Evidence of a timing mechanism for predictive smooth pursuit in frontal cortex

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Introduction

Predictive smooth-pursuit eye movements rely on both short-term and long-term mechanisms. Short-term mechanisms compute derivatives of target position or use some similar scheme to determine a target's future path (Deno *et al.*, 1990). Long-term mechanisms could drive the eyes based on a memory of the previous path of a target, or by coding the temporal characteristics of the trajectory, much as an "internal clock" would, as Robinson (1968) has speculated. So far, a neurophysiological substrate for predictive eye movement generation has been lacking. This report describes a neuronal candidate for a long-term predictive mechanism. The data presented here were recorded from neurons in the dorsomedial frontal cortex (DMFC), an area previously implicated in saccade generation. Neurons here code for saccade metrics (Schlag & Schlag-Rey, 1987), as well as higher-order aspects of saccade generation such as motor "set" (Schall, 1991). General functions of the DMFC are extremely interesting, as they are related more to planning than to executing movements, leading some to refer to it as a "supramotor region." Cerebral blood flow increases have been seen here during mental rehearsal of complex sequences of motor movements (Roland *et al.*, 1980), sequences of learned saccades, or alternating self-paced saccades (Petit *et al.*, 1993). Preparatory or motor set activity of DMFC neurons also occurs during arm movement tasks (Matsuzaka *et al.*, 1992). The neurons recorded in the current study seem to be coding the timing of intervals during smooth-tracking trials, and this activity could be used in predictive smooth-pursuit generation.

Methods

Two *Macaca fascicularis* monkeys were used. Animals were trained to smoothly track a small (.25 deg) spot of light that ramped out from the center of the screen at a constant velocity. Neurons were recorded during this task, or during pursuit of periodic target motion (standard frequencies 0.3-0.5 Hz). Eye position was recorded with the search coil (Fuchs & Robinson, 1966). Single neurons (n=158) were recorded with tungsten microelectrodes lowered into the DMFC using stereotaxic coordinates. The spike density function was used to determine the time of peak discharge of a neuron.

Results

Most neurons recorded in the DMFC (60 %) responded during smooth pursuit of the small spot, and most of those (92%) also responded when the spot was moved while the monkey fixated. Some of this activity probably reflects input from neurons in the middle superior temporal sulcus (MST), where cells also respond during pursuit and visual motion (Komatsu & Wurtz, 1988; Newsome *et al.*, 1988). However, many DMFC cells had a novel component to their response. During periodic tracking, these cells responded for usually one, but sometimes both, directions of target motion with a ramp-like profile (Fig. 1).

The response usually peaked before the target reversed direction (mean lead = 151 msec). The timing and waveform of the response raised the possibility that these cells were involved in generating predictive eye movements and not just coding simple metrics or dynamics of smooth pursuit (*e.g.*, position and velocity). Figure 1 shows the responses of a DMFC neuron and the eye while the monkey tracked 0.3 Hz sinusoidal or triangle-like motion.

In neither case can the cell's response be described strictly in terms of eye position or velocity, since the response is so nonlinear. Rather, the predominant characteristic is a buildup of activity as the target moves from left to right. Of 35 cells tested, 17 showed such behavior. Tuning was evident in 6/7 units that were isolated long enough to assess directionality in more detail, and neuronal firing for the preferred direction averaged 97% over that for the opposite direction.

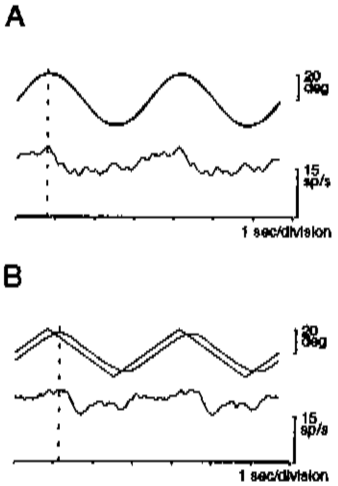

Figure 1. Cycle averages of a neuron recorded in the DMFC during two trials of periodic tracking. In both cases, the top trace shows eye and target position superimposed vertically and the bottom trace represents neuronal activity as a spike density function (σ = 50 ms). Two identical cycles are shown. A) Target motion is sinusoidal (0.3Hz). Note ramp-like activity that rises to a peak (dotted line) 70 ms before target direction reverses (and before the eye reverses). Short-term mechanisms can aid prediction in this situation. B) Target motion is triangle-like (0.3Hz). The cell seems to be incorrectly signaling target reversal here, and the animal's prediction is poorer as well. The peak however still leads eye reversal. Only long-term mechanisms can be used to predict in this case.

Some neurons (n=20) had a similar activity profile during ramp tracking, as their activity peaked just before the end of the ramp motion. When the trajectory length was changed in a new block of trials, the peak shifted gradually over trials to a new position near the end of that trajectory, indicating that the response profile of the neuron could be modified.

