to fish from the *Gal4mpn354* line targeted a specific subset of periventricular interneurons (nsPVINs) (Nevin et al. 2010), resulting in disruptions of orientation toward small stimuli. Furthermore, optogenetic activation of *GAL4mpn354*-labeled neurons had the opposite effect and facilitated orienting and approach behaviors. These findings support a tectal decision mechanism that mediates switching between approach and avoidance behaviors via dedicated pathways.

Helmbrecht et al. (2018) extended this work by selectively labeling tectofugal neurons and tracing the resulting output pathways to visualize a teleost tectal projectome of at least seven classes of projection neurons across the tectum, revealing multiple distinct pathways. For instance, the ipsilateral tectobulbar tract (iTb) consistently showed a division of behavioral function, with axons in the medial iTb (iTb-M) responding primarily to larger looming stimuli and axons in the lateral iTb (iTb-L) selective for smaller prey-like stimuli. A combination of optogenetic, calcium imaging, and behavioral tracking methods also revealed different patterns of iTb-L and -M projections to downstream targets. iTb-L projections exhibited an orderly topography along the anterior to posterior axes, suggesting that functional responses reflect the spatial location of stimuli resembling potential prey, while the iTb-M projections mediating escape behaviors were localized to the posterior visual field (Figure 2).



**Figure 2**

Zebrafish tectofugal sensorimotor decision pathways that mediate (a) avoidance behaviors in response to looming targets via the iTb-M pathway and (b) approach behaviors for smaller targets via the iTb-L pathway. Figure adapted with permission from Helmbrecht et al. (2018). Abbreviations: iTb-L, lateral ipsilateral tectobulbar tract; iTb-M, medial ipsilateral tectobulbar tract; VPNI, velocity-to-position neural integrator.

Collectively, these findings suggest a broader role for the teleost optic tectum in forming fly-by-wire representations from primarily visual information (but integrating other sensory information as well) that can be transformed into a representation that is selectively channeled to specific targets in brainstem motor centers to effect appropriate behavioral responses (Northmore 2011). Helmbrecht et al. (2018) observed distinct pathways to mediate stimulus-dependent orienting behaviors in the optic tectum. However, in comparison, the SC of the rodent brain is more complex due to its more extensive use of environmental context in the decision process to switch between behavioral responses. We return to this discussion in the following section.

## 5. ROLE OF THE MURINE SUPERIOR COLLICULUS IN COMPLEX MOVEMENTS

Mammals evolved more complex sensorimotor systems and more nuanced cognitive capabilities but also inherited some basic neural wiring principles from lower vertebrates; this is apparent in a well-conserved structure like the SC (Butler 2008, Schneider 2014). Indeed, early electrophysiology experiments in the mammalian SC yielded perplexing results. For example, while the murine SC exhibits an orderly retinotopic visual map across its superficial layers and an underlying gaze motor map (Stein 1981), some stimulation studies also elicited complex behaviors, including approach, aversion, defensive posturing, aggression, and other responses (McHaffie & Stein 1982, Imperato & Di Chiara 1981, Olds & Olds 1963, Panksepp 1971, Valenstein 1965, Waldbillig 1975, Weldon et al. 1983). How could the same structure elicit seemingly contradictory (approach versus aversion) movement patterns? The complex and contrasting behaviors observed in these studies challenge the predominant view that the mammalian SC primarily guides gaze movements to visual targets.

While recent findings in the optic tectum of lampreys, teleost fish, and other lower vertebrate species provide phylogenetic context for these varied behavioral responses, the work of Redgrave and colleagues systematically characterizes the behaviors observed from the murine SC and describes an ethological context. Sahibzada et al. (1986) manipulated stimulation current in the SC and observed two major patterns of behavior across distinct subregions, forming a functional mosaic: Lateral SC sites generally yielded contralateral behavioral responses, described as orienting movements toward stationary stimuli or approach (and chasing) movements toward moving targets (which we call pursuit in this review, not to be confused with smooth pursuit eye movements), while medial SC sites yielded ipsilateral defensive movements such as freezing, cringe-like postures, shying locomotion, and running or jumping behaviors. Generally, as stimulation current was increased, the pattern of behavioral responses graduated in intensity, with lower currents eliciting coordinated head and eye movements, such as orienting or cringing, and higher-current stimulation yielding more involved movement components, including shying locomotion or running and jumping behaviors. Dean et al. (1989, p. 140) argued that having a variety of fully integrated responses represented in the SC is advantageous: “It can be argued on general grounds that it is sensible for a device (SC) concerned with orienting to be concerned also with defensive responding. The reason is that only some novel stimuli are neutral ‘events’ for which orienting is a suitable response. Other novel stimuli may signal an impending emergency, for example the appearance of a predator, or of an object on a collision course.”

The lateral SC sites with orienting responses that resemble pursuit or chasing behaviors and the medial SC aversion responsive areas divide roughly across the SC midline and send projections along crossed and uncrossed descending pathways, respectively (Dean et al. 1989). For example, pursuit behaviors can be elicited by stimulation or inhibited by ablation of fibers projecting to the predorsal bundle (PDB) of the crossed descending pathway (Dean et al. 1986, 1988). Alternatively,



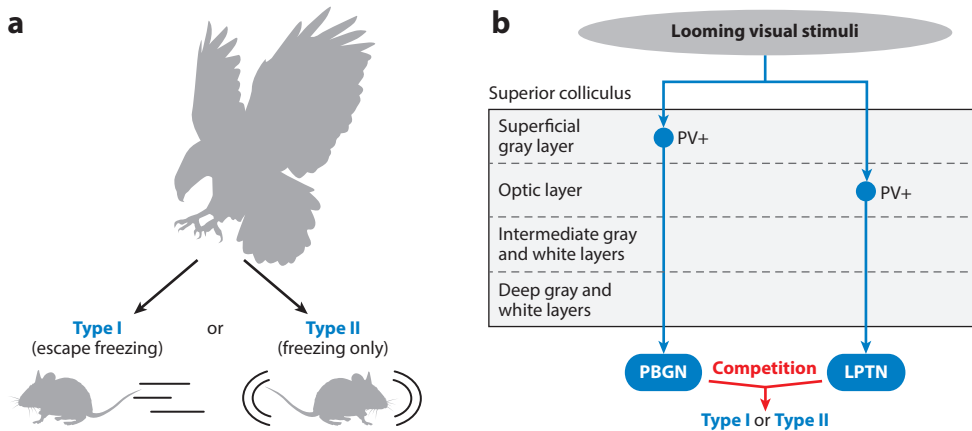
a variety of defensive behaviors are elicited by stimulation of fibers projecting to the cuneiform area (CNF) (Dean et al. 1988, Redgrave et al. 1988). Furthermore, crossed PDB fibers and uncrossed CNF projections receive distinct sensory inputs (Westby et al. 1990). Lateral SC efferents to the PDB are driven largely by multisensory stimuli that include visual input from the lower visual field, somatosensory vibrissae stimuli, and auditory stimuli. Medial SC efferents to the CNF, in contrast, are responsive to visual stimuli in the upper visual field. These topographically distinct functional pathways in the murine SC are thus not unlike the distinct pathways in the zebrafish tectum, which allow it to orient toward stimuli in front of the animal while remaining prepared to flee from visual stimuli approaching from behind. Taken together, these combinations of systematic mapping, ablation, and tracing studies identified the parallel pathways of murine SC that guide either orienting responses or escape behaviors to avoid threats; these pathways receive distinct sensory inputs, mediate distinct behavioral responses, and send downstream projections across segregated crossed and uncrossed pathways.

