

EDITORIAL

Saccade, search and orient – the neural control of saccadic eye movements

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One of the most important functions of the brain is to guide our behavior through an ever-changing environment as our goals and desires fluctuate. One simple, yet elegant system for investigating how sensory information and goal-related information combine to control and coordinate efficient behavior is the guidance of saccadic eye movements. The brain relies heavily on visual input to guide and coordinate our complex actions, but it is impossible for our brain to simultaneously process every aspect of visual information present in real world scenes at any given moment. Instead, the retina has evolved a highly specialized fovea in the center where we have the highest visual acuity. Therefore, to analyze a visual scene optimally, the eyes reorient in complex sequences so that the high acuity fovea of the retina can be directed to specific objects of interest. These saccadic eye movements are interspersed with periods of active fixation during which the visual system performs a detailed analysis of an object that may pertain to our current goals. Alternating between the serial process of making saccades and the analytical process of active fixation is repeated several hundred thousand times per day and is critical for numerous behaviors like reading this issue of *EJN*, driving an automobile or negotiating a busy sidewalk. In the laboratory, saccadic behavior can be measured easily and accurately. Quantitative analysis of saccade behavior can also serve as an important tool to investigate brain disorders in a host of neurological and psychiatric disorders (Leigh & Zee, 2006).

Over the past few decades, there has been a tremendous increase in our knowledge of the systems that contribute to the control of saccadic eye movements. There have been many recent and exciting advances. Anatomical, physiological, clinical and imaging studies have contributed to our extensive knowledge of the saccade control circuit (Fig. 1), which includes regions of the occipital, parietal and frontal cortex, basal ganglia, thalamus, superior colliculus, cerebellum, and brainstem reticular formation. Within each of these brain regions are multiple populations of neurons and subnuclei that perform critical operations to coordinate behavior.

In addition to overt eye movements that explicitly orient the visual system, visual selection may also be directed covertly to different locations or objects without any movement of the eyes. For example, we have the ability to shift attention away from where we look without initiating a saccade. Both overt (move the eyes) and covert (only shift attention) orienting can be directed voluntarily to a specific location or object, or involuntarily 'captured' by an abrupt change in the visual environment (Posner, 1980; Theeuwes, 1991; Fecteau & Munoz, 2006). There is significant overlap in the brain areas that participate in overt and covert orienting, which include several components of the frontoparietal network and the superior colliculus.

This special issue of *EJN* contains reviews and original articles by some of the leading experts in the fields of saccades and visual search. There have been many recent exciting advances in these fields that are captured in the contributions in this issue. The contributions focus on different brain areas but the content ranges from the sensory input to the motor output and everything in between (Fig. 1). There are several different state-of-the-art technologies employed including quantitative behavioral analysis, neurophysiology, neuroimaging, clinical investigation, transcranial magnetic stimulation and modeling.

Overview of the special issue

A hallmark of this field is rigorous quantification of saccade behavior. Multiple technologies have been developed to measure eye movements accurately and efficiently (Leigh & Zee, 2006). In addition, detailed quantitative analysis of eye movement behavior has revealed tremendous insight into how the brain is organized, not only for eye movement control but also for processes like the decision-making that is required when searching for visual targets in complex environments. This theme is carried forward in the current issue with a technical spotlight by Noorani & Carpenter (2011) in which they describe a novel technique for the analysis of reaction time distributions when data are sparse by using small numbers of quantiles to represent behavior, instead of large distributions of reaction times from many trials.

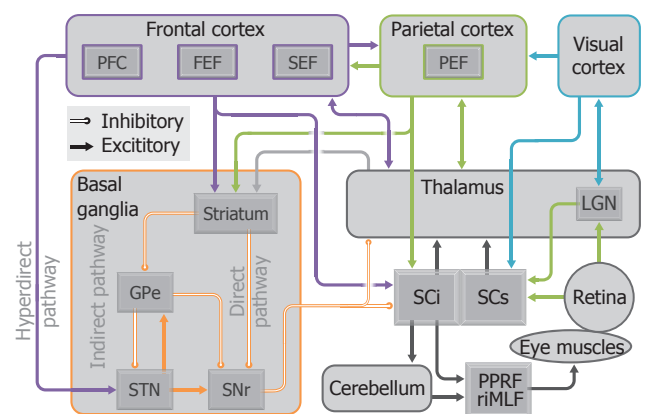


FIG. 1. Neural circuitry controlling the planning and production of saccadic eye movements. Many connections are not shown. FEF, frontal eye field; GPe, external segment of globus pallidus; LGN, lateral geniculate nucleus; PEF, parietal eye field; PFC, prefrontal cortex; PPRF, paramedian pontine reticular formation; riMLF, rostral interstitial nucleus of the medial longitudinal fasciculus; SCI, intermediate layers of superior colliculus; SCs, superficial layers of superior colliculus; SEF, supplementary eye field; SNr, substantia nigra pars reticulata; STN, subthalamic nucleus.

Visual input provides the essential bottom-up input to the saccade system (Fig. 1). The retina projects to the lateral geniculate nucleus of the thalamus, which relays visual input to the primary visual cortex. Some retinal ganglion cells also project to the superficial layers of the superior colliculus directly. There is ongoing debate as to the relative contribution of these parallel pathways, retino-geniculo-cortical vs. retino-tectal, to overall visual function, especially in patients with blindsight produced by a large lesion of the occipital cortex. Kato *et al.* (2011) address this question by exploring the relative contribution of the retino-tectal pathway to blindsight in monkeys with a unilateral lesion to the primary visual cortex.

