Visual-tracking neurons in area MST are activated during anticipatory pursuit eye movements

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Here, I report that rhesus monkeys are able to generate anticipatory smooth pursuit eye movements in the transient absence of a moving target, if this target moves periodically. The eye velocity before target reappearance was significantly larger if the target trajectory was predictable compared with the control condition consisting of unpredictable target trajectory. Parallel to the registration of the eye movements, single-unit activity was recorded from neurons in the middle superior temporal (MST) area of the two monkeys. The neuronal activity of visual-tracking neurons resembled the observed eye movements, i.e. these neurons increased their activity earlier if the movement of the target was predictable compared with the unpredictable control. These results provide further evidence for the existence of extra-retinal signals in the activity of visual-tracking neurons located in area MST. *NeuroReport* 14:2219–2223 © 2003 Lippincott Williams & Wilkins.

Key words: Extra-striate cortex; Goal-directed behavior; Prediction; Rhesus monkeys; Sensorimotor integration; Visual motion processing

INTRODUCTION

It has been shown that the expectation of the appearance of a moving target is able to influence the execution of smooth pursuit eye movements (SPEM) in humans [1–7]. The fact that SPEM were not exclusively dependent on the processing of retinal image motion signals was shown by the finding that SPEM were not delayed relative to the target if the target moved on a periodic trajectory [5,8,9]. Predictive mechanisms in the control of eye movements are able to compensate for the inevitable delay in the visual system.

Rhesus monkeys are frequently used in cognitive neuroscience studies. One reason therefore is the fact that their oculomotor repertoire is very similar to the human oculomotor behavior. In 1967, it was reported that monkeys were not able to perform predictive eye movements in the form of SPEM or saccades [10]. There was debate about whether this finding holds true for all conditions: first, the SPEM gain of monkeys tracking sum-of-two-sines or sum-of-three-sines trajectories was higher than predicted from a simple visual feedback system working with a delay between 100 and 200 ms [9]. Second, monkeys could learn to produce very fast responses to predictable perturbations of the target trajectory [11].

The role of extrastriate area MST in the generation of smooth pursuit eye movements is well documented based on three very different methodological approaches. First, single-unit responses recorded from monkeys performing SPEM revealed specific activation [12–17]. Second, intracortical microstimulation within area MST was able to modify ongoing SPEM [18,19]. Thirdly, SPEM deficits were shown following lesions of area MST [20].

The aim of the present study was two-fold: (1) I tried to elicit anticipatory SPEM in monkeys in a paradigm based on experiments with human subjects [7]; (2) I asked whether the activity in the extrastriate area MST reflected the execution of predictive eye movements.

MATERIALS AND METHODS

Experimental set-up: The experiments were performed with two male rhesus monkeys (*Macaca mulatta*) prepared for chronic recordings of eye position and neuronal activity (see [17] for details). At a viewing distance of 85.5 cm, the monkeys faced an $86 \times 66^\circ$ tangent screen onto which the visual stimuli were back-projected by a videoprojector (Electrohome ECP 4100, resolution 1280×1024 pixels, frame rate 60 Hz) connected to a stimulation PC. Eye movement recordings were achieved by the search coil technique [21,22]. Neuronal activity was recorded using glass-insulated tungsten electrodes inserted daily through chambers whose centers were aimed at area MST (lateral 19, posterior 3.5, dorsal 16 mm) tilted 30° upward from horizontal in a parasagittal plane. The microelectrode signal was preamplified, low-pass filtered at 10 kHz, and fed to a multispike detector (Alpha Omega, Model MSD). The temporal resolution of the sampling of the neuronal activity was 4 kHz. Horizontal and vertical eye position were sampled at 12 bits depth with 1 kHz per channel. All animal procedures

were carried out in accordance with the guidelines laid down by the National Institutes of Health and the German law and were approved by the local ethics committee.

Paradigm: Initially, the monkeys had to track a target (red, diameter 0.5°, luminance 0.5 cd/m^2) which moved periodically left- and rightward (velocity 12°/s, 3 s period, see Fig. 1a). Following the presentation of 10 periods, either the test or control stimulus was presented. In the case of the test stimulus, the target continued to move on the same trajectory but became invisible whenever the position of the target exceeded 50% of its maximal amplitude and reappeared if the target crossed this invisible line (Fig. 1b). In the case of the control stimulus (Fig. 1c), the target trajectory consisted in a simple non-periodic ramp movement. The target remained stationary in the center of the screen, was switched off for 100–300 ms pseudo-randomly and reappeared moving at 12°/s to either the right or left. The duration of a single trial was 3 s in all conditions.