Redgrave and collaborators' work also describes different pathways to process sensory stimuli to mediate behaviorally relevant reactions to either pursue a target or escape from a potential threat. However, the repertoire of behavioral responses guided by the SC is much more varied than a binary decision. For example, looming stimuli may elicit different defensive behaviors in rodents. Typically, rodents will either freeze or flee from a looming threat (De Franceschi et al. 2016, Eilam 2005, Yilmaz & Meister 2013), depending on the stimulus features and other factors, including the animal's access to shelter or previous experience.

Recent work by Shang et al. (2015, 2018) delineated the distinct pathways of parvalbumin-positive (PV+) SC neurons that guide defensive behaviors for looming stimuli. Generally, a rodent's escape behavior can be manipulated by an overhead looming visual stimulus: Escape behavior followed by freezing (Type I behavioral response) is typically triggered when a shelter is nearby, whereas immediate freezing behavior (Type II behavioral response) is triggered when shelter is not available. Two distinct classes of PV+ neurons that receive threat-relevant signals were identified and found to send distinct projections to the parabrachial nucleus (PBGN) or the lateral posterior thalamic nucleus (LPTN), respectively, in association with this behavior. Retrograde tracing revealed that the populations of SC PV+ PBGN and LPTN neurons are morphologically distinct in that they are clustered in different layers of the superficial SC. Furthermore, optogenetic activation of the PV+ SC PBGN pathway triggers impulsive escape behaviors followed by long-lasting freezing (Type I), whereas activation of the PV+ SC LPTN pathway induces immediate freezing (Type II) (**Figure 3**); this roughly mimics the dimorphic defensive behaviors triggered by looming visual stimuli. This work is significant because it demonstrates another functionally distinct SC pathway to mediate appropriate behavioral responses.

In a structure like the SC, where multimodal sensory information is combined and which lies in close proximity to the brainstem motor nuclei, such functionally distinct sensorimotor pathways provide an elegant way to consolidate the decision process to minimize response delay. However, having multiple pathways raises the important question of how to choose the right one (Redgrave et al. 1999). The decision rule for pursuit versus avoidance is relatively simple in the murine SC and similar to the teleost's rule: Lower visual field stimuli are to be approached, whereas unexpected overhead movement should trigger an escape behavior. However, the decision of whether to freeze or flee is more nuanced, involving variables from an animal's behavioral experience and environment (Eilam 2005). This indicates that additional information, beyond the immediate sensory stimulus triggering the response, is incorporated to reach an appropriate decision. It is currently unknown whether this higher-order information, presumably from the cortex, directly affects processing within the SC or whether it exerts an influence downstream.





**Figure 3**

Dimorphic defensive behavior in response to looming visual stimuli. (a) Looming stimuli can elicit either escape-freezing or freezing-only behavioral responses (Type I or II, respectively). (b) These two defensive behavioral responses are mediated by two distinct PV+ classes of neuron. PV+ neurons that project to the PBGN encode looming stimuli in the superficial gray retinal recipient layer, whereas PV+ neurons that project to the LPTN encode looming stimuli in the optic layer. PV+ SC PBGN and PV+ SC LPTN pathways send projections to their respective brainstem nuclei targets to effect Type I or Type II motor responses. Figure adapted with permission from Shang et al. (2018). Abbreviations: LPTN, lateral posterior thalamic nucleus; PBGN, parabigeminal nucleus; PV+, parvalbumin-positive.

## 6. FORELIMB-REACHING MOVEMENTS IN PRIMATES AND CATS

As discussed above, SC activity is associated with a variety of movements of varying complexity in lower animals. In primates, in contrast, the vast majority of studies of the SC have been confined to its role in vision and gaze control. It is possible that, due to encephalization, the SC has become a domain exclusively for the control of gaze shifts. This view is challenged, however, by a series of studies beginning in the 1990s, which brought to light new evidence for a connection between SC activity and arm-reaching behavior in primates.

### 6.1. Superior Colliculus Activity Related to Reaching in Nonhuman Primates

Werner (1993) discovered that a subset of neurons in the deeper SC and underlying reticular formation of monkeys shows activity related to arm-reaching movements. In a larger and more detailed follow-up study, Werner et al. (1997) demonstrated a strong temporal correlation between the onset of activity of these neurons and electromyographic (EMG) activity in muscles involved in reaching movements, including the trapezius, spinatus, and deltoid muscles. The observed activity often exhibited multiple phases, correlating with the onset of the reaching movement, contact with the reach target, and/or initiation of a return movement. In both of these studies, the reach target was fixated throughout each trial, thus eliminating eye movements as a likely explanation for the results. Moreover, when tested in saccade tasks, cells with reach-related activity typically had little or no saccade-related discharge. Depending on the cell, their reach-related activity could begin well before, at the onset, or during the reach movements. Most of these cells also showed tuning for the direction of the reaching movement (called the reach movement field).

Stuphorn et al. (2000) examined this spatial tuning in more detail to determine the extent to which reach direction tuning depends on gaze position. Their results provided evidence for

functional and anatomical distinctions indicating the existence of two different types of reaching cells. One population of cells, gaze-related neurons, is located in the intermediate and deeper layers of the SC. In these cells, the presence of activity for a given arm movement critically depends on the retinal location of the target. They also found an additional effect of orbital position on the reach-related activity (a gain field) when the retinotopic location of the target was kept constant, although their data did not permit a quantitative description of the gain fields.

The second population of cells, which were typically (although not exclusively) located deeper in the SC, and more often in the reticular formation, was gaze independent, meaning that they encode the direction of the reaching movement independently of where the eyes are fixated or where on the retina the reach target falls. These cells have overall lower firing rates and broader tuning than gaze-related cells. Furthermore, in contrast to gaze-related cells, gaze-independent cells display anticipatory activity, discharging even before a go signal is given to initiate a movement when the reach target is presented in the cell's reach movement field.

Importantly, all of these studies found that the preferred direction of reach-related cells is unrelated to the overlying retinotopic organization of SC visual and saccade-related cells. Indeed, in contrast to visual and saccade-related response fields, reach movement fields could even be located in the ipsilateral visual field. Furthermore, within the population of reach-related cells themselves, there was no clear topographic correspondence between reach movement field location and anatomical location in the SC. This lack of correspondence between the organization of the visual and saccadic cells and the reach-related cells suggests that the reaching cells comprise a separate functional compartment, even though they are intermingled with saccade-related neurons anatomically.

In all of these studies, the authors reported that the reach-related activity critically depends on the position of the reach target (and in some cases the direction of gaze) but does not depend on the trajectory of the reach movement itself, nor on the particular pattern of measured EMG activity accompanying the reach. This indicates that these neurons do not directly control the kinematics of the reaching movement, but instead likely provide more abstract descending (or ascending) signals related to the location of the reach goal.

