Role of Rostral Superior Colliculus in Gaze Stabilization during Visual Fixation

Robert A. Marino, Douglas P. Munoz, and Ron Levy

Abstract

Visual fixation (i.e., holding gaze on a specific visual object or location of interest) has been shown to be influenced by activity in the rostral pole of the intermediate layers of the superior colliculus (SCi)—a sensory–motor integration nucleus in the midbrain involved in visual fixation and saccadic eye movement generation. Neurons in the rostral SCi discharge tonically during visual fixation and pause during saccades to locations beyond their foveal visual-sensory or saccadic-motor response fields. Injection of muscimol to deactivate rostral SCi neurons also leads to an increase in fixation instability. However, the precise role of rostral SCi activity for controlling visual fixation has not been established and is actively debated. Here, we address whether this activity reflects signals related to task demands (i.e., maintaining visual fixation) or foveal visual stimulus properties. Two non-human primates performed an oculomotor task that required fixation of a central fixation point (FP) of varying luminance at the start of each trial. During this fixation period, we measured fixational saccades (≤ 2° of the FP, including microsaccades) and fixation-error saccades (> 2° from the FP) in combination with activity from the rostral SCi. Fixation of the lowest FP luminance increased the latency (onset time relative to initial FP foveation) for both fixational and fixation-error saccades. Fifty percent of the rostral SCi neurons exhibited activity that opposed the change in FP luminance and correlated with delayed fixational saccades and increased fixation-error saccades. Twenty-two percent of rostral SCi neurons exhibited activity that followed the change in FP luminance and correlated with earlier fixational saccades and decreased fixation-error saccades. This suggests the rostral SCi contains both sensory-driven and task-related motor signals related to foveal sensory stimuli and visual fixation. This evidence supports a role for the rostral SCi in gaze stabilization and can help inform artificial computational models of vision.

INTRODUCTION

As we scan the visual world, our eyes make quick movements (saccades) that move the fovea (the high acuity region of the retina encompassing ~2° of the central visual field) to align with objects of interest. These saccades are separated by periods of visual fixation during which the visual image is analyzed. This process of visual fixation involves numerous brain structures, including the brainstem premotor circuit, superior colliculus, frontal and parietal cortex, basal ganglia, and cerebellum, which exhibit sustained activity during fixation that shuts off during saccades (for a review see: Krauzlis, Goffart, & Hafed, 2017; Scudder, Kaneko, & Fuchs, 2002; Munoz, Dorris, Paré, & Everling, 2000; Scudder, Moschovakis, Karabelas, & Highstein, 1996). However, the neural mechanisms underlying the control of visual fixation have not been clearly established and are actively debated.

The superior colliculus (SCi) is an important sensorimotor midbrain structure involved in both visual fixation (Krauzlis et al., 2017; Goffart, Hafed, & Krauzlis, 2012; Munoz & Wurtz, 1992, 1993a, 1993b) and the sensorimotor transformations underlying saccade generation (Hall & Moschovakis, 2003; Sparks, 1986). The intermediate layers (SCI) contain neurons that discharge bursts of action potentials in response to the appearance of visual stimuli and/or the initiation of saccadic eye movements within distinct regions of the visual field (i.e., visual or motor response fields; Mohler & Wurtz, 1976; Sparks, Holland, & Guthrie, 1976). Importantly, SCi neurons are organized into a retinotopic (i.e., eye-centered) motor map in which responses to both sensory stimuli and saccade motor vectors are represented within spatially organized response fields (Marino, Rodgers, Levy, & Munoz, 2008; Ottes, Van Gisbergen, & Eggermont, 1986; Robinson, 1972). Within this map, foveal visual stimuli and small amplitude saccades are represented rostrally, whereas more peripheral visual stimuli and larger amplitude saccades are represented more caudally.

A subset of neurons in the rostral SCi exhibit low-frequency (typically < 50 Hz) tonic activity during active visual fixation, and reduced activity during generation of saccades beyond their small para-foveal response fields (Chen, Hoffmann, Distler, & Hafed, 2019; Hafed, Chen, & Tian, 2015; Krauzlis, 2003; Krauzlis, Basso, & Wurtz, 2000; Munoz & Wurtz, 1993b; Munoz & Guitton, 1991). Although mounting evidence indicates that this rostral SCi activity is important for the control of visual fixation and/or suppression of saccades (Krauzlis et al., 2017; Goffart et al., 2012; Munoz & Wurtz, 1992, 1993b), different theories have been proposed as to the mechanism by
which it influences fixation behavior. One theory (referred to here as "endogenous fixation") suggests that the rostral SCI neurons that discharge tonically during fixation are involved in maintaining fixation by (1) inhibiting saccade-related activity in the caudal SC (Munoz & Fecteau, 2002; Munoz & Wurtz, 1993a, 1993b) and (2) exciting brainstem omnipause neurons (OPNs) that inhibit the saccade burst neurons (Büttner-Ennever, Horn, Henn, & Cohen, 1999; Gandhi & Keller, 1997; Paré & Guitton, 1994; Raybourn & Keller, 1977). A more recent theory (referred to here as "exogenous equilibrium") suggests that the tonic activity in the rostral pole is related to the presence of the fixated sensory stimulus in the foveal position. The tonic sensory activity helps maintain visual fixation at a location by facilitating an equilibrium in the activity between the right and left SCI (Krauzlis et al., 2017; Goffart et al., 2012). Once this equilibrium is lost and the activity on one side of the SCI dominates, a contralateral saccade is generated.

One question that arises from both theories is whether the tonic activity recorded in the rostral SCI during visual fixation of a stimulus originates from purely exogenous sensory signals (such as retinotopic location, or stimulus luminance contrast relative to background) or whether it also includes more cognitive endogenous task-related signals involved in gaze stabilization. Rostral SCI activity has been shown to persist during fixation even after the disappearance of the fixated stimulus (Munoz & Wurtz, 1993a), which suggests an endogenous origin; however, such activity has never been linked behaviorally with eye immobilization during fixation.

Here, we address this question by investigating the tonic activity of rostral SCI neurons during fixation of a central fixation point (FP) stimulus whose sensory luminance relative to a dark background was systematically varied. We reanalyzed a previous data set (Marino, Levy, & Munoz, 2022) with a focus on rostral SCI activity and saccadic behavior that occurred during the initial visual fixation period of a visually guided saccade task (Figure 1A). Examining the initial visual fixation period is critical as this reflects when the only immediate task goal is to initiate

