Involvement of Neurons in Frontal Cortex in Learning Predictable Object Motion

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Abstract

The dorsomedial frontal cortex (DMFC) is a brain region known to be involved in planning for and executing movement. Our work targets the role that single brain cells play in planning and executing eye movements that are made to objects that are moving (smooth pursuit eye movements). Moving objects can take trajectories that are relatively random, such as the flight path of a fly, as well as highly predictable trajectories, such as the one that a ball would take if it were thrown. We study how brain cells adjust to or "learn" new trajectories in a predictable situation. The theory behind the activity of these neurons is that they function to keep track of elapsed time when the distance that the object will move is known. The timing signal conveyed by the neurons is then used by the system that controls the dynamics of the eye movement to more accurately follow an object in the face of processing delays inherent in any biological system.

1. Introduction

An important problem in the field of neuroscience concerns how the brain encodes the movement of an object in the world and then computes the appropriate response necessary to either avoid or acquire that object. This problem becomes even more difficult when one realizes that there is an inherent processing delay of approximately 200 msec between when sensory information enters the brain to the time that a movement can be made. If the path that a moving object takes is random, theoretically it would be impossible to acquire (and possibly avoid) that object, given the substantial processing delay. To circumvent this problem, biological systems utilize strategies that take advantage of recurrent patterns of object motion and compute movement based upon predictions about where the object will be located and how fast it will be moving at a future time.

Eye movements are a type of behavior which neuroscientists have studied in an attempt to address these questions. Why use eye movements for this type of research? The simplest reason is that an eye can only move with three degrees of freedom: horizontal and vertical rotation, and torsion. Furthermore, in most situations where the concern is to know where the eye is looking, it is safe to ignore torsion. Related to this, the measurement techniques for resolving eye movements are extremely accurate, for example, the magnetic-field search-coil method [1] allows discrimination of rotational angles which differ by as little as 2 minutes of arc (Figure 1). Therefore, quantifying the angle that a person is looking is relatively straightforward and accurate. Furthermore, the fact that other movement

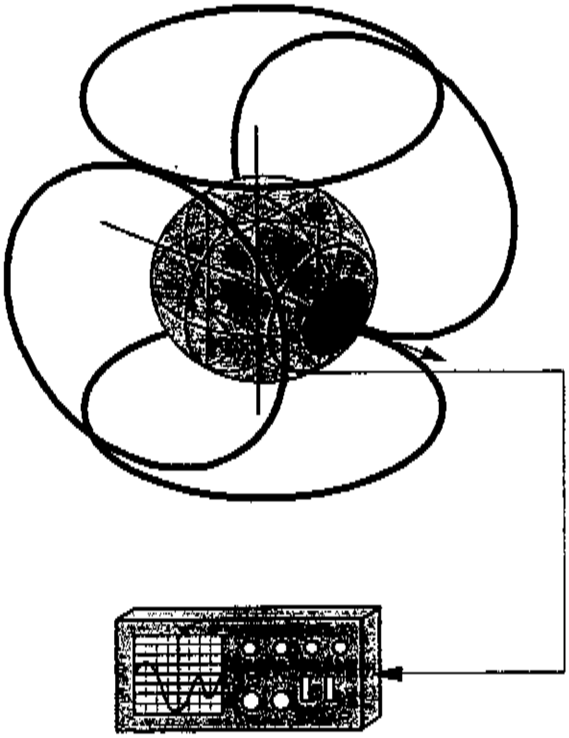

Figure 1. Measuring eye movements. The head is centered in a pair of orthogonal magnetic fields (only the eye is shown for simplicity). A coil of wire is wound around the front of the eye (darker circle) for the monkey, and worn on a contact lense in the human. Alternating the fields produces a small current in the coil proportional to the angle that the eye is rotated. The two fields yield separate horizontal and vertical eye rotation signals. These signals can then displayed on the oscilloscope and stored on disk for further analysis.

systems are governed by similar principles of neural control and are subserved by overlapping anatomical pathways as the eye movement system gives the results obtained from eye movement research a degree of generality. Finally, there are simple yet elegant control system models of eye movement systems that in many cases provide an accurate description of the neural circuitry involved in eye movement generation [*e.g.*, 2;3].