The monkeys had to pursue the moving target as precisely as possible; gaze deviation from target $> 4°$ resulted in an instantaneous trial abortion and lack of reward. If the target was absent, the gaze control window was located at the position predicted by the invisible target trajectory.

To classify individual recorded neurons as visual-tracking neurons, additional experiments were performed, consisting of a ramp-like pursuit task with or without brief target disappearances (for details see [17]). During the recordings reported here, the direction of the target movement was adjusted to the preferred direction of the individual recorded neuron.

Data analysis: The recorded eye position was low-pass filtered and differentiated to obtain eye velocity. Eye speed in the preferred direction of a given recording site was averaged in five 100 ms time windows before and after target reappearance (Fig. 1). The analysis started 100 ms before target reappearance and lasted until 400 ms following this event. To be able to analyze smooth pursuit eye movements exclusively, saccades were removed automatically from the eye velocity recorded based on an acceleration threshold algorithm. The saccadic periods were excluded from further processing. Statistical comparison of the mean eye speed in test and control conditions was achieved using *t*-tests. The latency of the response of an individual neuron to the appearance of the moving target was determined based on a threshold algorithm. In addition, to illustrate my findings, I calculated population responses of all recorded neurons.

All neurons were recorded from area MST based on the coordinates within the recording chamber and the typical response properties. Both monkeys are still in related experiments. The classification of an individual neuron as a visual-tracking (VT) or a non-visual-tracking (nVT) neuron was based on statistically significant differences in their response properties: a neuron was classified as a VT-neuron if, (1) the base activity during fixation of a stationary spot was significantly lower than during pursuit of a constant velocity target in the preferred direction ($p < 0.05$), (2) the neuron's response during pursuit in the