Figure 1. (A) Schematic representation of the temporal events in the visually guided saccade task denoting changes in the central fixation point (FP), target (T), and eye position (EYE). Vertical gray bars denote the fixation dissociation and baseline fixation epochs used for analysis (see Methods section). (B) Scatter plot of the two epochs used to group neural activity in the fixation period. Different symbols denote each individual neuron subpopulation group. (C) Mean population spike density function (Gaussian Kernel, $\sigma = 4$ msec), aligned to saccade onset for all 72 recorded rostral SCI neurons during a 10° saccade (directed ipsilaterally to the side of the brain where each neuron was recorded). (D) Comparison of activity between the saccade response (mean single neuron activity 0 to 15 msec after saccade onset) and the baseline fixation response (mean single unit activity during last 200 msec of the fixation period) for all 72 recorded rostral SCI neurons during ipsilateral 10° saccades. Different symbols denote each individual neuron subpopulation group.
and maintain fixation on a visual stimulus before any predictive warning cues that otherwise prompt a subject to prepare a saccade to an imminently appearing target. Thus, the fixation period provides an ideal epoch to study pure fixation mechanisms while minimizing the presence of potential confounding saccade preparation signals (Basso & Wurtz, 1998; Dorris & Munoz, 1995, 1998; Dorris, Paré, & Munoz, 1997). The existence of three hypothetical fixation-related signals in the rostral SC was investigated: (1) If the sustained activity during fixation is influenced by the exogenous sensory properties of the fixated stimulus, we hypothesize that the activity will co-vary with FP stimulus luminance at a latency consistent with a visual response in the caudal SC when a similar stimulus appears in the periphery (Marino et al., 2012). (2) If the activity is related to an endogenous task-related fixation signal, we hypothesize that the activity should dissociate from the sensory properties of the fixated stimulus and remain correlated with gaze stability (e.g., reflect changes in difficulty fixating a bright vs. a dim stimulus). (3) Finally, if the activity is related to the retinotopic location of the foveated stimulus, we hypothesize that the activity should be unchanged across FP luminance conditions because the retinotopic position and size of the fixation stimulus remains constant. We examine the extent to which these three possible signals are represented within the discharge patterns of individual neurons in the rostral SCi and discuss their implications for the role of the rostral SC in controlling visual fixation. The results provide new insight into the varied role of the rostral SC in the neural mechanisms underlying the control of visual fixation in primates.

METHODS
Animal Preparation
All animal care and experimental procedures were in accordance with the Canadian Council on Animal Care policies on the use of laboratory animals and approved by Queen’s University Animal Care Committee. The surgical techniques required to prepare animals for neuronal and eye movement recordings in our laboratory have been described previously (Marino et al., 2008). In brief, two adult male monkeys (Macaca mulatta) were trained to perform oculomotor tasks. Both animals underwent surgery under aseptic conditions for the insertion of an eye coil, a stainless steel head holder, and a recording chamber that was mounted on the skull using stainless steel bone screws and dental acrylic. The recording chamber was oriented toward the SC at an angle of 38° posterior of vertical in the mid-sagittal plane. Monkeys were given at least 4 weeks to recover before resuming of behavioral training.

Experimental Tasks and Behavioral Stimuli
Monkeys were seated in a primate chair with their heads restrained during the experiment. They faced a display cathode ray tube monitor that provided an unobstructed view of the central visual area 50° × 60°. Eye position was measured using the magnetic search coil technique (Robinson, 1963) and recorded at 1 kHz. Extracellular recording was performed with tungsten microelectrodes (0.5- to 5-MΩ impedance, Frederick Haer) inserted through guide tubes (23 gauge) that were anchored in delrin grids with 1-mm hole separations inside the recording chamber (Crist, Yamasaki, Komatsu, & Wurtz, 1988). Electrodes were advanced with a microdrive into the intermediate layers of the SC where we proceeded to isolate single neurons.

Each monkey was required to perform a visually guided saccade task where the luminance of the FP was manipulated (Figure 1A). Each trial started with a 250-msec period of unconstrained free viewing of a black screen (~0.0001 cd/m²). A circular (0.25° diameter spot) grayscale FP at one of three luminance levels (0.04 cd/m², 3.5 cd/m², 42.5 cd/m²) then appeared at the center of the screen. Monkeys were required to fixate upon the FP for 800–1100 msec after its appearance (i.e., the fixation period) until a small circular grayscale target (T) appeared with fixed luminance (0.25° diameter spot, 42.5 cd/m²) 10° to the left or right of the FP. The 10° amplitude target locations were selected to be beyond the optimal sensorimotor vector of each rostral SCi neurons’ response field (Figure 1C, 2A, for full results, see Marino et al., 2022). During the final 300 msec before T appearance (pretarget warning period), FP luminance could change to one of three different levels (0.04 cd/m², 3.5 cd/m², 42.5 cd/m²; see Figure 1A). The monkey was required to initiate a saccade to the T within 1000 msec of its appearance. This study focuses only on saccade behavior and rostral SCi activity during the fixation period of each trial (i.e., the time from initial foveation of the FP until the start of the pretarget warning period; Figure 1A). The effect of FP luminance on saccade behavior to the T as well as pretarget warning period activity in the SCi are described elsewhere (Marino et al., 2022) and are not included in this study.

The display screen was diffusely illuminated during the intertrial interval (800- to 1500-msec duration) to prevent dark adaptation. Luminance of the FP and T were measured with an optometer (UDT instruments, Model S471) that was positioned directly against the screen of the monitor and centered on the stimulus. On experimental recording days, fluids were rationed such that each monkey earned a portion of their daily water by performing saccade tasks. After each correct trial, the monkey was rewarded with 1–5 mL of water. Weight was monitored daily, and supplemental water was provided whenever weight dropped by more than 5%.

Analysis of Neural Activity during the Fixation Period
Here, we examined 72 neurons recorded in the rostral SCi of two monkeys that exhibited peak visual and/or motor
response fields with eccentricities within 2.3° of central visual angle (Figure 2A, B). Visual response fields were defined as all spatial T locations (relative to the FP) that elicited an increase in action potentials (~40 to 90 msec after T appearance) related to the appearance of the T (i.e., a visual response). Motor response fields were defined as all saccade vectors that elicited an increase in action potentials (around the time of the saccade) related to the initiation of a saccade toward the T (motor response). The peak location was defined by the spatial location of the T that elicited the highest frequency burst of action potentials related to the appearance of the T (visual response), or the initiation of a saccade toward the T (motor response). This peak location was used to determine the location on the SC map via a mathematical transformation. When mathematically transformed into anatomically modeled SC map coordinates, all neurons were within 1.1 mm (Ottes et al., 1986) or 2.2 mm (Chen et al., 2019) of the rostral pole, depending on which model was applied (Figure 2B, right side). Visual response fields were measured in real time via a rapid visual response field mapping task (Marino et al., 2012). This task mapped visual responses to briefly flashed visual stimuli (100-msec stimuli duration, 150-msec ISI) that appeared at 182 different locations throughout the visual field (Figure 2A). All neurons described in this article exhibited tonic activity during fixation of the visible FP during the last 200 msec of the fixation period (fixation baseline epoch) preceding the pretarget warning period (Figure 1A). All SCi neurons were recorded at electrode depths where saccade motor responses had been observed in some neurons (Marino et al., 2022). Neurons with peak visual and or motor responses > 2° but < 3° eccentricity were only included when neighboring neurons with peak responses < 2° were observed within the same electrode trajectory.

Each spike was convolved with a Gaussian kernel (σ = 4 to 5 msec) to create a continuous spike density function over time for analysis. Mean spike density functions were calculated from trial-averaged neural activity. When analyzing the fixation period activity, spike density functions were...
were aligned to either: (1) the appearance of the FP at the start of each trial or (2) the end of the saccade that aligned gaze with the central FP after its appearance. In the trials when the FP appeared at or near the current gaze location (i.e., < 2°), these two alignments were nearly equivalent. Saccade responses were aligned to the start of the eye movement and were measured from the mean spike density function ± 10 msec around the onset of the saccade (Marino et al., 2022).