Interestingly, while the reaching activity of gaze-related neurons is independent of which arm is used to effect the movement, gaze-independent neurons show a preference for movements of the contralateral arm. Moreover, the presence of anticipatory activity in the gaze-independent neurons suggests that they could be related to selection of an arm-reaching movement in a given direction in allocentric coordinates. This suggests that gaze-independent neurons may form a lower-level representation compared to the largely arm-independent and gaze-dependent activity seen in the gaze-related neurons. Indeed, the activity of gaze-related neurons could perhaps be thought of as coding the reach movement goal (or a reach movement intention) relative to the fovea.

However, based in part on the lack of early activity in gaze-related neurons, Stuphorn et al. (2000) argued against this view, reasoning instead that gaze-related neurons could be involved in rapid correction of reaching movements. When a reach to a target is made, the eyes normally fixate the target first, while the arm follows later due to its greater inertia. Stuphorn et al. (2000) hypothesized that the gaze-related neurons could be thought of as encoding the mismatch between the saccade goal (or currently fixated location) and the goal of the reaching movement and could thus be used to provide rapid online corrections, which are commonly seen when a target shifts position during a reaching movement (for a similar proposal in cats, see Alstermark et al. 1990).

## 6.2. Superior Colliculus Activity Related to Reach Target Contact

In addition to reach movement neurons, Hoffmann and colleagues identified another, more frequently encountered class of neurons: somatosensory-motor neurons that respond upon contact

with a reach target (Nagy et al. 2006). These cells are found intermingled among reach movement neurons at depths in the intermediate and deep SC layers of 1.2–4 mm below the SC surface. In general, they do not respond to visual stimuli during fixation or upon saccade onset, and they show little or no activity during reaching movements. Instead, they respond vigorously 50–100 ms after the hand makes contact with a reach target, and the strength of their response typically increases when greater force is applied to the target.

In a control condition, Nagy et al. (2006) tested the responses of these neurons when monkeys simply reached and held their arm near a target button without contact and found that this action elicits little or no response in most neurons. Approximately half of these cells show spatial tuning, and contact-related responses are seen for both the ipsilateral and contralateral hands. However, direct somatosensory stimulation of the hand was ineffective in driving these neurons, and only approximately half of the neurons were activated by passive forces on the arm, shoulder, neck, or trunk muscles. The origins of this reach target contact activity remain unclear, but Nagy et al. (2006) speculated that it could originate from the posterior parietal cortex, which provides strong input to the SC (e.g., Fries 1984), or via spinotectal neurons (Wiberg et al. 1987).

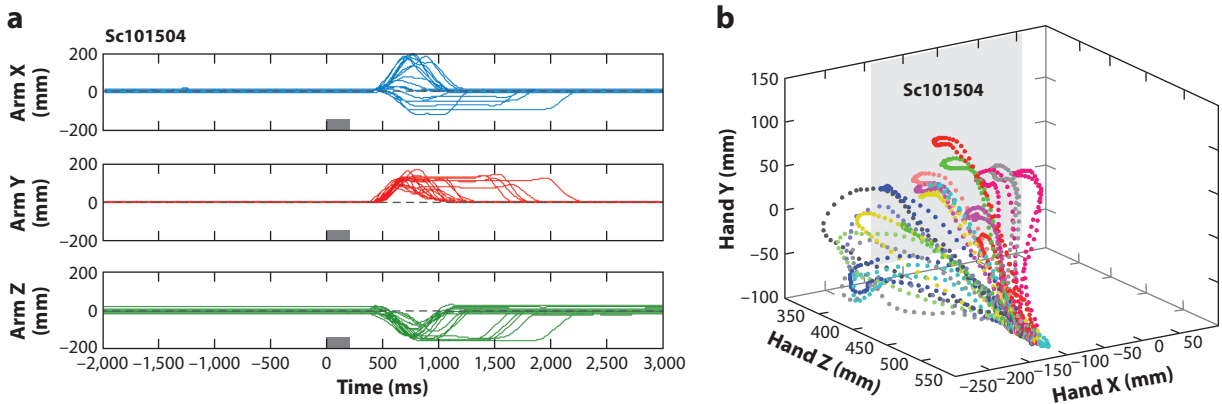
The presence of somatosensory-motor neurons provides further evidence for a role of the primate SC in movements beyond gaze shifts. More research is needed to characterize the afferent and efferent connections of these cells to understand their specific role in reaching. Nagy et al. (2006) speculated that, just as the so-called fixation neurons in the rostral SC monitor small motor errors during fixation (e.g., Krauzlis et al. 2017), the somatosensory-motor neurons could perhaps be similarly involved in monitoring the small changes in muscle force that are needed to interact effectively with a reach target.

### 6.3. BOLD Activity in the Human Superior Colliculus

SC activity related to reaching movements has also been reported in a pair of functional magnetic resonance imaging studies in humans. Linzenbold & Himmelbach (2012) compared the distribution of blood oxygen level–dependent (BOLD) activity in the human SC when reaches were made with either the left or the right arm to targets in the left or the right visual field. They found an increased BOLD signal in the SC contralateral to the hand used for reaching, regardless of target position. When contrasted with the signal seen for saccades, the reach-specific signal changes were located in the deeper layers of the SC and/or in the underlying reticular formation, similar to what is seen in monkeys. Importantly, the lateralization of this signal based on which hand was used to execute the reach (rather than on the hemifield location of the visual reach target) argues against a purely visual and/or attentional explanation of their results. In a follow-up study, Himmelbach et al. (2013) used a pro- and antireaching task in which subjects were cued to reach either toward or away from a visual target to explicitly separate visual and reach-related signals. They again found activation of the SC contralateral to the arm used for reaching, regardless of target position, in both the deep and the intermediate layers of the SC. This supports the idea that the SC may play a role in reaching movements in humans.

### 6.4. Electrical Microstimulation Studies of Reaching Movements in Primates and Cats

To look for a causal connection between SC activity and arm-reaching movements in monkeys, Philipp & Hoffmann (2014) used electrical microstimulation to demonstrate that activation of the SC and underlying reticular formation elicits arm movements in monkeys, typically with stimulation currents of approximately 20–40  $\mu$ A (**Figure 4**). They probed depths below the SC surface in a range of approximately 1–5.7 mm and found that the majority of effective sites lay in the deep SC



**Figure 4**

Examples of arm movements elicited by superior colliculus (SC) electrical microstimulation in primates. (a) Plots of 3D hand position as a function of time. Time zero marks the onset of microstimulation, and the gray bar shows its duration. (b) Spatial 3D plots of hand position during microstimulation trials in which movements toward a display screen were elicited. The screen lay in the *y* plane, and distance between the hand and the magnetic sensing device located behind the screen is given by the *z* axis. The *x* axis indicates horizontal hand position. Figure adapted with permission from Philipp & Hoffmann (2014).

and reticular formation at depths of 2.8–4.8 mm in the lateral, posterior portion of the SC. This portion of the conventional SC topography corresponds to large retinal eccentricities in the lower visual field. However, as mentioned above for the recording experiments, reach-related neurons do not appear to adhere to this organization. This deviation from the SC retinotopic organization was also found in the stimulation experiments: There was no systematic map of reach direction or amplitude as a function of location within the traditional SC map.