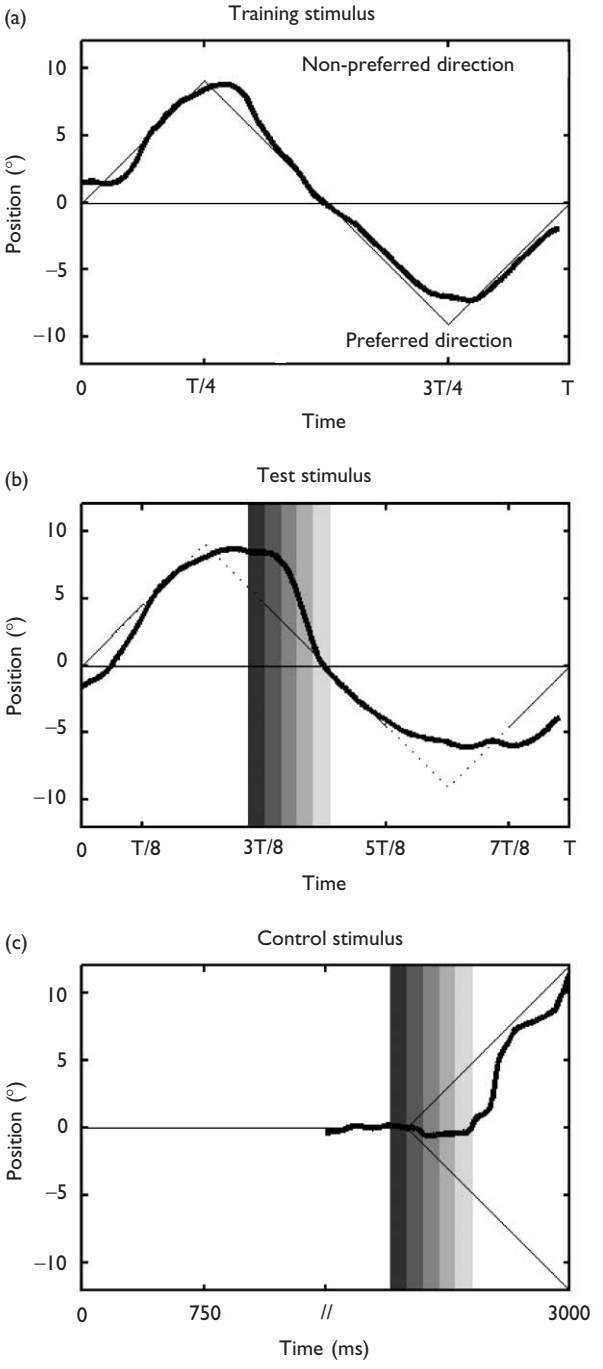

Fig. 1. Position–time plots of the moving stimuli in the training, test, and control stimulus. The solid lines give the mean eye position profiles based on 10 repetitions, thin lines show target position. (**a**) Training stimulus consisting in a periodically moving target. In all diagrams, downward represents the preferred direction of an individual recorded neuron. (**b**) The tachistoscopically illuminated, periodic test stimulus. Period duration (T = 3 s) and target velocity (12°/s) were constant in all conditions. The target was invisible as indicated by the dashed lines. The different gray bars represent 100 ms bins in which the eye speed was averaged. (**c**) The control stimulus consisted of a ramp paradigm beginning with a stationary target randomized for 1–2 s, followed by a gap with a random duration of 100–300 ms and finally a ramp-like target movement at 12°/s. Since the initial fixation duration was randomized, average eye position is only shown in a limited time interval.

preferred direction was significantly larger than the response during pursuit in the opposite direction ($p < 0.05$), and (3) the activity of the neuron did not decrease during a 200 ms gap in the presentation of the moving pursuit target ($p > 0.05$).

RESULTS

If the appearance of the moving target was predictable, our monkeys performed smooth pursuit eye movements prior to the appearance of the target in the context of our experimental paradigm. In Fig. 1b, the mean eye position profile reveals a slight deflection in the direction of the anticipated target movement before this target reappeared, which will be quantitatively analysed in the following.

As shown in Fig. 2a and b the mean eye velocity in the 100 ms time bin just before the target became visible again was clearly different from zero. If the eye velocity in the predictable test condition is compared with the eye velocity in the non-predictable control condition, the influence of anticipation on the execution of SPEM becomes especially evident. Since the mean eye velocity was computed from de-saccaded eye velocity profiles, it can be excluded that the differences in eye velocity were due to saccades. Only 200 ms after reappearance of the moving target, the significant difference in eye velocity between test and control condition disappeared as a consequence of the visual feedback which was present at this time. This eye movement behavior was very robust and was observed in all performed experiments. It is important to note that the physical stimulus condition before the reappearance of the

