Abstract In previous studies of saccadic eye movement reaction time, the manipulation of initial eye position revealed a behavioral bias that facilitates the initiation of movements towards the central orbital position. An interesting hypothesis for this re-centering bias suggests that it reflects a visuo-motor optimizing strategy, rather than peripheral muscular constraints. Given that the range of positions that the eyes can take in the orbits delimits the extent of visual exploration by head-fixed subjects, keeping the eyes centered in the orbits may indeed permit flexible orienting responses to engaging stimuli. To investigate the influence of initial eye position on central processes such as saccade selection and initiation, we examined the activity of saccade-related neurons in the primate superior colliculus (SC). Using a simple reaction time paradigm wherein an initially fixated visual stimulus varying in position was extinguished 200 ms before the presentation of a saccadic target, we studied the relationship between initial eye position and neuronal activation in advance of saccade initiation. We found that the magnitude of the early activity of SC neurons, especially during the immediate pre-target period that followed the fixation stimulus disappearance, was correlated with changes in initial eye position. For the great majority of neurons, the pre-target activity increased with changes in initial eye position in the direction opposite to their movement fields, and it was also strongly correlated with the concomitant reduction in reaction time of centripetal saccades directed within their movement fields. Taking into account the correlation with saccadic reaction time, the relationship between neuronal activity and initial eye position remained significant. These results suggest that eye-position-dependent changes in the excitability of SC neurons could represent the neural substrate underlying a re-centering bias in saccade regulation. More generally, the low frequency SC pre-target activity could use eccentric eye position signals to regulate both when and which saccades are produced by promoting the emergence of a high frequency burst of activity that can act as a saccadic command. However, only saccades initiated within ~200 ms of target presentation were associated with SC pre-target activity. This eye-dependent pre-target activation mechanism therefore appears to be restricted to the initiation of saccades with relatively short reaction times, which specifically require the integrity of the SC.

Keywords Saccadic eye movement · Saccade initiation · Saccade selection · Reaction time · Express saccade · Superior colliculus · Motor preparation · Fixation · Eye position · Monkey

Introduction

Behavioral studies in head-restrained subjects (humans: Fuller 1996; Zambarbieri et al. 1995; monkeys: Albano and Wurtz 1982; Paré and Munoz 1996a) have shown that the initiation of saccadic eye movements is systematically modified by the starting position of the eyes in the orbits: movements made from eccentric initial eye positions and towards central positions have a shorter reaction time (RT) than those made to further eccentric positions. The implication of this re-centering bias for eye–head coordination was examined by Fuller (1996), who suggested that it helps to alter the relative timing of the initiation of eye and head movements, given the existing “orbital reserve”, i.e. the extent of eye movement possible either by counter-rotation at the beginning of a head movement, or by per-rotation at the end of the gaze shift. With the visual field extending beyond the range that can be explored with saccades, this strategy can also help to minimize excursions away from the central position, preventing the eyes from reaching their boundaries even when the head is restrained. Unless this re-centering bias is caused by a peripheral muscular phenomenon,
the neural mechanisms implicated in both the selection and the initiation of saccades may therefore be influenced by eye position. In this paper, we investigate this hypothesis by recording from saccade-related neurons in the intermediate layers of the primate superior colliculus (SC), a structure critical for both the initiation and the execution of saccades.

The intermediate layers of the SC contain an ensemble of neurons that display a saccade-related pattern of activity: a burst of action potentials time-locked to saccades of specific metrics that define a neuron’s movement field (Sparks et al. 1976; Wurtz and Goldberg 1971). Saccade-related neurons are topographically organized and, within this neural map, the metrics of saccades are encoded in relative coordinates, i.e. neurons discharge for a particular range of saccade vectors irrespective of initial eye position (Schiller and Koerner 1971; Wurtz and Goldberg 1972). A recent study by van Opstal and colleagues (1995), however, showed that eye position does influence the magnitude of the saccade-related burst of activity of several SC neurons, thereby revealing their access to eye position signals. The same neurons can additionally display low frequency activity well in advance of saccade onset (Glimcher and Sparks 1992; Mohler and Wurtz 1976; Munoz and Wurtz 1995; Sparks 1978), and it was recently demonstrated that the level of this early activation could predict RT (Dorris et al. 1997). The hypothesis that the SC plays a role in saccade initiation was further supported by results obtained in microstimulation (Paré et al. 1994; Robinson 1972; Stanford et al. 1996) and pharmacological experiments (Aizawa and Wurtz 1998; Hikosaka and Wurtz 1985, 1986; Quaia et al. 1998; Schiller et al. 1987; Sparks et al. 1990). The question arises as to whether eye position can exert its effect on RT through the early activation of SC neurons?