Neurons were separated into groups for analysis based on their low-frequency tonic activity (< 50 spikes/sec) during fixation of different FP luminance levels (see Figure 1A). Analysis groups were determined from increases or decreases in firing rate between the highest (42.5 cd/m²) and lowest (0.04 cd/m²) FP luminance condition. Individual neurons were considered as increasing or decreasing their activity during the fixation period if they exhibited a mean difference in firing rate between the highest and lowest FP conditions of at least 3.5 spikes/sec during the first 100- to 400- and 100- to 300-msec epochs (i.e., fixation dissociation epochs) of the fixation period (Figure 1B). Two different epoch durations were used when separating activity differences between neurons to account for variability in the timing and duration of peak activity modulation during the fixation period. This ensured that neuron group sorting was as accurate as possible for all neurons in the recorded population. Thus, the two fixation dissociation epochs ensured that the 3.5-spikes/sec threshold and varied fixation epoch durations were arbitrarily chosen to best separate activity during the fixation period as well as exclude/remove neurons with little or no modulation from the analysis. The first 100 msec of the fixation period was not used for grouping to conservatively account for efferent and afferent visual processing delays that precede visual sensory information arriving in the SCi (Marino et al., 2012). Left and right target locations were collapsed together for analysis as the upcoming target location was unknown to the subject during the fixation period.

Once neuronal activity was separated into groups, we examined the differences in activity between each FP luminance condition within the same group before and during the fixation period using a running rank sum test ($p \leq 0.05$) with a 10-msec temporal resolution. The onset of activity differences across FP luminance conditions was then determined relative to two different events: (1) task-aligned to the initial appearance of the FP during the unconstrained eye position period or (2) behavior-aligned to the onset of FP foveation at the beginning of the fixation period (Figure 1A). The extrafoveal appearance of the FP (before it is fixated in the fixation period) conveyed information related to the task condition (i.e., initial FP luminance; Figure 1A). Thus, initial FP appearance time was used to align neural activity related to the task condition. In contrast, when examining activity related to changes in foveal sensory input after saccades, neural activity was aligned to the start of the fixation period (i.e., the end of the saccade that aligned the fovea on the FP), as this reflects the onset time of when the FP first visually stimulates the fovea during each trial.

**Saccade Analyses**

Data were analyzed offline with custom MATLAB (MATLAB Release 2017a, The Mathworks Inc.) software. The start and end of both fixational and fixation error saccades (see below) were determined from saccadic eye velocity. Saccade velocity was calculated from a smoothed (repeated 5-point moving average) radial eye position. **Fixational saccades** were defined as saccades made within the square 2° region of the visual field that surrounded the FP (i.e., fixation window). Saccades made within this area were permitted during the fixation period and did not affect the completion of a correct trial. Saccades (> 2° amplitude) that directed gaze outside this area during the fixation period were defined as **fixation-error saccades** and resulted in the trial being aborted and scored as an error. A subset of error trials, where gaze entered and then left the fixation window without stopping, were excluded from analysis as these trials did not reflect an error related to maintaining visual fixation (percentage excepted trials by FP luminance: 3.5% at 0.04 cd/m², 3.6% at 3.5 cd/m², and 4.8% at 42.5 cd/m²). Visual fixation was defined within this study as the maintenance of gaze (i.e., the fovea) within the 2° fixation window surrounding the FP. Visual fixation includes fixational saccades, microsaccades, as well as the periods where the fovea was relatively immobile other than positional drift (i.e., stable gaze). We define gaze stability in this study as the subset of visual fixation when the fovea was immobile (other than positional drift) and directed toward the FP.

**Fixation-error saccade latency** was calculated from the start of the fixation period (i.e., end of saccade to look at the FP) to the time when another saccade directed the gaze beyond the 2° square fixation region surrounding the FP. **Fixational saccade latency** was likewise calculated from the start of the fixation period to the start of the first fixational saccade directed within the 2° square fixation region surrounding the FP. Fixational saccades could also include corrective saccades made to better align the fovea on the FP. Trials where gaze drifted into the fixation window without a clear saccade were excluded from all analyses as no precise onset time for initial FP fixation could be determined. Trials where the monkey utilized a > 2° saccade to fixate the FP after its appearance were included in all analyses (i.e., the gaze position originated outside the fixation window when the FP appeared). Trials where gaze was already located within 2° of the FP when it appeared were eliminated from the correlation analysis but were analyzed separately in the neural population activity analysis. Excluding these trials from the correlation analysis enabled all trials to be aligned to the same event, that is, the start of visual fixation following a saccade. Separating and including these trials in the population activity
enabled the temporal dissociation of stimulus-related sensory responses from task-related responses.

Saccadic behavior and physiological data were consistent across both participants and were collapsed for analysis. All statistical comparisons of neuronal activity and saccade behavior were tested for normalcy using the Kolmogorov–Smirnov goodness-of-fit test. Nonparametric statistical comparisons were calculated with Kruskal–Wallis tests with pairwise comparisons using the Tukey–Kramer method unless stated otherwise. Proportional differences were tested using a chi-square test of proportions. All mean and median values reported also included standard error unless stated otherwise. In total, 3157 (0.04 cd/m²), 3850 (3.5 cd/m²), and 3873 (42.5 cd/m²) correct trials were performed at each FP luminance level from which fixational saccades were extracted and analyzed. Likewise, 594 (0.04 cd/m²), 263 (3.5 cd/m²), and 294 (42.5 cd/m²) fixation error trials were performed (totals collapsed across both monkeys).

Correlation of Activity with FP Luminance and Task Performance

We investigated possible goal-driven (linked to the endogenous decision to maintain fixation) and sensory-driven (linked to the exogenous external FP luminance) signal sources for the observed modulations of activity in the rostral SC. This is done by correlating neural activity recorded from individual neurons within each modulated analysis group (i.e., neurons that increased or decreased discharge during the fixation period for decreasing FP luminance; see above) to both task performance and raw FP luminance values. Mean neural activity for each condition was calculated from the proportion of fixation error saccades during the fixation period (Figure 1A). We assessed the effects of FP luminance on fixational and saccadic behavior (Chen et al., 2019; Krauzlis et al., 2017). We correlated fixational saccade latency with rostral SC activity irrespective of FP luminance as each bin contained trials from several different luminance conditions. Correlations were calculated using Pearson’s rho because the 10 data points per correlation allowed for a parametric linear investigation.

Before correlation with fixational saccade latency, rostral SC activity was aligned to the beginning of the fixation period (i.e., initial fixation of the FP) to ensure consistent alignment between correlated quantities. To demonstrate that the correlation between rostral SC activity and fixational saccade latency was insensitive to the temporal epoch over which the rostral SC activity was sampled, multiple correlations utilizing multiple epoch start times and durations were calculated. Rostral SC activity was calculated from a range of epoch durations (10–100 msec) and epoch start times (0–800 msec) relative to the start of the fixation period. Rostral SC activity epochs were calculated every 5 msec within the ranges of both start times and durations. This resulted in a total of 3059 independent correlations for each of the three subpopulations in this study.

Correlation Significance and Timing

Significance of each mean correlation from zero was calculated using a sign rank test from each individual neuron’s tau or rho values for each subpopulation. The temporal epoch when the mean correlation value (tau or rho) significantly changed from its initial value at the onset of each alignment was determined from a running rank sum test ($p < .05$) that compared the correlation value at the initial epoch to each subsequent epoch (calculated individually for each subpopulation). The onset of significant change in correlation relative to the start of each alignment was calculated as the first significantly different epoch in a consecutive sequence of at least 10 significant epochs. The individual significance of each correlation (relative to 0) was calculated at every epoch. The temporal resolution of each epoch was dependent on the duration over which the neural activity was calculated. Here, the onset of correlation changes was calculated at a fixed epoch duration of 20 msec. This duration yielded adequate temporal resolution while still allowing a long enough sample period of neural activity during the fixation period to minimize variability and noise in the spike train.