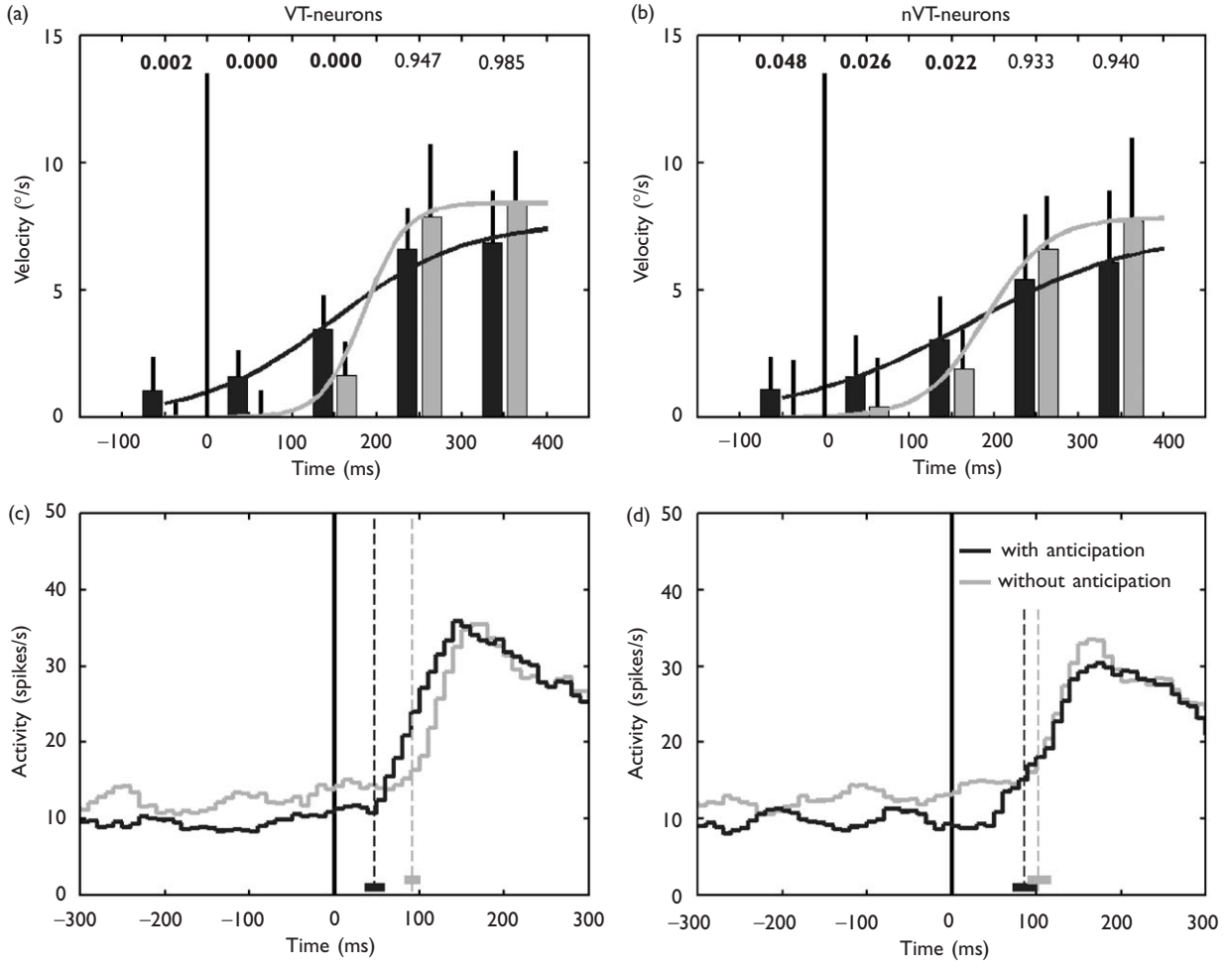

Fig. 2. Mean eye speed within 100 ms bins in various conditions and the related population responses recorded from different pools of neurons in area MST. (**a**) Mean eye speed from 26 experiments in which VT-neurons were recorded. Dark bars give the eye speed in the test condition with anticipation, gray bars inform about the eye speed in the control condition without anticipation. Mean and standard error are given in each bin and *p*-values (significantly different values bold) obtained by *t*-tests comparing the eye velocity in test and control conditions. (**b**) Very similar eye speeds resulting from 19 experiments in which nVT-neurons were recorded. Note that the observed eye movement behavior did not depend on which neurons were recorded. (**c**) Population response of all 27 VT-neurons; black gives test stimulus with anticipation, gray gives control stimulus without anticipation. Note the shorter latency of the population response in the case of anticipation, the vertical dashed lines give the mean latencies and the horizontal bars show standard errors determined by the analysis of individual neurons as shown in Table 1. (**d**) Population response for 19 nVT-neurons lacking this significant difference in latency.

Table I. Latency of discharge rates of VT- and nVT-neurons.

	Test (ms)	Control (ms)	*n*	*p*-value
VT-neurons	47 ± 11	91 ± 9	27	0.001
nVT-neurons	86 ± 14	103 ± 13	19	0.185
p-value	0.014	0.212		

target was identical in test and control conditions: a black screen without any visual structure.

Forty-six single-units from area MST in the posterior parietal cortex of two rhesus monkeys were recorded during the execution of the anticipatory smooth pursuit eye movements described above. All recorded single neurons displayed a clear directionally selective response during the execution of SPEM. As explained in the methods, 27 neurons were classified as visual-tracking (VT) and 19 neurons were classified as non visual-tracking (nVT) neurons.