The smooth pursuit eye movement system is specialized for voluntary tracking of objects that are moving, in comparison with saccades, which are generated to inspect features of a stationary environment. This system is thought to be driven by the velocity of motion on the retina, and has been modeled as a feedback system which attempts to minimize the amount of motion on the retina and thereby keep the image stabilized. The smooth pursuit system is unique among movement systems in that a moving visual stimulus must usually be present for an eye movement to occur, *i.e.*, smooth pursuit cannot be made voluntarily without the appropriate stimulus. However, there are exceptions to this rule. One of the most notable ones, and the one which we will discuss here concerns the case when the motion of an object becomes predictable. This situation usually comes about if the object moves in a repetitive fashion, for example back and forth across the scene. When this happens, the eyes start to move or reverse directions before the object, in anticipation of its motion [*e.g.*, 4;5]. These eye movements are thought to be generated from memory of previous velocity of the object, and the timing of the repetitive motion [6]. Together, this information can be used to calculate the trajectory of an

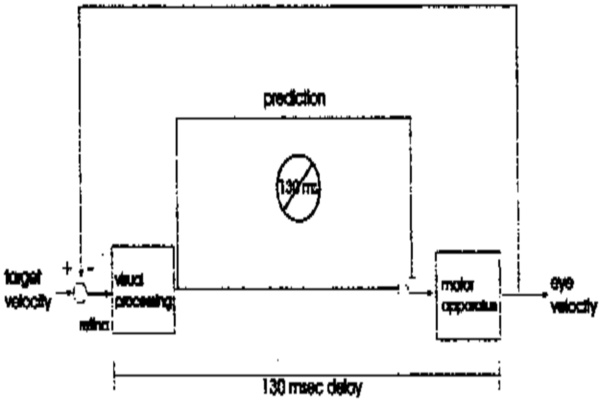

Figure 2. A model of the predictive circuit. When target motion is unpredictable, the velocity of the target on the retina is first processed by the visual system, and then sent to the motor apparatus to move the eyes. The system uses the outer negative feedback loop to minimize the error between eye velocity and target velocity. This process is subject to a propagation delay of ~130 msec. When target motion becomes predictable, an internal circuit is used that overcomes the propagation delay.

object, and hence place the eyes on that object at an earlier time than would be permitted given the anatomical delays imposed by neural circuitry (Figure 2). Our studies explore how neurons in a region of premotor cortex known as the dorsomedial frontal cortex (DMFC) are involved in encoding the timing of repetitive object motion for the purpose of generating anticipatory eye movements.

2. Methods

We study the electrical activity of single-neurons recorded from the DMFC of monkeys using insulated tungsten microelectrodes that are lowered on a daily basis into the brain through a small stainless steel chamber which is surgically implanted before the experiments. The monkeys are trained with behavioral techniques to perform smooth pursuit eye movements to follow a spot of light (.25 degree visual angle) that is generated by an oscilloscope and rear-projected on a tangent screen. The target spot in our experiments initially comes on in the center of the screen allowing the monkey to direct his gaze towards it. The monkey then fixates this spot for a period before it starts to move. The duration of this fixation period can be manipulated to change the predictability of when the spot will move. When the spot moves, it maintains a constant velocity until it stops. The total time that the target moves can also be manipulated to change the predictability of when the target will stop.

The eye movements are recorded using the magnetic-field search-coil method [1]. In this method, the rotational angle of the eye is obtained by inducing current with a alternating magnetic fields into a coil of wire wound around the monkey's eye (Figure 1). Two orthogonal fields are generated, one horizontal and the other vertical. The two fields are alternated with different phase which allows extraction of separate horizontal and vertical eye movement components. The coil of wire is surgically implanted between the conjunctiva and sclera of the eye before experiments begin.

3. Results

The typical response of a neuron during these tasks when the fixation and/or motion period is predictable is initially low activity that builds during the period up to a peak that occurs when the period ends. This activity has been shown to