RESULTS

Fixation Stimulus Luminance Modulated Fixational Saccades

We assessed the effects of FP luminance on fixational and error saccades during the fixation period (Figure 1A).
Figure 3 illustrates the effects of FP luminance on the occurrence of fixation-error saccades (Figure 3A, B; i.e., saccades > 2° away from the FP during the fixation period, thereby resulting in an error trial) and fixational saccades (Figure 3C, D, i.e., saccades < 2° away from the FP) during the fixation period. When the FP was at the lowest luminance (0.04 cd/m²), there was a significant increase in the proportion of fixation-error saccades; chi-square test of proportions, 0.04 to 3.5 cd/m²: $\chi^2 = 123.8, p < .01$; 0.04 to 42.5 cd/m²: $\chi^2 = 96.3, p < .01$; Figure 3A).

Figure 3B denotes the latency of the first fixation-error saccade relative to the beginning of the fixation period for each FP luminance condition. There was a main effect of FP luminance on the time of fixation-error saccades (Kruskal–Wallis $H(2, 1050) = 71.8$; Kolmogorov–Smirnov goodness-of-fit test for normalcy $p > .05$). The
lowest FP luminance condition (0.04 cd/m$^2$) resulted in longer latency fixation-error saccades compared with the highest (42.5 cd/m$^2$) or intermediate (3.5 cd/m$^2$) luminance FP conditions (Kruskal–Wallis post hoc pairwise comparisons: 0.04 to 3.5 cd/m$^2$: $p < .01$; 0.04 to 42.5: $p < .01$). The median fixation-error saccade latencies were 279 msec (0.04 cd/m$^2$), 156 msec (3.5 cd/m$^2$), and 150 msec (42.5 cd/m$^2$).

Figure 3C denotes the median number of fixational saccades performed during the fixation period for each FP luminance condition. There was a main effect of the FP luminance on the median number of fixational saccades performed (Kruskal–Wallis $H(2, 13635) = 574.4$; Kolmogorov–Smirnov goodness-of-fit test for normalcy $p > .05$). The highest and intermediate FP luminance condition (42.5 cd/m$^2$ and 3.5 cd/m$^2$) resulted in more fixational saccades per trial compared with the lowest (0.04 cd/m$^2$) luminance FP conditions (Kruskal–Wallis post hoc pairwise comparisons: 0.04 to 3.5 cd/m$^2$: $p < .01$; 0.04 to 42.5 cd/m$^2$: $p < .01$). The median number of fixational saccades per FP luminance condition was 0.9 (0.04 cd/m$^2$), 1.22 (3.5 cd/m$^2$), and 1.24 (42.5 cd/m$^2$).

FP luminance also impacted the timing of the first fixational saccade during the fixation period (Figure 3D). There was a main effect of FP luminance on median fixation-error saccade latency (Kruskal–Wallis $H(2, 10899) = 1482.7$; Kolmogorov–Smirnov goodness-of-fit test for normalcy $p > .05$). The lowest FP luminance condition (0.04 cd/m$^2$) resulted in longer latency fixation-error saccades compared with the highest (42.5 cd/m$^2$) or intermediate (3.5 cd/m$^2$) luminance FP conditions (Kruskal–Wallis post hoc pairwise comparisons: 0.04 to 3.5 cd/m$^2$: $p < .01$; 0.04 to 42.5 cd/m$^2$: $p < .01$). The median fixation-error saccade latencies were 296 msec (0.04 cd/m$^2$), 195 msec (3.5 cd/m$^2$), and 184 msec (42.5 cd/m$^2$).

In summary, FP luminance modulated gaze stability (defined here as foveal immobility) during FP fixation such that the lowest luminance stimulus increased stable gaze duration (i.e., there were longer periods of foveal immobility on the FP during fixation before the occurrence of either a fixational or fixation-error saccade). However, the increased periods of gaze stability came at a cost of higher proportions of fixation error saccades, which could indicate increased difficulty or neural effort when fixating the lowest luminance FP.

**FP Luminance Modulated SC Activity during Visual Fixation**

We investigated whether changes in the luminance of fixated stimuli modulated tonic activity of single neurons in the rostral SC and whether this modulation was related to sensory or task-related signals (Figure 4). The continuum of neural activity from 72 neurons recorded in the rostral SC was aligned to both FP appearance and initial FP foveation (i.e., the start of the fixation period) and divided into three subpopulations based on differences in activity between the highest (42.5 cd/m$^2$) and lowest (0.04 cd/m$^2$) luminance conditions (see Figure 4 and Methods section). Based on these criteria: 16/72 neurons increased their activity between the lowest and highest FP luminance conditions (i.e., their modulation was congruent with the change in the visual sensory stimulus), 36/72 neurons decreased their activity between the lowest and highest FP luminance conditions (i.e., the modulation was opposite to the change in the visual sensory stimulus), and 20/72 neurons did not exhibit modulation by FP luminance.

For neurons that increased with increasing luminance, when aligned to both FP appearance (Figure 4A left, Figure 4D) and the start of the fixation period (Figure 4A right), activity in the highest (42.5 cd/m$^2$) and middle (3.5 cd/m$^2$) FP luminance conditions significantly increased relative to the lowest (0.04 cd/m$^2$) FP luminance condition. When the monkey made a saccade to the FP, the activity in the highest (42.5 cd/m$^2$) and middle (3.5 cd/m$^2$) luminance conditions both increased relative to the lowest luminance condition at 280 and 320 msec, respectively (Figure 4A, aligned to FP appearance). In a subset of trials for which gaze was already within the fixation window at FP appearance, the activity in the highest (42.5 cd/m$^2$) and middle (3.5 cd/m$^2$) luminance conditions increased relative to the lowest luminance condition at 70 and 350 msec, respectively (Figure 4D). When aligned to the start of the fixation period (Figure 4A right, colored arrows), the activity in the highest (42.5 cd/m$^2$) and middle (3.5 cd/m$^2$) luminance conditions significantly increased compared with the lowest luminance condition at 80 and 430 msec, respectively (running rank sum tests, $p \leq .05$).

Figure 4B and 4E illustrates the subpopulation of rostral SC neurons that decreased their activity with the largest increase in FP luminance. When aligned to both FP appearance (Figure 4A left, Figure 4E) and the start of the fixation period (Figure 4A right), activity in the highest (42.5 cd/m$^2$) and middle (3.5 cd/m$^2$) FP luminance conditions significantly decreased relative to the lowest (0.04 cd/m$^2$) FP luminance condition regardless of gaze position at the time of FP appearance. When aligned to the time of FP appearance, the activity in the highest (42.5 cd/m$^2$) and middle (3.5 cd/m$^2$) luminance conditions significantly decreased from the lowest luminance condition at 110 msec when the FP was saccaded to (Figure 4B left) and at 100 and 110 msec, respectively (Figure 4E), when gaze was already within the fixation window at FP appearance. Furthermore, the middle FP luminance condition (3.5 cd/m$^2$) also increased from the highest FP luminance condition (42.5 cd/m$^2$) later into the epoch at 410 msec (Figure 4B). When aligned to the start of the fixation period (Figure 4B right, colored arrows), the activity in the highest (42.5 cd/m$^2$) and middle (3.5 cd/m$^2$) luminance conditions significantly decreased from the lowest luminance condition at 20 and 10 msec.