Philipp & Hoffmann (2014) described the elicited arm movements as extend, lift, or twitch movements, depending on the amplitude of the movement. These movements could also be accompanied by eye, head, and pinnae movements, and they were typically larger in amplitude, and more common, in more highly trained animals. In discussing the possible pathways underlying the stimulation-elicited arm movements, Philipp & Hoffmann (2014) noted that the lateral and posterior locations of the effective stimulation sites correspond well with the locations of tectospinal neurons in the deeper layers of the SC (e.g., Castiglioni et al. 1978, Nudo et al. 1993, Robinson et al. 1994). Some SC neurons also have bilateral connections to the mesencephalic reticular formation, which sends its own bilateral projections to the spinal cord (Horn 2006, May 2006).

In cats, a different pattern of results has been observed. Despite the presence of direct connections from the feline SC to regions of the spinal cord involved in forepaw-reaching movements (e.g., Illert et al. 1978, Olivier et al. 1991), electrical stimulation in the SC has not been found to initiate forelimb movements (Guillaume & Pélisson 2001). However, Courjon et al. (2004) demonstrated that stimulation during an ongoing reaching movement results in a marked deceleration, with downward and backward deviation of the movement, even in the absence of stimulation effects on the eyes or head. These reach movement perturbations, which were typically elicited when the stimulating electrode was approximately 2 mm from the SC surface, were obtained with short latencies (on the order of 50 ms after stimulation onset) at all stimulation sites tested. Eye and head movements could also be elicited at these same locations but were not observed in the reaching experiments due to the shorter duration of the stimulation train used. After cessation of stimulation, the reaching movements were quickly corrected online (typically within approximately

30 ms) and continued accurately to the target. One limitation of this study is that it examined a relatively restricted set of SC locations encoding downward contralateral gaze movements.

In a follow-up study, Courjon et al. (2015) made a more detailed investigation of the topography of the perturbation effect at stimulation sites across the collicular map. Confirming the previous results, they found that, at depths of 1.3–2.6 mm below the SC surface, transient perturbation of ongoing reaches could be obtained in approximately 75% of tested sites. As observed in the earlier study, an accurate reaching movement to the target resumed shortly after the end of the stimulation train. However, surprisingly, they found that the direction of the stimulation-induced perturbation did not depend on the location within the SC map that was stimulated. Rather, movements were consistently decelerated and deviated down and backward regardless of the stimulation site.

The stereotyped nature of the trajectory perturbations led Courjon et al. (2015) to conclude that the cat SC is not directly involved in coding reaching movements. Instead, they suggested that SC stimulation could indirectly affect reaches, either due to an effect on reach target selection or by triggering an orienting response, which in turn leads to a change in the cat's posture. It should be noted that one clear difference between the monkey and cat studies reviewed above is that, in cats, stimulation sites were more superficial and always within the boundaries of the SC, whereas in monkeys, sites in both the deep SC and the underlying reticular formation were probed.

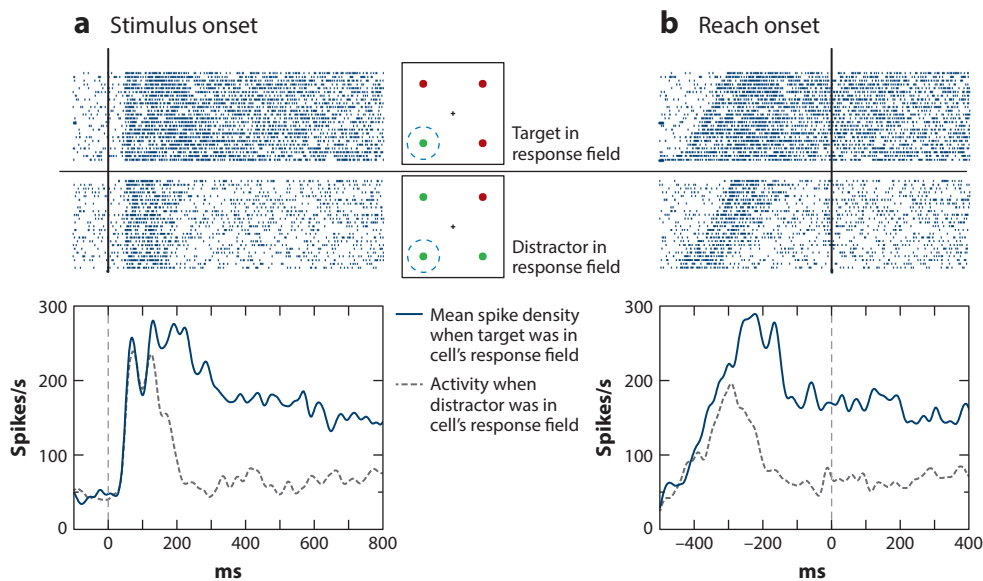
## 6.5. Role of the Superior Colliculus in Reach Target Selection in Primates

The important role of the primate SC in the selection of targets for eye movements has been demonstrated in recording (e.g., Basso & Wurtz 1998, Glimcher & Sparks 1992, McPeck & Keller 2002, Shen & Paré 2007), microstimulation (e.g., Carello & Krauzlis 2004), and inactivation studies (e.g., McPeck & Keller 2004). A more recent body of work has also implicated the primate SC in target selection for manual movements.

**6.5.1. Inactivation studies.** The first evidence came from Nummela & Krauzlis (2010), who compared the effects of intermediate-layer SC inactivation on target selection not only for saccadic and smooth pursuit eye movements, but also for manual button presses. For all three response modalities, two stimuli of different colors were presented, one in the response field of the inactivated SC site and the other in the opposite hemifield. A color cue in the center indicated which of the two stimuli was the target. In the eye movement tasks, monkeys were rewarded for performing either a saccade or a pursuit movement to the cued stimulus. In the button-pressing task, monkeys maintained fixation and responded by pressing a left or right button on a response pad corresponding to the hemifield location of the target. As expected based on earlier work, Nummela & Krauzlis (2010) found that SC inactivation produced a strong bias against selecting eye movement targets presented in the inactivated field. However, more unexpectedly, they also found a weaker but consistent bias against responding manually to targets in the inactivated field, indicating that SC inactivation can influence target selection for manual button-press responses as well as eye movements.

Song et al. (2011) followed up on this, but rather than using a button-press task, which requires an indirect mapping between the target location and the response location, they investigated the effects of SC inactivation on reach target selection by training monkeys to directly reach to, and touch, a target presented on a touchscreen with a distractor while maintaining fixation. This allowed the difficulty of target selection to be manipulated by changing the time between the onsets of the target and distractor stimuli (stimulus onset asynchrony). As before, one stimulus was placed in the response field of the inactivated SC site, while the other was placed in the opposite





**Figure 6**

Activity of an example superior colliculus (SC) neuron during a reach target selection task. (a) Activity aligned to the onset of a color singleton target and accompanying distractor stimuli. (b) Activity aligned to the onset of reaching movement. In the lower panels, blue lines show mean spike density when the target was in the cell's response field (RF); dashed gray lines show activity when a distractor was in the RF. The upper panels show single-trial spike raster plots, grouped according to target location (in versus out of the RF) and ordered by reach latency. Insets show stimulus schematics for the two RF conditions. Monkeys maintained eye fixation at the center point throughout each trial. Figure adapted with permission from Song & McPeck (2015).

this experiment was the same: Monkeys showed a clear bias against selecting the stimulus in the inactivated field, supporting the idea that SC inactivation results in a reach target selection deficit.