We studied the activity of SC neurons using a simple reaction time paradigm wherein the initially fixated visual stimulus varied in position. The extinction of this fixation stimulus 200 ms before the presentation of the saccadic target provided a warning signal sufficient for the expression of ‘pre-target’ activity in these neurons. We examined the relation linking this neuronal activation to both initial eye position and RT to determine whether it is influenced by eye position and whether this influence is consistent with the known relationship between RT and eye position. We found that the SC pre-target activation could indeed contribute to the facilitation of movements towards the orbital center, consistent with the hypothesis that the central processes regulating the selection and the initiation of saccades use eye position signals.

Some results have been reported in abstract form (Paré and Munoz 1996b).

### Materials and methods

Animal preparation and experimental procedures

Three male rhesus monkeys (*Macaca mulatta*, 5–10 kg) were prepared for behavioral training along with eye position and extracellular single-neuron recording in a single surgical procedure carried out under general anesthesia and aseptic conditions as described previously (Dorris et al. 1997; Munoz and Istvan 1998; Paré and Munoz 1996a). Animals received both antibiotics and analgesic medications during the post-surgery recovery period that lasted about 2 weeks. Animal health status was monitored closely and under supervision of the university veterinarian. All animal care and experimental procedures were approved by Queen’s University Animal Care Committee and were in accordance with the Canadian Council on Animal Care policy on use of laboratory animals.

Two stereotaxic craniotomies were made to access both SC with microelectrodes. Stainless steel recording cylinders were positioned over each craniotomy: one centered on the midline and tilted 35° posterior of vertical and the other centered on the interaural axis and tilted 25° lateral. A PC-compatible computer running a UNIX-based real-time data acquisition system (REX) (Hays et al. 1982) controlled behavioral paradigms, visual displays, and reward delivery. Eye movements were monitored by the magnetic search coil technique using phase angle detection (Collewijn 1977), which permitted the absolute calibration of the horizontal eye position signals. Neuronal recordings were made with tungsten microelectrodes that were inserted into the brain via guide tubes positioned in the cylinders with the aid of a grid system (Crist et al. 1988). Action potentials of single neurons that met distinct amplitude and time constraints were isolated with the use of a window discriminator. The resulting output pulses were digitized at 1 kHz, whereas horizontal and vertical eye position signals were digitized at 500 Hz.

During the experiments, the monkeys were seated in a primate chair with the head restrained and facing an opaque tangent screen positioned 86 cm away. Each behavioral task was initiated by the appearance on the screen of a light spot, referred to as the fixation point, followed after a fixation period by a second light spot serving as a saccade target. The light spots (light-emitting diodes, 2.0 cd/m²) were back-projected onto the tangent screen and their positions controlled by an x–y mirror galvanometer positioned 86 cm from the screen. This arrangement ensured that any angular deviations in the light source equaled the angular deviations in the cyclopean view of the monkey, and therefore fully corrected for any tangent errors. Except for the light spots, the room was kept dark during the experimental trials. To prevent dark-adaptation, the screen was illuminated with diffuse white light during the inter-trial intervals.

#### Behavioral paradigms

The activity of SC neurons was studied while the animal performed a warned, simple RT paradigm commonly known as the gap saccade task (Fig. 1A) (Saslow 1967). Once the fixation point appeared at the center of the screen, the monkey had to look at it and maintain visual fixation for 500–800 ms. The fixation point was then extinguished, and the monkey had to maintain steady non-visual fixation during a 200-ms gap interval before the saccade target appeared. The gap period was kept constant, allowing it to act as a warning interval. The monkey was required to make a saccade to the target within 500 ms of its presentation, and then maintain fixation for 300–500 ms before a liquid reward was given.

We ascended the general properties of the neuronal discharge with respect to saccades within a few trials and then varied systematically (in steps of 1°) the position of the saccade target to determine the movement field of saccade-related neurons (Wurtz and Goldberg 1971; Sparks et al. 1976; Munoz and Wurtz 1995). This was accomplished by graphically displaying online rasters and histograms of the spike occurrences aligned on the onset of the saccades made to each target position. After the center of the movement field (the saccade vector for which neuronal discharge was optimally) was well defined, we introduced the orbital gap saccade task (Fig. 1B). In this task, the initial position of eye fixation was varied randomly between three different positions, each spatially separated by ~15° and distributed along the same axis as the saccade targets: central (straight-ahead), contralateral or ipsilateral.