Marino, Munoz, and Levy 187
Figure 4C and 4F illustrates the subpopulation of rostral SC neurons that were unmodulated with the largest increase in FP luminance. This subpopulation did not exhibit any significant changes in activity across FP luminance conditions.

**Correlation of Rostral SC Activity with Sensory and Task-related Signals**

We investigated the strength and timing of the modulation of each rostral SCi subpopulation (extracted from the...
continuum of neural responses; see Methods section) with respect to FP luminance and task performance. To accomplish this, we correlated the activity of all neurons in each subpopulation with both FP luminance (visual-sensory properties) and the proportion of fixation breaks (i.e., fixation-error saccades) over time. Correlation timing was determined separately for each alignment (i.e., relative to FP appearance and initial FP foveation) and was calculated over multiple overlapping temporal windows (5-msec resolution, 10- to 100-msec epoch duration). Activity was calculated over multiple epoch durations (10–100 msec) to validate that the results were robust across different epoch durations (see Methods section). Figure 5 illustrates the nonparametric correlation coefficients (Kendal’s ρ) of both subpopulations with FP luminance (Figure 5A, 5C, and 5E) and task performance (Figure 5B, 5D, and 5E).

In the subpopulation that increased fixation period activity with increasing FP luminance (Figure 5A and 5B), there was a significant positive correlation with FP luminance (Figure 5A; FP appearance aligned: 67.9% epochs positively correlated; ρ = 0.58 ± 0.12, p < .05; FP foveation aligned: 81.9% epochs positively correlated, ρ = 0.56 ± 0.1, p < .05). There were no significant instances of negatively correlated epochs with FP luminance (p > .05). When this population was correlated with task performance (Figure 5B), significant negative correlations were observed (FP appearance aligned: 19.8% epochs negatively correlated, ρ = −0.39 ± 0.06, p < .05; FP foveation aligned: 22.5% epochs negatively correlated, mean ρ = −0.36 ± 0.04, p < .05), whereas almost no epochs were positively correlated (Figure 5B; FP appearance aligned: 0% epochs positively correlated, p > .05; FP foveation aligned: 0.4% epochs positively correlated, ρ = 0.36 ± 0.04, p < .05). There were significantly more positive correlations with FP luminance (Figure 5A) than negative correlations with task performance (Figure 5B) across both alignments (FP appearance aligned: chi-square test of proportions χ² = 1436, p < .01, FP foveation aligned: chi-square test of proportions χ² = 2160, p < .01). This indicates that the subpopulation that increased fixation period activity with increasing FP luminance also exhibited activity that correlated with reduced saccade errors.

Figure 5E denotes the correlation values at the 20-msec epoch duration (black outlined arrows from Figure 5A–5D) from each subpopulation aligned to FP appearance (Figure 5E, left) and initial FP foveation (Figure 5E, right). For this same subpopulation that increased fixation activity with increasing FP luminance, the onset of positive correlation with FP luminance occurred earliest when aligned to FP foveation onset (91 msec at 20-msec epoch durations; Figure 5E, right, vertical dashed lines above the solid black triangle below the abscissa) relative to when it was aligned to the time of FP appearance (261 msec at 20-msec epoch durations; Figure 5E, left, vertical dashed lines above the solid black triangle under the abscissa). If the correlation of this subpopulation with FP luminance was linked with a sensory response to the FP stimulus, then the timing of this correlation would be expected to be similar to known visual response onset latencies (VROIs) in the caudal SCi (Marino et al., 2012). Here, the correlation timing is consistent with SCi VROIs when aligned to FP foveation (91 msec at 20-msec epoch durations; Figure 5A and 5E right), not FP appearance (261 msec at 20-msec epoch durations; Figure 5A and 5E left). That is, the correlation timing is linked to the arrival of the visual response to the FP stimulus aligning with the fovea (the retinal location coded by the rostral SCi).

For the subpopulation that decreased fixation activity with increasing FP luminance (Figure 5C and 5D), there was a significant negative correlation with FP luminance (Figure 5C; FP appearance aligned: 65.6% epochs negatively correlated, ρ = −0.41 ± 0.14, p < .05; FP foveation aligned: 68.9% epochs negatively correlated, ρ = 0.40 ± 0.1, p < .13) as well as some positive correlation before the appearance of the FP (FP appearance aligned: 4.7% epochs positively correlated, ρ = 0.35 ± 0.06, p < .05; FP foveation aligned: 0% epochs positively correlated, p > .05). There was significant positive correlation with task performance (Figure 5D; FP appearance aligned: 55.3% epochs positively correlated; ρ = −0.42 ± 0.1, p < .05; FP foveation aligned: 57.4% epochs correlated, ρ = 0.42 ± 0.9, p < .05) as well as sparse negative correlations (Figure 5D; FP appearance aligned: 3.6% epochs negatively correlated, ρ = −0.30 ± 0.06, p < .05; FP foveation aligned: 5.7% epochs negatively correlated, ρ = −0.29 ± 0.05 p > .05). This indicates that the subpopulation that decreased fixation period activity with increasing FP luminance also exhibited activity that correlated with increased saccade errors.

In addition for this subpopulation that decreased fixation activity with increasing FP, stable correlation with FP luminance and task performance was already present at the time of FP foveation (Figure 5C, 5D, and 5E), whereas when aligned to FP appearance, stable correlation only required 76 msec at 20-msec epoch durations to emerge (Figure 5E, left, gray arrow). Thus, for this subpopulation, activity became correlated before the arrival of the visual response in the rostral SCi to FP foveation.

Different Subpopulations of SCi Neurons Correlate Positively and Negatively with Fixational Saccades

We investigated the influence of rostral SCi activity on fixational saccade generation by correlating fixational saccade latency with rostral SCi activity during the fixation period. Activity was again calculated over multiple epoch durations and start times relative to the start of the fixation period (see Methods section). Figure 6 illustrates the mean Pearson correlation coefficients calculated from each subpopulation of individual rostral SCi neurons during a wide range of epochs within the fixation period. The two modulated rostral SCi subpopulations exhibited the strongest and most consistent correlations between fixation period activity and fixational saccade latency.
Figure 5. Correlation (Kendall’s τ) heat maps from the populations that increased in response with higher FP luminance (A, B) or decreased their response between the lowest and highest FP luminance (C, D). Population fixational activity was correlated with FP luminance (A, C) and task difficulty (B, D), i.e., the proportion of error saccades by the FP luminance condition. Correlations were calculated across a range of epoch durations (ordinate axis) and start times (abscissa axis) during the fixation period. Horizontal black outlined arrows denote the 20-msec epoch duration over which correlation timing was calculated in E. (E) Mean correlations from A–D during 20-msec epoch durations only. Gray lines, data points, and arrows represent the subpopulation with a decreased response for increasing FP luminance. Black lines, data points, and arrows represent the subpopulation with increased response for increasing FP luminance. Triangles represent correlations with changes in FP luminance, whereas circles represent correlations with the proportion of fixation errors. Significantly correlated epochs are denoted by solid data points. Arrows denote epoch onset times when mean correlation values begin to significantly differ from the initial correlation value at alignment start.
compared with the unmodulated population (Figure 6, Table 1). For the subpopulation that increased their response with increasing FP luminance (Figure 6A), the correlation switched from positive to negative after a delay that was generally consistent with the VROL in the SC previously calculated (VROL: 42.5 cd/m² = 56.5 ± 0.7 msec; 3.5 cd/m² = 63.9 ± 0.8 msec; 0.04 cd/m² = 86.3 ± 1.0 msec; see Marino et al., 2012). To ensure that correlations were only calculated from epochs that occurred after the visual response arrived in the SC (because of retinal transduction and afferent delays), we utilized luminance specific cutoff times (Marino et al., 2012, Figure 6A–6C dotted vertical lines) calculated from VROLs to identical peripherally appearing visual stimuli (calculated previously). For the epochs occurring before the earliest visual response to the highest luminance stimuli (42.5 cd/m², < 55 msec), 87% of the epochs were positively correlated with fixational saccade latency across the subpopulation with a maximum mean correlation of $r = .31$. For all epochs occurring after the earliest visual response to the middle and highest luminance stimuli (3.5 cd/m², > 65 msec; 0.04 cd/m², > 85 msec), 90%–91% of the epochs were