How does inactivation of the SC affect reach target selection? Many models of target selection posit the existence of a priority map that represents both the physical salience and behavioral relevance of potential targets (e.g., Zelinsky & Bisley 2015). After a winner-take-all competition, the target with the highest priority on this map is selected as the target for action (or attention). Indeed, there is good evidence that the SC comprises such a map for eye movements and attention (Basso & May 2017, Krauzlis et al. 2013). The effects of SC inactivation on reach target selection reviewed in this section suggest that the SC priority map also contributes to target selection for other movements, such as reaches.

**6.5.2. Recording studies.** To gain insight into the SC neuronal activity occurring during reach target selection, Song & McPeck (2015) recorded intermediate-layer SC neurons during a task in which monkeys remained fixated and reached to touch a peripheral target that was presented with distractors. Even though no eye movement was made, when the reach target was in the recorded cell's response field, a subpopulation of SC neurons showed greater activity than when a distractor was in the response field. When this activity is aligned on the onset of the target and distractors, the initial burst of activity does not discriminate the reach target, but soon after, activity evolves to signal whether the reach target is in the response field (**Figure 6a**). Furthermore, when activity is aligned on execution of the reaching movement, there is no modulation in association



with the onset of the movement itself (**Figure 6b**). This indicates that these cells select the reach target but are not involved in triggering execution of the movement, which is what one might expect if they serve as a priority map for reach target selection. Song & McPeck also tested the cells in a standard saccadic delay task to further characterize them. They found that neurons that discriminated the reach target typically (but not always) showed sustained activity during the delay period. In contrast, virtually all of the cells that were not selective for the reach target lacked delay period activity.

How do these cells compare with the reach movement cells discussed in Section 6.1? Those cells are sparsely found, often (but not exclusively) deep in the SC and reticular formation; are largely confined to the lateral and caudal aspect of the SC; and show directional preferences that do not conform to the overlying SC retinotopic topography. In contrast, the cells recorded by Song & McPeck (2015) are fairly common, are found in the intermediate layers throughout the SC map, and show spatial preferences conforming to the usual SC retinotopy. Thus, it is clear that the reach target selection cells described in this section are from a different subpopulation than the gaze-related and gaze-independent movement cells discussed above. Interestingly, however, all three populations of cells seem to be concerned with encoding the locations of reach targets, relative either to gaze or to the hand, rather than with lower-level control of the reach movement trajectory.

## 7. IN SUMMARY

The SC is a well-studied area of the midbrain that integrates sensory information to guide behavioral responses to stimuli in an animal's environment. In structure, the SC is remarkably well preserved across phyla. However, the behavioral responses guided by SC activity vary widely across animal species. In this review, we place the basic underlying structure of the SC in phylogenetic and ethological context using several model animal systems to emphasize that the SC can play a broader role in behavior than is usually considered. While it is true that the primate SC serves primarily as an important node in the neuronal circuitry controlling gaze shifts, it also plays a role in guiding diverse orienting and defensive behaviors (DesJardin et al. 2013) to facilitate appropriate reactions to environmental stimuli.

Speed is often of the essence, particularly when survival hinges on reacting appropriately to novel stimuli. The midbrain likely evolved to expedite the integration of sensory modalities and give access to the underlying circuitry of the brainstem as a conduit to effect rapid behavioral responses (Schneider 2014). This review walks through several examples of collicular circuitry doing just this: multiplexing visuotopic information with multimodal sensory inputs and cortical or pallial inputs and applying ethologically valid decision algorithms to yield fast responses mediated by distinct pathways to effector nuclei in the brainstem. The lamprey has survived hundreds of millions of years using very simple rule sets. For instance, if something is small and moving in front of me, an appetitive response is required. If it is large and coming from behind me, an aversive response is required. However, ethological validity is not one size fits all. The murine midbrain has more sophisticated circuitry that incorporates information about environmental context and previous experience from higher cortical centers that are lacking in the lamprey.

In the lamprey, teleost, and murine models, studies have demonstrated the existence of morphologically, anatomically, and functionally distinct pathways that support a role for the SC in actively participating in shaping complex behavioral responses. While such pathways have not yet been identified in the primate, Section 6 of this review focuses on the evidence for a role of the primate SC in arm-reaching movements. The presence of reach-related responses and somatosensory-motor responses in the SC is intriguing, as are the effects of SC microstimulation on reach initiation and SC inactivation on reach target selection. Yet the precise role of these

neuronal responses in normal reaching behavior is still unclear. It is possible that the reach-related SC pathways are involved in the rapid initiation or correction of reaching movements, in eye–hand coordination, or in the rapid adjustment of small reaching motor errors when contacting reach targets. Resolution of these questions and deeper understanding of the role of the SC in reaching movements in primates, as well as the relationships among SC activity, reach target selection, and the coupling of visual attention with reaching movements, require further research and discovery. Eventually, the genetic tools that have been exploited in lower vertebrates may be able to provide even greater clarity on the roles of specific cell types and the flow of information within the primate SC to help address these open questions.

## SUMMARY POINTS

1. The SC is a phylogenetically well-conserved structure that integrates multimodal sensory information with inputs from disparate cortical and subcortical centers to guide appropriate behavioral responses to environmental stimuli.
2. In the SC of mammals and the optic tectum of lower vertebrates, there exist morphologically, anatomically, and functionally distinct pathways that mediate motor responses that range in complexity (from saccades or pinnae movements to fleeing behaviors, for example) and purpose (i.e., approach or orienting versus avoidance).
3. The SC in mammals and the optic tectum in lower vertebrates implement ethologically valid decision rules that increase in complexity as the sophistication and diversity of connectivity increases.
4. In primates, the SC plays a prominent role in the guidance of saccades. Although the repertoire of responses elicited by SC stimulation does not match the diversity seen in lower vertebrates (such as murine models), results suggest involvement in a variety of orienting behaviors, as well as more complex behaviors such as reaching and touching.
5. In primates, different subpopulations of SC reach-related cells have been observed. While the prevalence and localization of these cell classes differ, collectively, these cells appear to represent aspects of reach goal or target selection rather than the lower-level execution or trajectory of reach movements.

## FUTURE ISSUES

1. Are there examples of midbrain-mediated behavioral switches similar to those of the lamprey, teleost, or murine models in other animals? If so, can these examples be used to investigate the circuits of decision making as well?
2. How is information from different sensory modalities integrated to select ethologically valid decision rules? In particular, for animals that do not rely primarily on vision, how does the SC incorporate auditory, somatosensory, or echolocation input to select appropriate responses?
3. How similar is the organization of the intracollicular circuits in primates, murines, and nonmammalian species, and to what extent can we apply insights from lower species to higher ones?

4. To what extent does the selection of ethologically valid decision rules occur within the SC, as opposed to relying on upstream or downstream areas?
5. In primates, what is the role of the different classes of reaching and somatosensory-motor SC neurons in natural reaching movements and eye–hand coordination? How do these cells interact with neurons involved in orienting and gaze control?

## DISCLOSURE STATEMENT

The authors are not aware of any affiliations, memberships, funding, or financial holdings that might be perceived as affecting the objectivity of this review.