Visual saliency is defined as the conspicuousness of a stimulus or object in the visual field. Priority is a term that has been defined to represent the combination of bottom-up saliency and top-down goals (Fecteau & Munoz, 2006; Serences & Yantis, 2006). The coding of visual saliency is critical for efficient neural processing (Itti & Koch, 2001). What are the neural mechanisms used to enhance the processing of some visual stimuli so that they are more salient than other stimuli? Although the frontoparietal network is clearly involved, recent work has shown that subcortical structures also play an important role (Boehneke & Munoz, 2008; Knudsen, 2011; Shen *et al.*, 2011). Recent work from the barn owl has identified key elements of a subcortical circuit for coding saliency that may have analogies in the primate brain (Knudsen, 2011).

Automatic (sensory-triggered) and voluntary saccade control are mediated by different cortical and basal ganglia inputs to the intermediate layers of the superior colliculus. The visual and parietal cortices and the superficial collicular layers provide important visual input that is necessary for initiating saccades to visual stimuli. Areas of the parietal and frontal cortex and basal ganglia provide many important inputs for voluntary saccade control. Several contributions in this special issue focus on recent advances in our understanding of the frontoparietal network and superior colliculus in visual selection and saccade control. The contributions rely on different approaches such as functional brain imaging (Jerde *et al.*, 2011; Medendorp *et al.*, 2011), neurophysiology (Bisley *et al.*, 2011; Shen *et al.*, 2011; Wardak *et al.*, 2011) and modeling (Schall *et al.*, 2011; Zirnsak *et al.*, 2011).

There is a growing body of literature demonstrating the important roles of the basal ganglia and thalamus in voluntary saccade control. Within the basal ganglia, the classical nuclei (caudate, globus pallidus external, subthalamic nucleus and substantia nigra pars reticulata; see Fig. 1) and pathways (direct, indirect and hyperdirect) have been implicated. However, there is growing evidence that other nuclei (e.g. putamen and pedunculo-pontine nucleus) also play important roles. Recent advances in this field are reviewed by Watanabe & Munoz (2011) with a focus on the use of microstimulation as a technique with tremendous clinical potential and the ability to compare between human and monkey species. Isoda & Hikosaka (2011) then go on to discuss how specific elements in the cortico-basal ganglia network of monkey can be used as an experimental model for flexible control over automatic prepotent behaviors. Tanaka & Kunimatsu (2011) review the role of various thalamic nuclei in saccade control, discussing how these nuclei are heavily interconnected with the cortex, basal ganglia and cerebellum. Finally, lesions in these different cortical and basal ganglia nuclei lead to specific abnormalities in saccade control. Van Stockum *et al.* (2011) exploit this to investigate saccade control in Parkinson's disease and they reveal a hypersensitivity to visual inputs in patients.

Saccade production is controlled by brainstem elements within a saccade-generating circuit that are well understood (Scudder *et al.*, 2002; Sparks, 2002). Briefly, the position of the eyes in the orbits is controlled by the actions of six muscles (superior, inferior and lateral, and medial rectus, superior and inferior oblique) organized into three orthogonal pairs. The motoneurons that innervate these muscles reside

in cranial nerve nuclei III, IV and VI. The activity of the extraocular muscle motoneurons is under the precise control of a saccade-generating circuit in the brainstem reticular formation. Horizontal gaze is coordinated in the paramedian pontine reticular formation and vertical gaze is coordinated in the mesencephalon. The intermediate layers of the superior colliculus, brainstem reticular formation and cerebellum are heavily interconnected to coordinate the metrics of each saccade.

Microsaccades are very small eye movements that occur during the periods of fixation between macrosaccades. Recent evidence has shown that microsaccades are influenced by attentional processing and they may play an important role in the orienting/attention system. Hafed (2011) reviews recent evidence showing how microsaccades may be controlled by the neural elements within the superior colliculus and brainstem premotor circuit.

The cerebellum also plays a very important role in saccade control, especially in maintaining the accuracy of saccades. As such, saccade adaptation has emerged as a very useful model for investigation into the role of the cerebellum in motor learning in general. Prsa & Their (2011) review some of the recent findings in this field, showing how the cerebellum participates in saccade adaptation.

Rapid eye movements are also present in a specific stage of normal sleep, i.e. rapid eye movement (REM) sleep. Although the precise function of rapid eye movements during sleep has remained elusive, it is important to determine whether similar physiological mechanisms control saccades and rapid eye movements during sleep. Sanchez-Lopez & Escudero (2011) present original data showing that, at the beginning of REM sleep, normal rodents have a tendency to converge the eyes and rotate them downward in a similar pattern to that observed previously in the cat. These data are important for demonstrating the similarity of the rodent behavior to other animals so that detailed physiological mechanisms of REM sleep can now be pursued.

Most work on how the brain controls saccades has ignored the fact that the brain must actually control two eyes that are separated by a few centimeters. Having vision from two eyes provides important depth cues to help guide our behavior in three dimensions. However, it also complicates the control mechanisms because the two eyes do not always move together, especially when looking between visual targets located at different depths, a situation that occurs for almost all saccades made in a three-dimensional world. Recent advances in the role of brainstem elements in the binocular control of eye movements are reviewed by King (2011) and Cullen & Van Horn (2011).

Orientation of the visual axis often involves more than movement of just the eyes. Head and body motion can also participate in the orienting response. Goonetilleke *et al.* (2011) use transcranial magnetic stimulation of human frontal eye fields to explore the role of this structure in coordinating eye and head movements and activating the neck musculature.

In conclusion, the saccade system provides an excellent model system to investigate the neural mechanisms underlying sensory, motor and cognitive functions. There has been a tremendous increase in knowledge of this system and it now has direct experimental, applied and clinical applications. We predict that this system will continue to provide important information about brain function and, as your eyes peruse the pages of this special issue, we hope that you will come away with a deeper appreciation of how the oculomotor network brings the world to you.

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