![Figure 6. Heat map of mean correlation coefficients (Pearson's rho) calculated between the fixation activity in the rostral SC and the latency of the first fixational saccade during the fixation epoch for each subpopulation of neurons. All epochs occur before the mean onset of a visual response to a 42.5-cd/m² stimulus in the SCi. Correlations were calculated from fixation activity across a range of epoch durations (ordinate axis) and start times (abscissa axis) during the fixation period. This provides an estimate of the minimum lower bound for when the sensory response to a newly fixated stimulus reaches the SC. The boundary of the white triangular area in the upper right of each part denotes the median fixational saccade latency (collapsed across all FP luminance values) and demarcates the upper bound for calculating correlation epochs based on minimum necessary statistical power requirements. The vertical dashed lines denote the VROL times in the SC previously calculated (Marino et al., 2012) for stimuli matching each FP luminance condition. (A) Correlation heat map from the population that increased in response with higher FP luminance. (B) Correlation heat map from the population that decreased their response between the lowest and highest FP luminance. (C) Correlation heat map from all neurons unmodulated by FP luminance. (D) Mean correlations from A to C during 20-msec epoch durations only. Grayscale lines and circles represent each of the three subpopulations: increased response with higher FP luminance, decreased response with higher FP luminance, and unmodulated. Significantly correlated epochs are denoted by solid data points. Arrows denote epoch onset times when mean correlation values from each population begin to significantly differ from its initial correlation value at the start of the fixation period.](http://direct.mit.edu/jocn/article-pdf/35/2/180/2065828/jocn_a_01949.pdf)
negatively correlated across the subpopulation mean with a maximum correlation of \( r = -0.47 \) (Figure 6A, Table 1).

For the subpopulation of neurons that decreased their response between the lowest (0.04 cd/m\(^2\)) and highest (42.5 cd/m\(^2\)) FP luminance (Figure 6B), the correlation was consistently positive during the fixation period. For the epochs occurring between the earliest visual response to the highest luminance stimuli (42.5 cd/m\(^2\), \(< 55\) msec), 100% of the epochs were positively correlated across the subpopulation mean with a maximum correlation of \( r = -0.53 \) to 0.54 (Figure 6B, Table 1).

For the subpopulation of neurons that were unmodulated between the lowest (0.04 cd/m\(^2\)) and highest (42.5 cd/m\(^2\)) FP luminance (Figure 6C), the overall correlation between fixational saccade latency and fixation period activity was significantly reduced across all epoch ranges (Table 1). In addition, unlike the modulated subpopulations where individual neurons all correlated in the same direction, both positive and negative correlations were found within individual neurons of the unmodulated subpopulation (Table 1).

**Table 1.** Correlation Summary between Time of First Fixational Saccade and Mean Activity in the Rostral SC across Neuron Subclasses during the Fixation Period

<table>
<thead>
<tr>
<th>VROL Cutoff</th>
<th>Correlation Measures (within Cutoff Boundary)</th>
<th>Neuron Subpopulation (Modulation Resulting from Max Increase in FP Luminance)</th>
<th>Correlation Measures (within Cutoff Boundary)</th>
<th>Neuron Subpopulation (Modulation Resulting from Max Increase in FP Luminance)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Increased Response</td>
<td>Decreased Response</td>
<td>Not Modulated</td>
</tr>
<tr>
<td>Pre Min VROL (&lt;55 msec)</td>
<td>% Epochs correlated**</td>
<td>87</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Max single epoch correlation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Min single epoch correlation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Total correlated neurons (+ve)*</td>
<td>4/16</td>
<td>9/36</td>
<td>5/20</td>
</tr>
<tr>
<td>42.5 cd/m(^2) (55 msec)</td>
<td>% Epochs correlated**</td>
<td>91</td>
<td>100</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>Max single epoch correlation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Min single epoch correlation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Total correlated neurons (+ve)*</td>
<td>0/16</td>
<td>20/36</td>
<td>4/20</td>
</tr>
<tr>
<td>3.5 cd/m(^2) (65 msec)</td>
<td>% Epochs correlated**</td>
<td>90</td>
<td>100</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>Max single epoch correlation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Min single epoch correlation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Total correlated neurons (+ve)*</td>
<td>0/16</td>
<td>19/36</td>
<td>4/20</td>
</tr>
<tr>
<td>0.04 cd/m(^2) (85 msec)</td>
<td>% Epochs correlated**</td>
<td>90</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Max single epoch correlation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Min single epoch correlation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Total correlated neurons (+ve)*</td>
<td>0/16</td>
<td>19/36</td>
<td>4/20</td>
</tr>
</tbody>
</table>

* Significant Pearson correlation within a neuron, \(p < .05\).

** Significant mean Pearson correlation across a neuron population, rank sum test \(p < .05\).
DISCUSSION

Here, we have shown in monkeys that the luminance of a visual FP stimulus influences gaze stability as well as the timing and likelihood of producing both fixational and larger saccades. Thus, the intensity of the FP influenced the degree to which it acted as an anchor for steadying gaze and inhibiting saccades to other locations. When the FP was presented at the lowest luminance level (0.04 cd/m²), monkeys made the largest proportion of saccade errors (saccades > 2° away from the FP), indicating increased difficulty for maintaining fixation of the lowest FP luminance. In contrast, the lowest FP luminance also resulted in longer periods of stable fixation (before both fixational saccades and saccade errors) as well as fewer fixational saccades during the fixation period. This finding is broadly consistent with the understanding that fixational saccades act to correct eye position on a fixated target (Krauzlis et al., 2017; Hafed et al., 2015; Martinez-Conde, Macknik, & Hubel, 2004) and could also indicate a potential trade-off relationship between the duration of gaze stability during fixation and the proportion of fixation errors. The proportion of fixation errors (i.e., breaks in fixation that result in individual trial failure) provides a measure of task difficulty across conditions. In this case, decreased signal-to-noise ratio on the retina (resulting from lower luminance FP stimuli) leads to an increased neural effort for detecting, processing, and holding gaze on the FP.

Within the continuum of neural activity in the rostral SCi, we identified two subpopulations based on their modulation with FP luminance. Interestingly, both subpopulations exhibited activity that was consistent with both exogenous sensory-driven and endogenous task-related like elements. The first subpopulation (16 out of 72 neurons) increased activity with increasing FP luminance (exogenous sorted) and exhibited activity that: (1) temporally arrived with the visual response to FP foveation (exogenous-like), (2) inhibited saccade errors during fixation (endogenous-like), and (3) facilitated fixational saccades (endogenous-like). The activity of this subpopulation facilitated task performance because saccade errors were punished via aborted trials and fixational saccades were permitted during successfully performed trials.