## ACKNOWLEDGMENTS

The authors are supported by National Institutes of Health grant R01EY030669.

## LITERATURE CITED

- Adamuk E. 1870. Über die Innervation der Augenbewegungen. *Zbl. Med. Wiss.* 8:65–67
- Alstermark B, Gorska T, Lundberg A, Pettersson LG. 1990. Integration in descending motor pathways controlling the forelimb in the cat. 16. Visually guided switching of target-reaching. *Exp. Brain Res.* 80(1):1–11
- Apter JT. 1946. Eye movements following strychninization of the superior colliculus of cats. *J. Neurophysiol.* 9(2):73–86
- Barker AJ, Baier H. 2015. Sensorimotor decision making in the zebrafish tectum. *Curr. Biol.* 25(21):2804–14
- Basso MA, May PJ. 2017. Circuits for action and cognition: a view from the superior colliculus. *Annu. Rev. Vis. Sci.* 3:197–226
- Basso MA, Wurtz RH. 1998. Modulation of neuronal activity in superior colliculus by changes in target probability. *J. Neurosci.* 18(18):7519–34
- Bianco IH, Kampff AR, Engert F. 2011. Prey capture behavior evoked by simple visual stimuli in larval zebrafish. *Front. Syst. Neurosci.* 5:101
- Bilotta J, Saszik S. 2001. The zebrafish as a model visual system. *Int. J. Dev. Neurosci.* 19(7):621–29
- Bodznick D, Northcutt RG. 1981. Electrorception in lampreys: evidence that the earliest vertebrates were electrosensitive. *Science* 212(4493):465–67
- Burnett LR, Stein BE, Chaponis D, Wallace MT. 2004. Superior colliculus lesions preferentially disrupt multisensory orientation. *Neuroscience* 124(3):535–47
- Butler AB. 2008. Evolution of brains, cognition, and consciousness. *Brain Res. Bull.* 75(2–4):442–49
- Carello CD, Krauzlis RJ. 2004. Manipulating intent: evidence for a causal role of the superior colliculus in target selection. *Neuron* 43(4):575–83
- Castiglioni AJ, Gallaway M, Coulter JD. 1978. Spinal projections from the midbrain in monkey. *J. Comp. Neurol.* 178(2):329–45
- Cornide-Petronio ME, Barreiro-Iglesias A, Anadón R, Rodicio MC. 2011. Retinotopy of visual projections to the optic tectum and pretectum in larval sea lamprey. *Exp. Eye Res.* 92(4):274–81
- Courjon JH, Olivier E, Pélisson D. 2004. Direct evidence for the contribution of the superior colliculus in the control of visually guided reaching movements in the cat. *J. Physiol.* 556(3):675–81
- Courjon JH, Zénon A, Clément G, Urquizar C, Olivier E, Pélisson D. 2015. Electrical stimulation of the superior colliculus induces non-topographically organized perturbation of reaching movements in cats. *Front. Syst. Neurosci.* 9:109
- Cowie RJ, Robinson DL. 1994. Subcortical contributions to head movements in macaques. I. Contrasting effects of electrical stimulation of a medial pontomedullary region and the superior colliculus. *J. Neurophysiol.* 72(6):2648–64

- De Francheschi G, Viyattanasam T, Saleem AB, Solomon SG. 2016. Vision guides selection of freeze or flight defense strategies in mice. *Curr. Biol.* 26(16):2150–54
- Dean P, Redgrave P, Mitchell IJ. 1988. Organisation of efferent projections from superior colliculus to brain-stem in rat: evidence for functional output channels. *Prog. Brain Res.* 75:27–36
- Dean P, Redgrave P, Sahibzada N, Tsuji K. 1986. Head and body movements produced by electrical stimulation of superior colliculus in rats: effects of interruption of crossed tectoreticulospinal pathway. *Neuroscience* 19(2):367–80
- Dean P, Redgrave P, Westby GWM. 1989. Event or emergency? Two response systems in the mammalian superior colliculus. *Trends Neurosci.* 12(4):137–47
- DesJardin JT, Holmes AL, Forcelli PA, Cole CE, Gale JT, et al. 2013. Defense-like behaviors evoked by pharmacological disinhibition of the superior colliculus in the primate. *J. Neurosci.* 33(1):150–55
- Drager UC, Hubel DH. 1975. Responses to visual stimulation and relationship between visual, auditory, and somatosensory inputs in mouse superior colliculus. *J. Neurophysiol.* 38(3):690–713
- Dunn TW, Gebhardt C, Naumann EA, Riegler C, Ahrens MB, et al. 2016. Neural circuits underlying visually evoked escapes in larval zebrafish. *Neuron* 89(3):613–28
- Edwards SB, Ginsburgh CL, Henkel CK, Stein BE. 1979. Sources of subcortical projections to the superior colliculus in the cat. *J. Comp. Neurol.* 184(2):309–29
- Eilam D. 2005. Die hard: a blend of freezing and fleeing as a dynamic defense—implications for the control of defensive behavior. *Neurosci. Biobehav. Rev.* 29(8):1181–91
- Freedman EG, Stanford TR, Sparks DL. 1996. Combined eye-head gaze shifts produced by electrical stimulation of the superior colliculus in rhesus monkeys. *J. Neurophysiol.* 76(2):927–52
- Fries W. 1984. Cortical projections to the superior colliculus in the macaque monkey: a retrograde study using horseradish peroxidase. *J. Comp. Neurol.* 230(1):55–76
- Gandhi NJ, Katnani HA. 2011. Motor functions of the superior colliculus. *Annu. Rev. Neurosci.* 34:205–31
- Gess RW, Coates MI, Rubidge BS. 2006. A lamprey from the Devonian period of South Africa. *Nature* 443(7114):981–84
- Glimcher PW, Sparks DL. 1992. Movement selection in advance of action in the superior colliculus. *Nature* 355(6360):542–45
- Goldberg ME, Wurtz RH. 1972. Activity of superior colliculus in behaving monkey. I. Visual receptive fields of single neurons. *J. Neurophysiol.* 35(4):542–59
- Goodale MA, Murison RC. 1975. The effects of lesions of the superior colliculus on locomotor orientation and the orienting reflex in the rat. *Brain Res.* 88(2):243–61
- Graf W, Meyer DL. 1978. Eye positions in fishes suggest different modes of interaction between commands and reflexes. *J. Comp. Physiol.* 128(3):241–50
- Green SA, Bronner ME. 2014. The lamprey: a jawless vertebrate model system for examining origin of the neural crest and other vertebrate traits. *Differentiation* 87(1–2):44–51
- Grillner S, Wallén P, Saitoh K, Kozlov A, Robertson B. 2008. Neural bases of goal-directed locomotion in vertebrates—an overview. *Brain Res. Rev.* 57(1):2–12
- Guillaume A, Pélisson D. 2001. Gaze shifts evoked by electrical stimulation of the superior colliculus in the head-unrestrained cat. I. Effect of the locus and of the parameters of stimulation. *Eur. J. Neurosci.* 14(8):1331–44
- Harris LR. 1980. The superior colliculus and movements of the head and eyes in cats. *J. Physiol.* 300(1):367–91
- Helmbrecht TO, Dal Maschio M, Donovan JC, Koutsouli S, Baier H. 2018. Topography of a visuomotor transformation. *Neuron* 100(6):1429–45
- Herrero L, Rodríguez F, Salas C, Torres B. 1998. Tail and eye movements evoked by electrical microstimulation of the optic tectum in goldfish. *Exp. Brain Res.* 120(3):291–305
- Himmelbach M, Linzenbold W, Ilg UJ. 2013. Dissociation of reach-related and visual signals in the human superior colliculus. *NeuroImage* 82:61–67
- Horn AK. 2006. The reticular formation. *Prog. Brain Res.* 151:127–55
- Huerta MF, Harting JK. 1984. Connectional organization of the superior colliculus. *Trends Neurosci.* 7(8):286–89