The type of responses seen in both of these tracking conditions could provide information about how far the target had moved in a given direction, or alternatively, about the amount of time that the target had been moving. Data from another class of DMFC neurons suggest that cells here are in fact involved in the latter, *i.e.*, timing the stimulus trajectory. These cells build up activity during the fixation interval preceding pursuit trials. Here, eye position is maintained around the stationary target, and the cell still shows the ramp-like discharge pattern. Such a signal could be used to anticipate upcoming target motion.

Conclusions

DMFC neurons that respond during smooth pursuit do not simply encode oculomotor metrics or dynamics. Rather, they seem to be involved in timing "periodic" intervals of target motion. These cells could function as elements in a dynamic network that integrates the output of a clock until a threshold is reached. This threshold would shift closer to the time of an abrupt target trajectory change by sampling the time that the retinal-slip error signal conveyed from the visual system was maximal during the previous cycle/trial of tracking. In this scheme, the activity profile of the cell evolves systematically so that the peak approximates the time of abrupt target trajectory changes. The oculomotor system could use such a signal to predict trajectory changes.

The anatomy supports this hypothesis in that the DMFC both receives visual motion projections from MST (Huerta & Kaas, 1990), and sends appropriate connections back to the oculomotor system. The predictive signal could be coupled with eye velocity and acceleration signals present in the nucleus reticularis/pontine nuclei complex (Suzuki *et al.*, 1991) that directly drive the eyes, since the DMFC projects to this brainstem area (Huerta & Kaas, 1990). Alternatively, this signal could go to the frontal eye fields (FEF), since the FEF is reciprocally connected to the DMFC (Huerta & Kaas, 1990), contains eye velocity cells (MacAvoy *et al.*, 1991) and projects to the nucleus reticularis/pontine nuclei complex (Stanton *et al.*, 1988).

Previous work has implicated the DMFC in cognitive events. Motor set or preparatory activity has been documented for both saccade (Schall, 1991) and arm movement (Matsuzaka *et al.*, 1992) tasks. One study found cells with a similar buildup of activity before arm movements (Matsuzaka *et al.*, 1992) as seen before target motion change in the present study. Again, this could be an internal timing mechanism controlling predictable movement initiation.

One of the most interesting characteristics of neurons in the DMFC is a ramp-like temporal profile of activity during periodic or ramp-tracking trials. This activity can be dissociated from the dynamics of the eye movement, and could be used to initiate or fine-tune predictive oculomotor behavior.

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Differential processing of eye movement induced retinal image slip in monkey visual cortex

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In afoveate vertebrates, stability of the visual world during voluntary movements is preserved by synergistic vestibular and optokinetic reflexes which attempt to stabilize the retina in space. The evolution of a fovea in primates, however, introduced an additional requirement since slow, pursuit eye movements override reflex attempts to stabilize eye position. Goal-directed eye and head movements such as smooth-pursuit force the visual system to receive and somehow discriminate those visual motion signals which are caused entirely by the voluntary movement. Yet adequate spatial orientation is obviously maintained during pursuit, and incidental retinal image motion is not consciously perceived (otherwise the visual world would appear to move during pursuit). To address the question of where and how in the visual system this is achieved, the responses of cells in 4 visuo- cortical areas (V1, V4, MT, and MST) of trained rhesus monkeys were compared when comparable retinal image motion was caused by object motion as opposed to ego motion.

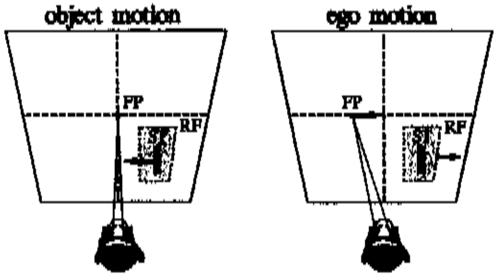

Fig. 1

Experimental Paradigm, **Object motion**: Retinal image slip results from the movement of a behaviorally irrelevant visual stimulus (ST) while the eyes maintain fixation of a stationary laser target (FP). RF=receptive field. **Ego motion**: the same retinal slip of the image of ST is a consequence of a smooth pursuit eye movement, guided by the laser target (FP), while ST is stationary on the screen in front of the monkey. In other words, in the ego motion stituation, the eyes move the receptive field (RF) across the stationary visual stimulus (ST).

Methods

Standard extracellular recording techniques were used to examine the responses of 400 cells recorded from cortical areas V1, V4, MT and MST of four awake rhesus monkeys. General methods for surgery, anesthesia, stimulus presentation and single unit extracellular recordings have been described previously (Thier and Erickson, 1992). The scleral search coil technique (Robinson, 1963) was used to monitor eye movements. While the monkey maintained fixation of a stationary target (diameter: 0.2°), the receptive field of an isolated cell was mapped and its preferences for the size, orientation and structure of the pattern, and the direction and speed of movement were established. Cells responding to retinal image motion of comparatively small velocity (i.e. $<25^{\circ}$/sec) were subjected to a quantitative comparison of the responses to object and self-induced retinal image slip. As depicted in figure 1, object-induced retinal image slip was realized by moving a suitable behaviorally irrelevant visual