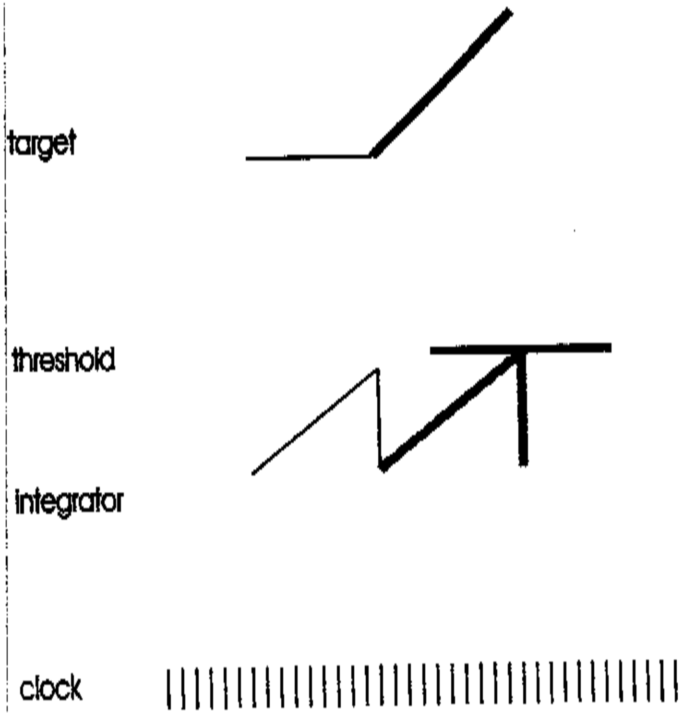

Figure 3. How neurons in the DMFC are hypothesized to keep track of elapsed time. Top: the position of the target over time. The thin line represents fixation when the target is stationary. The thick line represents when the target moved, here the motion is to the right. Middle: Schematic of the cell response. In this theory, activity of the cell increases to a peak which drops either around the time the target moves, or around the time that it stops. The thin line corresponds to activity during the fixation period, the thick line activity during the motion. Usually different cells encode the time of different periods. Bottom: Schematic of the clock that feeds the integrator.

be greater when target events are predictable than when they are not [7]. We hypothesize that the activity is part of a timing mechanism that can encode the elapsed time of the target event. The mechanism is hypothesized to work by integrating the output of a clock until a threshold is reached (Figure 3). When the activity level of the neuron reaches the threshold, the activity resets to zero. In this theory, it is the process of resetting that sends a signal to the smooth pursuit system to move (or stop) the eyes.

Since these neurons appear to encode temporal characteristics of repetitive motion, it might be interesting to ask how the activity of the cells develops over successive trials of exposure to the same motion. Figure 4 shows the activity of a neuron after the duration of the fixation period has been changed from a random time to a fixed time. In the previous block of trials, the fixation period had been randomly assigned on each trial. In the block of trials shown, the fixation period was set to a constant value of 500 msec. Note that on the first trial the activity of the neuron is low and the temporal pattern of the activity is diffuse. In subsequent trials the amplitude of the activity increases, and a discrete peak in the temporal pattern becomes evident. As the block of trials progresses, this peak shifts to a position in time that is near the point where the target begins to move.

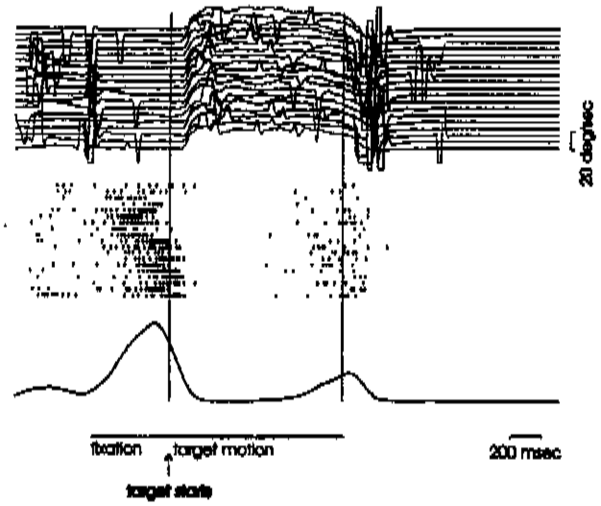

Figure 4. The pattern of activity of a neuron in the DMFC adjusts to align with the start of target motion. In the previous block of trials the fixation period was random, and therefore the start of target motion could not be known. In this block of trials, the fixation period was set to 500 msec and was therefore predictable. Top: eye velocity traces from sequential trials. Middle: activity of the neuron during sequential trials. Each small vertical dash represents a single action potential from the neuron. Each horizontal strip dashes corresponds to one trial. Trial 1 at top. Bottom: Average neural activity over the block of trials. Note that initially activity is weak and diffuse. Over trials, a robust and discrete peak evolves in the pattern of activity to eventually coincide with when the target moves.

To better assess the ability of these neurons to readjust their firing rate, we systematically tested a sample of neurons in a paradigm designed for more straightforward quantification of the results. Neuronal activity during both the fixation period and the period of ongoing motion was studied. In this paradigm, the animal tracked in a block of trials where the duration of the fixation period (or the period of target motion) was set at a constant value. The neuron was monitored while the animal tracked for at least 20 trials in this condition. In the next block of trials the duration of the fixation period (or the period of target motion) was suddenly changed to a new value where it remained for a block of at least another 20 trials. The activity of the neuron was again monitored over the block. The mean time of peak activity was analyzed for the last 5 trials in the new block and compared to that occurring in the first 5 trials of that block. For shifts of *fixation* period duration that ranged from 250- 500 msec, peak activity was found to shift by as much as 373 msec over the new block of trials. For shifts of *motion* period duration that ranged from 100-400 msec, peak activity was found to shift by as much as 253 msec over the new block of trials.