- Illert M, Lundberg A, Padel Y, Tanaka R. 1978. Integration in descending motor pathways controlling the forelimb in the cat. 5. Properties of and monosynaptic excitatory convergence on C3–C4 propriospinal neurones. *Exp. Brain Res.* 33(1):101–30
- Imperato A, Di Chiara G. 1981. Behavioural effects of GABA-agonists and antagonists infused in the mesencephalic reticular formation-deep layers of superior colliculus. *Brain Res.* 224(1):185–94
- Jones MR, Grillner S, Robertson B. 2009. Selective projection patterns from subtypes of retinal ganglion cells to tectum and pretectum: distribution and relation to behavior. *J. Comp. Neurol.* 517(3):257–75
- Kaas JH. 1997. Topographic maps are fundamental to sensory processing. *Brain Res. Bull.* 44(2):107–12
- Kardamakis AA, Perez-Fernandez J, Grillner S. 2016. Spatiotemporal interplay between multisensory excitation and recruited inhibition in the lamprey optic tectum. *eLife* 5:e16472
- Kardamakis AA, Saitoh K, Grillner S. 2015. Tectal microcircuit generating visual selection commands on gaze-controlling neurons. *PNAS* 112(15):E1956–65
- Kennedy MC, Rubinson K. 1977. Retinal projections in larval, transforming and adult sea lamprey, *Petromyzon marinus*. *J. Comp. Neurol.* 171(4):465–79
- King AJ. 2004. The superior colliculus. *Curr. Biol.* 14(9):R335–38
- Kosareva AA. 1980. Retinal projections in lamprey (*Lampetra fluviatilis*). *J. Hirnforsch.* 21(3):243–56
- Krauzlis RJ, Goffart L, Hafed ZM. 2017. Neuronal control of fixation and fixational eye movements. *Philos. Trans. R. Soc. Lond. B* 372(1718):20160205
- Krauzlis RJ, Lovejoy LP, Zénon A. 2013. Superior colliculus and visual spatial attention. *Annu. Rev. Neurosci.* 36:165–82
- Kumar S, Hedges SB. 1998. A molecular timescale for vertebrate evolution. *Nature* 392(6679):917–20
- Land MF. 2015. Eye movements of vertebrates and their relation to eye form and function. *J. Comp. Physiol. A* 201(2):195–214
- Linzenbold W, Himmelbach M. 2012. Signals from the deep: reach-related activity in the human superior colliculus. *J. Neurosci.* 32(40):13881–88
- May PJ. 2006. The mammalian superior colliculus: laminar structure and connections. *Prog. Brain Res.* 151:321–78
- McArthur KL, Chow DM, Fetcho JR. 2020. Zebrafish as a model for revealing the neuronal basis of behavior. In *The Zebrafish in Biomedical Research*, ed. S Cartner, J Eisen, S Farmer, K Guillemin, M Kent, G Sanders, pp. 593–617. Amsterdam: Elsevier
- McCauley DW, Docker MF, Whyard S, Li W. 2015. Lampreys as diverse model organisms in the genomics era. *BioScience* 65(11):1046–56
- McHaffie JG, Stein BE. 1982. Eye movements evoked by electrical stimulation in the superior colliculus of rats and hamsters. *Brain Res.* 247(2):243–53
- McPeck RM, Keller EL. 2002. Saccade target selection in the superior colliculus during a visual search task. *J. Neurophysiol.* 88(4):2019–34
- McPeck RM, Keller EL. 2004. Deficits in saccade target selection after inactivation of superior colliculus. *Nat. Neurosci.* 7(7):757–63
- Meredith MA, Stein BE. 1986. Visual, auditory, and somatosensory convergence on cells in superior colliculus results in multisensory integration. *J. Neurophysiol.* 56(3):640–62
- Mort E, Cairns S, Hersch H, Finlay B. 1980. The role of the superior colliculus in visually guided locomotion and visual orienting in the hamster. *Physiol. Psychol.* 8(1):20–28
- Munoz DP, Guitton D. 1989. Fixation and orientation control by the tecto-reticulo-spinal system in the cat whose head is unrestrained. *Rev. Neurol.* 145(8–9):567–79
- Nagy A, Kruse W, Rottmann S, Dannenberg S, Hoffmann KP. 2006. Somatosensory-motor neuronal activity in the superior colliculus of the primate. *Neuron* 52(3):525–34
- Nevin LM, Robles E, Baier H, Scott EK. 2010. Focusing on optic tectum circuitry through the lens of genetics. *BMC Biol.* 8(1):126
- Nikitina N, Bronner-Fraser M, Sauka-Spengler T. 2009. The sea lamprey *Petromyzon marinus*: a model for evolutionary and developmental biology. *Cold Spring Harb. Protoc.* 2009(1):pdb-emo113
- Northmore D. 2011. The optic tectum. In *Encyclopedia of Fish Physiology: From Genome to Environment*, ed. AP Farrell, pp. 131–42. Amsterdam: Elsevier