Figure 2c shows the population response of 27 VT-neurons to predictable and unpredictable target trajectory in the preferred direction. It can be seen that in the case of the predictable target, the neuronal responses of the VT neurons had a clearly shorter latency, which parallels the observed eye movements shown in Fig. 2a. In the case of the 19 nVT-neurons (Fig. 2d), this reduction in the latency of the population response was not present although the onset of the eye movements was also clearly different in predictable and unpredictable condition. However, the population responses shown in Fig. 2c and d only give qualitative results without statistical tests. To assess quantitative results, we calculated the latency of the neuronal response of every individual recorded neuron and based statistical procedures on these values. As shown in Table 1, the latency of the neuronal responses of VT-neurons was $\sim$50 ms shorter if the target moved predictably. This difference was highly significant ($p = 0.001$). The marginal difference in latency for nVT-neurons in test and control conditions was not significant ($p = 0.185$). Independent of whether the target trajectory was predictable or not, the VT-neurons had a shorter latency than the nVT-neurons. This difference was only significant for the predictable test condition ($p = 0.014$). In summary, the response latency of VT-neurons in the predictable condition was significantly shorter than the latencies of all other conditions, in which no significant difference in latency was found.

DISCUSSION

In this study, rhesus monkeys were able to perform anticipatory smooth pursuit eye movements elicited by a tachistoscopically illuminated and periodically moving target. The observed eye movements were accompanied by the activity of visual-tracking (VT) neurons recorded from area MST.

It was shown earlier that rhesus monkeys, unlike human subjects, could not use prediction for the generation of eye movements [10]. Human subjects tended to perform eye movements preceding the target movement if the target moved periodically; this observation holds true for saccades and SPEM. However, the two monkeys used in the study by Fuchs [10] did not perform such preceding eye movements. Obviously, there is some contradiction between this older report and the data presented here. The most likely explanation for this discrepancy consists in different training procedures applied. Here, two monkeys were specifically trained to produce anticipatory eye movements, since the gaze control window was moved according to the anticipated position of the invisible target. However, it must be noted that with identical experimental settings, human subjects generated eye velocities around 5°/s on average during the 100 ms interval before the predictable target became visible, whereas our monkeys only performed average eye velocities around 2°/s. In support of my findings, there are other reports in the literature indicating that monkeys were indeed able to perform predictive smooth pursuit eye movements [9,11]. However, it seems also that the ability of rhesus monkeys to perform anticipatory SPEM is clearly reduced compared to humans.

With respect to the pursuit-related activity recorded from area MST, the existence of extra-retinal signals related to the ongoing eye movements was shown in a subgroup of neurons named visual-tracking neurons. The activity of those neurons turned out to be insensitive either to short temporal removals of target, to stabilization of the retinal image of the target or to spatial removals of the target [13,14,17]. Essentially, retinal image motion signals are combined with eye and head movement related signals to internally reconstruct target trajectory in space. Therefore, the neuronal responses of VT-neurons during execution of anticipatory SPEM are probably due to the execution of the eye movement itself. It is not likely that the activity of the VT-neurons reflect the generation of an anticipatory signal. On the other hand, the latency of nVT-neurons was not significant different between test and control condition. This can easily be explained since the activity of nVT-neurons was only influenced by retinal image motion, obviously identical in predictable and non-predicable conditions, but not by eye movement related extra-retinal signals.

There is experimental evidence that the cerebellum is involved in the generation of anticipatory SPEM [23]. Neuronal responses from the flocculus and paraflocculus preceded eye movements by 12 ms. This very short lead indicates that the cerebellum is directly involved in the generation of the motoneuron discharge pattern underlying the execution of SPEM. However, if one addresses the question of where the anticipatory signal itself, eventually independent of the specific elicited motor program, is generated, the frontal cortex comes into play. It is well documented that a sub-area of the frontal eye field, the frontal pursuit area (FPA) contributes to the execution of SPEM [24,25]. Fukushima and colleagues [26] documented predictive responses from periarcuate neurons, even if the monkey did not produce predictive eye movements in this study. So it remains to future experiments to show whether the frontal cortex gives the drive for signals to cause the observed anticipatory SPEM.

CONCLUSIONS

If the monkeys could anticipate the reappearance of a moving target, they performed smooth eye movements before the target became visible. Visual-tracking neurons

recorded from area MST responded to the execution of anticipatory eye movements in the absence of any visual stimulation. This demonstrates that these neurons are responsive to extra-retinal signals related to the ongoing eye movement. The combination of retinal image motion signals and eye movement related signals yields in the presentation of the target trajectory within an external frame of reference. This transformation of reference frames is most likely an important function of the posterior parietal cortex.

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