4. Discussion

We found that neurons in the DMFC respond during smooth pursuit with a peak of activity that occurs around the time of predictable motion onset or predictable motion offset. This activity has a profile consistent with the idea that these neurons are in a network of cells which integrate the output of a clock thereby encoding elapsed time during a predictable period. The activity of the cells is hypothesized to reset after reaching a threshold, and in the process of resetting relay a signal to the region of the brain that generates the actual eye movements for the purpose of triggering the start or stop of a movement in anticipation of the target event. Furthermore, the network that these neurons are in is apparently able to adjust the time of peak activity of the cell to accommodate different duration fixation or motion periods.

How does the integrator work to maintain accurate tracking of a target? In our theory, the system attempts to optimize itself by achieving a balance between the amount of motion on the retina when the target is stopped and when it is moving. In a sense, the smooth pursuit system "hedges its bet" and departs from the target early when it changes speed so that it does not fall too far behind the new target speed. How then might these cells readjust their firing in the face of a different-length interval? We think that this occurs by recalibration of the threshold in the face of the new interval (Fig 5). The readjustment is hypothesized to occur as follows. On the first trial when a new interval is presented to the system, the timing circuitry conveys the same signal to the smooth pursuit system that it did with the previous interval, since no new information has yet been received. As a result, smooth pursuit perseveres for this first trial in the same fashion as it did in the last trial of the previous block. However, the target is now on for a longer (or shorter) time than it was in the past. This results in an imbalance between motion on the retina before and after the target event. As a result, on the next trial the threshold is moved up to accommodate longer periods, and down to accommodate shorter periods. This causes the integrator to reset later or earlier respectively thus conveying a more appropriate signal to the pursuit system. This process then iterates until a new balance is reached.

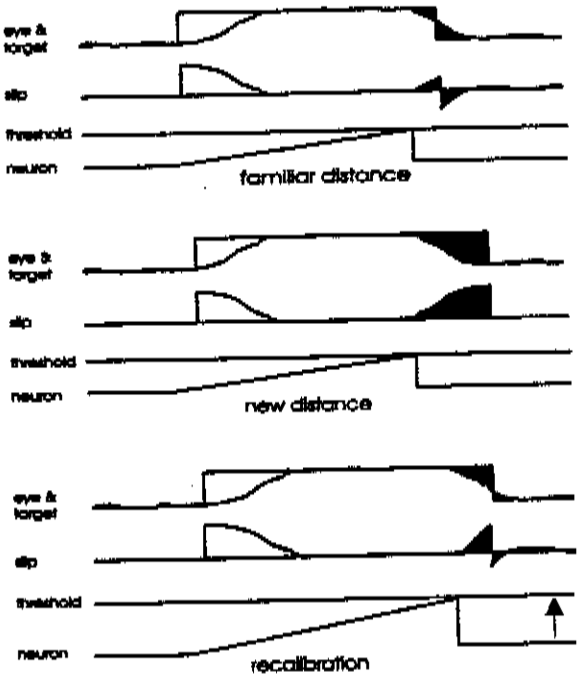

Figure 5. Recalibration of the predictive mechanism. Shown are schematics of three sequential trials, starting at the top. Here, target motion duration is manipulated. At top, the system has optimized slip at the end of the motion period; *i.e.*, positive and negative retinal motion (slip) are equal. Middle: The duration of motion is extended, resulting in more positive slip. Bottom: The system begins to readjust by raising the threshold, enabling the integrator to build up longer. For each trial, eye and target are at top, retinal slip in the middle, and the activity of the neuron is at the bottom.

Anticipatory eye movements are a sophisticated means to cope with relatively long delays imposed by neuronal processing. The problem that anticipatory eye movements solve is similar to that which a baseball player must solve when standing up to the plate to swing at a fastball. A fastball thrown by a good pitcher takes less than 500 msec to cross home plate. Since the reaction time to make most movements is about half of this time, the decision to swing or not and what type of swing to make must be decided when the ball is still only halfway to the plate. This requires that the batter make rather complex computations based upon the early trajectory of the ball. These calculations require (but are probably not limited to) knowing the speed of the ball and the time that it was released. Although the problem that the smooth pursuit system faces is not identical to this one, it involves some of the same calculations. And although the pursuit system does not have the same job as the system that swings the bat, it does need to perform precise calculations. Since retinal motion of only 2-3 degrees/second can reduce acuity [8], it is vital that the pursuit system perform adequate stabilization of a moving object on the retina to insure resolution of fine detail.

Neurons in the DMFC respond for other movements besides smooth pursuit. Activity during limb movements has been well documented (*e.g.*, [9;10;11], and activity for the other major class of voluntary eye movements known as saccades has also been seen [12]. Some of this activity has been linked to planning these types of movements as well [13]. We feel that the neurons we have studied in the DMFC may be more involved in generating a higher-order movement command that can be selectively interfaced with the eye movement or some other movement system. That movement system would in turn specify the exact dynamics of the movement.

5. References

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