- Nudo RJ, Sutherland DP, Masterton RB. 1993. Inter- and intra-laminar distribution of tectospinal neurons in 23 mammals. *Brain Behav. Evol.* 42(1):1–23
- Nummela SU, Krauzlis RJ. 2010. Inactivation of primate superior colliculus biases target choice for smooth pursuit, saccades, and button press responses. *J. Neurophysiol.* 104(3):1538–48
- Olds ME, Olds J. 1963. Approach-avoidance analysis of rat diencephalon. *J. Comp. Neurol.* 120:259–95
- Olivier E, Chat M, Grantyn A. 1991. Rostrocaudal and lateromedial density distributions of superior colliculus neurons projecting in the predorsal bundle and to the spinal cord: a retrograde HRP study in the cat. *Exp. Brain Res.* 87(2):268–82
- Panksepp J. 1971. Aggression elicited by electrical stimulation of the hypothalamus in albino rats. *Physiol. Behav.* 6(4):321–29
- Philipp R, Hoffmann KP. 2014. Arm movements induced by electrical microstimulation in the superior colliculus of the macaque monkey. *J. Neurosci.* 34(9):3350–63
- Preuss SJ, Trivedi CA, vom Berg-Maurer CM, Ryu S, Bollmann JH. 2014. Classification of object size in retinotectal microcircuits. *Curr. Biol.* 24(20):2376–85
- Redgrave P, Dean P, Mitchell IJ, Odekunle A, Clark A. 1988. The projection from superior colliculus to cuneiform area in the rat. *Exp. Brain Res.* 72(3):611–25
- Redgrave P, Prescott TJ, Gurney K. 1999. The basal ganglia: a vertebrate solution to the selection problem? *Neuroscience* 89(4):1009–23
- Robinson DA. 1972. Eye movements evoked by collicular stimulation in the alert monkey. *Vis. Res.* 12(11):1795–808
- Robinson FR, Phillips JO, Fuchs AF. 1994. Coordination of gaze shifts in primates: brainstem inputs to neck and extraocular motoneuron pools. *J. Comp. Neurol.* 346(1):43–62
- Roucoux A, Guitton D, Crommelinck M. 1980. Stimulation of the superior colliculus in the alert cat. *Exp. Brain Res.* 39(1):75–85
- Sahibzada N, Dean P, Redgrave P. 1986. Movements resembling orientation or avoidance elicited by electrical stimulation of the superior colliculus in rats. *J. Neurosci.* 6(3):723–33
- Saitoh K, Ménard A, Grillner S. 2007. Tectal control of locomotion, steering, and eye movements in lamprey. *J. Neurophysiol.* 97(4):3093–108
- Sajad A, Sadeh M, Crawford JD. 2020. Spatiotemporal transformations for gaze control. *Physiol. Rep.* 8(16):e14533
- Salas C, Herrero L, Rodriguez F, Torres B. 1997. Tectal codification of eye movements in goldfish studied by electrical microstimulation. *Neuroscience* 78(1):271–88
- Schaefer KP. 1970. Unit analysis and electrical stimulation in the optic tectum of rabbits and cats. *Brain Behav. Evol.* 3(1–4):222–40
- Schiller PH, Stryker M. 1972. Single-unit recording and stimulation in superior colliculus of the alert rhesus monkey. *J. Neurophysiol.* 35(6):915–24
- Schneider GE. 2014. *Brain Structure and Its Origins: In Development and in Evolution of Behavior and the Mind*. Cambridge, MA: MIT Press
- Scott EK, Mason L, Arrenberg AB, Ziv L, Gosse NJ, et al. 2007. Targeting neural circuitry in zebrafish using GAL4 enhancer trapping. *Nat. Methods* 4(4):323–26
- Shang C, Chen Z, Liu A, Li Y, Zhang J, et al. 2018. Divergent midbrain circuits orchestrate escape and freezing responses to looming stimuli in mice. *Nat. Commun.* 9(1):1232
- Shang C, Liu Z, Chen Z, Shi Y, Wang Q, et al. 2015. A parvalbumin-positive excitatory visual pathway to trigger fear responses in mice. *Science* 348(6242):1472–77
- Shen K, Paré M. 2007. Neuronal activity in superior colliculus signals both stimulus identity and saccade goals during visual conjunction search. *J. Vis.* 7(5):15
- Song JH, McPeck RM. 2015. Neural correlates of target selection for reaching movements in superior colliculus. *J. Neurophysiol.* 113(5):1414–22
- Song JH, Rafal RD, McPeck RM. 2011. Deficits in reach target selection during inactivation of the midbrain superior colliculus. *PNAS* 108(51):E1433–40
- Sparks DL. 1988. Neural cartography: sensory and motor maps in the superior colliculus. *Brain Behav. Evol.* 31(1):49–56

- Stein BE. 1981. Organization of the rodent superior colliculus: some comparisons with other mammals. *Behav. Brain Res.* 3(2):175–88
- Stuphorn V, Bauswein E, Hoffmann KP. 2000. Neurons in the primate superior colliculus coding for arm movements in gaze-related coordinates. *J. Neurophysiol.* 83(3):1283–99
- Suzuki DG, Pérez-Fernández J, Wibble T, Kardamakis AA, Grillner S. 2019. The role of the optic tectum for visually evoked orienting and evasive movements. *PNAS* 116(30):15272–81
- Temizer I, Donovan JC, Baier H, Semmelhack JL. 2015. A visual pathway for looming-evoked escape in larval zebrafish. *Curr. Biol.* 25(14):1823–34
- Torres B, Luque MA, Pérez-Pérez MP, Herrero L. 2005. Visual orienting response in goldfish: a multidisciplinary study. *Brain Res. Bull.* 66(4–6):376–80
- Torres B, Pastor AM, Cabrera B, Salas C, Delgado-García JM. 1992. Afferents to the oculomotor nucleus in the goldfish (*Carassius auratus*) as revealed by retrograde labeling with horseradish peroxidase. *J. Comp. Neurol.* 324(3):449–61
- Valenstein ES. 1965. Independence of approach and escape reactions to electrical stimulation of the brain. *J. Comp. Physiol. Psychol.* 60:20–30
- Valentine DE, Sinha SR, Moss CF. 2002. Orienting responses and vocalizations produced by microstimulation in the superior colliculus of the echolocating bat, *Eptesicus fuscus*. *J. Comp. Physiol. A* 188(2):89–108
- Waldbillig RJ. 1975. Attack, eating, drinking, and gnawing elicited by electrical stimulation of rat mesencephalon and pons. *J. Comp. Physiol. Psychol.* 89(3):200–12
- Wallace MT, Wilkinson LK, Stein BE. 1996. Representation and integration of multiple sensory inputs in primate superior colliculus. *J. Neurophysiol.* 76(2):1246–66
- Welch RB, DuttonHurt LD, Warren DH. 1986. Contributions of audition and vision to temporal rate perception. *Percept. Psychophys.* 39(4):294–300
- Weldon DA, Calabrese LC, Nicklaus KJ. 1983. Rotational behavior following cholinergic stimulation of the superior colliculus in rats. *Pharmacol. Biochem. Behav.* 19(5):813–20
- Werner W. 1993. Neurons in the primate superior colliculus are active before and during arm movements to visual targets. *Eur. J. Neurosci.* 5(4):335–40
- Werner W, Dannenberg S, Hoffmann KP. 1997. Arm-movement-related neurons in the primate superior colliculus and underlying reticular formation: comparison of neuronal activity with EMGs of muscles of the shoulder, arm and trunk during reaching. *Exp. Brain Res.* 115(2):191–205
- Westby GWM, Keay KA, Redgrave P, Dean P, Bannister M. 1990. Output pathways from the rat superior colliculus mediating approach and avoidance have different sensory properties. *Exp. Brain Res.* 81(3):626–38
- White BJ, Munoz DP. 2011. The superior colliculus. In *The Oxford Handbook of Eye Movements*, ed. SP Liversedge, I Gilchrist, S Everling, p. 195. Oxford, UK: Oxford Univ. Press
- Wiberg M, Westman J, Blomqvist A. 1987. Somatosensory projection to the mesencephalon: an anatomical study in the monkey. *J. Comp. Neurol.* 264(1):92–117
- Wurtz RH, Goldberg ME. 1971. Superior colliculus cell responses related to eye movements in awake monkeys. *Science* 171(3966):82–84
- Xu Y, Zhu S-W, Li Q-W. 2016. Lamprey: a model for vertebrate evolutionary research. *Zool. Res.* 37(5):263–69
- Yilmaz M, Meister M. 2013. Rapid innate defensive responses of mice to looming visual stimuli. *Curr. Biol.* 23(20):2011–15
- Zelinsky GJ, Bisley JW. 2015. The what, where, and why of priority maps and their interactions with visual working memory. *Ann. New York Acad. Sci.* 1339(1):154–64