The second subpopulation (36 out of 72 neurons) decreased their activity with increasing FP luminance (endogenous sorted) and exhibited activity that: (1) temporally arrived after initial FP appearance (i.e., task information) but before the visual response to FP foveation (endogenous-like), (2) facilitated saccade errors during fixation (endogenous-like), and (3) inhibited fixational saccades (endogenous-like). Activity in this subpopulation negatively impacted task performance as it facilitated saccade errors during fixation while inhibiting benign or potentially beneficial fixational saccades (see below).

The remaining neurons (20 out of 72 neurons) were not modulated by FP luminance and also not consistently correlated with fixation-error or fixational saccade latency. This suggested these neurons may lack a motor signal during fixation for either steadying gaze or generating future saccades.

Different Roles for Fixational versus Fixation Error Saccades

In primates, visual fixation relies on aligning the fovea (the high acuity region of the retina encompassing ~2° of the central visual field; Bringmann et al., 2018) on objects or locations of interest in the visual field for sufficient durations of time to adequately perceive and process the visual information at that location. Fixation error saccades act to interrupt visual fixation of a specific spatial location or target stimulus by moving the entire foveal region to a new location in the visual field. In contrast, fixational saccades generally do not interrupt visual fixation and can even act to facilitate visual processing of currently fixated regions of the visual environment (for a review see: Krauzlis et al., 2017; Martinez-Conde et al., 2004). For example, unlike fixation error saccades, many fixational saccades are small enough (< 2° of visual angle) that they do not move the fovea off the currently fixated location and can even correct for intersaccadic eye drift (Cornsweet, 1956). Fixational saccades also fulfill an important role in enhancing or refreshing visual processing during fixation because, without them, visual perception of the visual environment can otherwise fade as a result of adaptation mechanisms on the retina (Martinez-Conde, Macknik, Troncoso, & Dyar, 2006; Yarbus, 1967; Riggs, Ratcliff, Cornsweet, & Cornsweet, 1953; Ditchburn & Ginsborg, 1952). These adaptation mechanisms result in the visual system when steady or constant visual stimuli elicit successively weaker neural responses whereas abrupt or transient visual changes elicit stronger more robust responses (i.e., sustained and uniform stimulation of retinal receptors; Hubel & Wiesel, 1965; Kuffler, 1952). In this study, fixational saccades were not penalized and could have acted to assist in FP fixation (Figure 1A), whereas fixation error saccades were always detrimental and penalized as an unrewarded and aborted error trial.
Expanding the Role of the Rostral SCi for Visual Fixation and Saccade Generation

Different roles have been proposed for the sustained activity in the rostral SC during visual fixation. One theory (referred to here as endogenous fixation) proposes that the rostral SC aids fixation via the lateral inhibition of saccade-related activity in the caudal SC (Ikeda et al., 2015; Phongphanphanee, Kaneda, & Isa, 2008; Dorris, Olivier, & Munoz, 2007; Trappenberg, Dorris, Munoz, & Klein, 2001; Munoz & Istvan, 1998) and excitation of OPNs in the paramedian pontine reticular formation (PPRF; Munoz & Wurtz, 1992, 1993a). A second more recent theory (referred to here as exogeneous equilibrium) asserts that visual fixation is maintained via the equilibrium of activity between the right and left SCs. This theory proposes that the tonic activity in the rostral SC is solely reflective of the exogenous foveal location of the fixed stimulus that helps maintain fixation by keeping the equilibrium both balanced and centered between the left and right SCs thereby preventing peripheral saccades (Krauzlis et al., 2017; Goffart et al., 2012). This theory further hypothesizes that the tonic activity in the rostral SC during fixation has nothing to do with any endogenous motor commands for maintaining visual fixation.

The tonic activity in the rostral SCi that we observed here includes aspects that were consistent with both theories. For example, we observed evidence of exogenous sensory-driven signals related to the appearance or foveation of the FP stimulus, which is more consistent with the exogeneous equilibrium theory. However, we also observed evidence of endogenous task-related signals that either (1) inhibited saccade errors and facilitated fixational saccades, or (2) facilitated saccade errors and inhibited fixational saccades, which is more consistent with elements of the endogenous fixation theory.

This contrasts with a previous study that found that rostral SC activity during the gap period of the gap saccade task did not correlate with saccadic RT to a peripherally appearing saccade target (Dorris et al., 1997), despite the fact that fewer fixational saccades are observed during the gap period preceding target appearance (Watanabe, Matsuo, Zha, MacAskill, & Kobayashi, 2014). It is important to note several methodological differences that could account for the emergence of correlations between rostral SC activity and saccade latency that we observed in this study. First, we limited our analysis to small fixational saccades during the fixation period where the goal of the task was to maintain fixation on the FP for 500–800 msec. In contrast, Dorris et al. (1997) examined activity during the gap period where there was both no stimulus to fixate, and the monkey was preparing a larger saccade to a peripheral visual target appearing within a couple hundred milliseconds. Thus, task goals, fixation duration, saccade amplitude, and visual stimulus presence may likely modulate rostral SC activity during visual fixation.

Given that we observed rostral SC activity that was consistent with both sensory responses to foveated stimuli and endogenous fixation maintenance signals, and that these signals differentially correlated with fixational saccade latency, it is possible that these subpopulations may have different connectivity both within the SC and between the SC and PPRF. For example, the neurons coding an apparent fixation maintenance signal that delays fixational saccades could be more likely to project both a lateral inhibitory signal toward the caudal SC (Ikeda et al., 2015; Phongphanphanee et al., 2014; Trappenberg et al., 2001; Munoz & Istvan, 1998) and/or an excitatory connection to the OPNs in the PPRF to maintain stable fixation (Büttner-Ennever et al., 1999; Munoz & Wurtz, 1992, 1993b). Within the SC, such lateral inhibition could result from either local inhibitory mechanisms (Ikeda et al., 2015; Phongphanphanee et al., 2014; Meredith & Ramoa, 1998; Munoz & Istvan, 1998) or via interactions with global inhibitory signals from nigrotectal inputs (Hikosaka, Takikawa, & Kawagoe, 2000; Hikosaka & Wurtz, 1983a). In contrast, the neurons coding an apparent sensory response to the FP and facilitating earlier fixational saccades may only exert a more local excitatory influence (Phongphanphanee et al., 2014) on nearby surrounding regions of the SC map that code fixational saccade vectors within 2° of the FP. Such local-only influence is also consistent with observations that saccade-related activity in the caudal SCi can increase independently of fixation-related activity in the rostral SC when fixation is disrupted (Jagadisan & Gandhi, 2016).

Potential Sources for Endogenous Fixation Signals in the Rostral SCi

Exogeneous sensory-linked activity can reach the rostral SC via retino-tectal and retino-geniculo-cortical pathways (Krauzlis, Lovejoy, & Zénon, 2013; Boehnke & Munoz, 2008; Isa, 2002). Endogenous-fixation linked activity in the rostral SCi could be influenced by signals from several potential upstream oculomotor brain regions. One potential signal could relay broad inhibition to the caudal SCi. This could facilitate rostral SCi activity by suppressing competing activity elsewhere in the topographic SCi map (Rodgers, Levy, Marino, & Munoz, 2004; Robinson, 1972) because of extrafoveal visual stimuli or potential saccade locations (Dorris et al., 2007; McPeek & Keller, 2002; Trappenberg et al., 2001; Munoz & Istvan, 1998). Such a broad inhibition signal to the caudal SCi could originate from the substantia nigra pars reticulata (an oculomotor-linked output structure of the basal ganglia), which has been shown to project broad GABAergic inhibitory inputs to the SCi (Hikosaka, 2007; Hikosaka & Wurtz, 1983b). Previously identified neurons in the substantia nigra pars reticulata that are active during visual fixation and pause during saccades could relay this inhibition (Handel & Glimcher, 1999; Hikosaka & Wurtz, 1983a).
Endogenous rostral SCi fixation signals could also be relayed to the SCi from oculomotor cortical areas. One candidate region is the FEFs in frontal cortex. The FEF contains neurons with visual-sensory and saccadic-motor related activities (Hanes & Wurtz, 2001; Schall, 1997), as well as sustained activity during visual fixation (Suzuki & Azuma, 1977; Bizzi, 1968) that are similar to activity patterns in the SCi. Stimulation of the FEF regions with the highest concentrations of fixation-linked neurons has been shown to suppress both saccadic and smooth pursuit eye movements (Izawa, Suzuki, & Shinoda, 2004, 2011). Furthermore, these same fixation-linked FEF neurons also increase their activity in response to canceling planned saccades (Hanes, Patterson, & Schall, 1998), which indicates the presence of a top-down controlled endogenous fixation signal. In addition to the FEF, other oculomotor cortical areas project to the SCi and similarly exhibit elevated activity during fixation including posterior parietal association cortex (Sakata, Shibutani, & Kawano, 1980), dorsomedial frontal cortex (Bon & Lucchetti, 1992), and supplementary eye fields (Amador, Schlag-Rey, & Schlag, 2004). Further research is needed to identify other oculomotor areas potentially involved in generating or relaying endogenous fixation signals and their interactions with the rostral SCi.

From the Endogenous Fixation Theory to the Exogenous Equilibrium Theory

The exogenous equilibrium theory addresses several unresolved questions with the endogenous fixation theory that involve the role of the OPNs in the nucleus raphe interpositus of the PPRF and its relationship with the rostral SCi. Located one synapse away from the motor output, OPNs have been theorized to be involved in gaze stability during visual fixation because they (1) discharge tonically during visual fixation and pause for all saccades in a pattern similar to rostral SCi neurons, and (2) directly inhibit saccade-related premotor burst neurons in the mesencephalic and pontomedullary reticular formations, which drive the motor neurons innervating extraocular muscles (Scudder et al., 2002; Moschovakis, Scudder, & Highstein, 1996; Ohgaki, Markham, Schneider, & Curthoys, 1989; Strassman, Evinger, McCrea, Baker, & Highstein, 1987; Evinger, Kaneko, & Fuchs, 1982; Luschei & Fuchs, 1972). However, the role of OPNs in fixation has been questioned because local OPN inactivation via ibotenic acid injections into the nucleus raphe interpositus does not lead to problems maintaining fixation on a stationary stimulus (Kaneko, 1996). For this reason, it has been suggested that the inhibitory effect of OPNs on the motor neurons may only be related to synchronizing and coordinating the vertical and horizontal components of saccades (Krauzlis et al., 2017). OPNs receive monosynaptic excitatory input from the SCi (Büttner-Ennever et al., 1999; Everling, Paré, Dorris, & Munoz, 1998; Gandhi & Keller, 1997; Paré & Guitton, 1994). Although OPN input is most dense from the rostral SCi, OPNs also receive more caudal projections up to and including 10°–15° saccade eccentricities (Büttner-Ennever et al., 1999; Gandhi & Keller, 1997) on the SC motor map (Robinson, 1972). Thus, it is unclear how OPNs integrate peripheral saccade activity from the caudal SCi when this input is theorized to be primarily related to visual fixation signals from the rostral SCi.

Our results partially contradict the exogenous equilibrium hypothesis because we observed rostral SCi neurons that are consistent with a motor command to maintain fixation and or delay the generation of a fixational saccade. However, it should be noted that half of the neurons recorded (36 of 72 neurons) were unmodulated during the fixation period and could be reflective of the equilibrium maintaining rostral SCi activity proposed by the equilibrium hypothesis. Furthermore, the exogenous and endogenous signals observed here could still be reconciled with the general idea of the equilibrium hypothesis in that they could still facilitate equilibrium between the left and right SCs in two ways: (1) Constant activity could be maintained in the rostral SC if the decreases in endogenous fixation-maintenance activity that occurred for higher luminance FP stimuli were balanced by the reciprocal increases in sensory-related responses by exogenous neurons, and (2) inhibitory lateral interactions could also facilitate and maintain equilibrium between the left and right SCs. Such reconciliation of theories is further consistent with the results from a saccade study by Everling and colleagues (Everling, Dorris, Klein, & Munoz, 1999) who showed that rostral SCi neurons exhibited increased fixation-related activity during anti-saccade trials (i.e., directing a saccade away from a peripherally appearing stimulus) relative to pro-saccade trials (i.e., directing a saccade toward a peripherally appearing stimulus). This increased rostral SCi activity before an anti-saccade is consistent with the increased saccade suppression demand necessary to prevent the generation of a saccade to the peripheral stimulus when it appeared (Munoz & Everling, 2004). Such saccade suppression (which would be consistent with the endogenous population observed here) could be achieved both by increased activity in the rostral SCi to facilitate equilibrium and also by increased input to the OPNs.

Conclusions

These results indicate that activity in the rostral SC during fixation plays a role in endogenous fixation maintenance beyond the inhibition of saccade-triggering activity in caudal colliculus (via either direct inhibition or equilibrium maintenance mechanisms). Furthermore, these results indicate a more direct role for different populations of neurons in the rostral SC for the control of gaze stability, because changes in tonic activity during FP fixation correlate with either inhibiting or facilitating the production of fixational and error saccades.
Acknowledgments

We thank Ann Lablans, Mike Lewis, and Sean Hickman for outstanding technical assistance. We also thank members of the Munoz and Levy laboratories for their comments on earlier versions of the manuscript. This work was funded by a research grant from the Canadian Institutes of Health Research (MOP-FDN-148418). D.P.M. was supported by the Canada Research Chair Program.

Reprint requests should be sent to Robert A. Marino, Centre for Neuroscience Studies, Queen’s University, Bottleer Hall, 18 Stuart Street, Kingston, ON, Canada K7L 3 N6, or via e-mail: marinor@queensu.ca.

Data Availability Statement

Shared via e-mail to lead author.

Funding Information

Canadian Institutes of Health Research (https://dx.doi.org /10.13039/501100000024), grant number: MOP-FDN-148418. Douglas P. Munoz, Canada Research Chair Program.

Diversity in Citation Practices

Retrospective analysis of the citations in every article published in this journal from 2010 to 2021 reveals a persistent pattern of gender imbalance: Although the proportions of authorship teams (categorized by estimated gender identification of first author/last author) publishing in the Journal of Cognitive Neuroscience (JoCN) during this period were M(an)/M = .407, W(oman)/M = .32, M/W = .115, and W/W = .159, the comparable proportions for the articles that these authorship teams cited were M/M = .549, W/M = .257, M/W = .109, and W/W = .085 (Postle and Fulvio, JoCN, 34:1, pp. 1–3). Consequently, JoCN encourages all authors to consider gender balance explicitly when selecting which articles to cite and gives them the opportunity to report their article’s gender citation balance.

REFERENCES