Short communication

Hand position modulates saccadic activity in the frontal eye field

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Abstract

Recent neurophysiological studies have begun to uncover the neuronal correlates of eye hand coordination. This study was designed to test whether the frontal eye field (FEF) saccadic activity is modulated by hand position. Single neurons were recorded in two macaque monkeys performing visually guided saccades while holding their hand at given locations on a touchscreen. To determine the relative contributions of hand vision and its proprioception, monkeys executed the task with or without vision of the hand. We found that saccadic activity of more than half of the neuronal sample (54%; n = 130) was dependent on hand position relative to the saccade end point. Both visual and proprioceptive signals contributed to this modulation. These data demonstrate that the oculomotor function of the FEF takes into account hand position in space.

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Psychophysical studies have amply demonstrated the mutual links between the arm motor system and the oculomotor system at the behavioral level (e.g. [4]). Less is known about the underlying neural mechanisms and available knowledge concerns more how the eyes affect the planning of hand/arm movements than the opposite.

On the one hand, there is a large body of evidence that spatial accuracy and kinematics of hand movements are influenced by retinal signals coding target location, eye orientation at the time of pointing, and coordinated eye movements (e.g. [12,21,22]). Accordingly, neurophysiological recordings in monkeys showed that several areas devoted to the planning of arm movements contain neurons whose properties integrate eye and hand/arm movement signals. They include the posterior parietal cortex [2], ventral [5,18] and dorsal [6,14] premotor areas, prefrontal cortex [5] and superior colliculus [29].

On the other hand, the oculomotor system uses information derived from the hand/arm. Saccade latencies [3,10,16,19], trajectories [31] or speed [25], have been reported to depend on coordinated hand movements. Also, subjects are able to follow with their eyes the displacement of their hand, even when it is unseen [1,32]. These behavioral data indicate that signals derived from the arm motor system are integrated during the planning and execution of eye movements (see also [30]). How and which brain areas are involved is still unclear, as only one study has addressed this issue [17].

As we have previously shown that static eye position modulates arm-related activity in the dorsal premotor cortex [6], here we asked the question whether, conversely, the static hand position modulates the activity of neurons in one of the main oculomotor areas, the frontal eye field (FEF, for a review see [24]). Our hypothesis is that ocular exploration integrates hand position signals derived from vision and/or proprioception. To test this hypothesis, we recorded single neurons from the FEF of two monkeys trained to make saccades to visual targets, while they held their hand static either close to or far from the saccade target. To tease apart the relative contributions of proprioceptive and visual signals, the task was performed both with and without vision of the hand.

Two male monkeys, one Macaca fascicularis (monkey A) and one Macaca mulatta (monkey S) participated to this study. Both were implanted, under anesthesia and aseptic conditions with a bolt for head fixation, and a recording chamber over the hemisphere contralateral to the hand used to perform the task (right, monkey A; left, monkey S). Surgery, testing procedures, and animal care were in accordance with the European
The testing apparatus consisted of a resistive touchscreen (36 cm × 27 cm) inclined at a 45° angle under a mirror onto which stimuli were projected from an above computer monitor (Fig. 1A). The semi-reflective properties of the mirror made the visual stimuli appear as if located on the underneath touchscreen together with the hand. In this condition (“hand visible”), saccades were made while hand position was provided through both vision and proprioception. Insertion of a black paper board under the mirror made it fully reflective. Under this condition (“hand invisible”), visual stimuli still appeared on the touchscreen, but the invisible hand position was mostly felt through proprioception. The hand visible and hand invisible conditions were tested in separate blocks of trials, in a pseudorandom order.

A trial began with the presentation of a white square (2° × 2°) at the bottom left or the bottom right of the screen (11° from the center), instructing the monkey on where to put his hand on that trial (Fig. 1B). Then, a white circle (0.25°) appeared at the screen center, which the monkey had to fixate. After 500 ms of fixation, a target (white square, 1° × 1°; 10.3° eccentricity) appeared at one of two potential locations, immediately above the two hand positions. The target and the hand were spatially congruent or non-congruent from trial to trial. After either 0.5 or 1 s of set period, the fixation point was turned off (go signal), and the monkey had to make a saccade to the target to receive a liquid reward. If the animal moved the hand, or made the saccade before the go signal, the trial was aborted.

The recording chamber was centered on the genu of the arcuate sulcus in each animal using MRI scans (Fig. 1C), and FEF was localized within the chamber by means of intracortical microstimulation. Neuronal activity was first recorded, using tungsten electrodes (FHC Instruments, impedance: 0.5–2 MΩ) to detect the surface of the cortex. Then, microstimulation was applied every 250 µm using standard procedures (parameters: 40 ms duration trains of 20 pulses, 0.2 ms each) with currents ranging from 5 to 100 µA. Sites where microstimulation evoked saccades with currents less than 50 µA were considered as part of FEF [7] and were subsequently recorded from during the visually guided saccade task. During the recording sessions, action potentials were isolated on line using a waveform based sorting software (MSD, Alpha Omega).

Eye position was recorded as two analog inputs sampled at 250 Hz, one for the horizontal and one for the vertical position of the eyes, and analyzed offline using custom MATLAB routines (MathWorks, Inc., Natick, MA). Onset and end point of a saccade was detected by deriving the eye position signals. Saccade onset, used to determine saccade latencies, was defined as the first measure after saccade onset. Saccade onset, used to determine saccade latencies, was defined as the first measure after saccade onset. Saccade onsets were used to determine saccade latencies, which were defined as the time from saccade onset to 50 ms after saccade onset. The end point, used to assess saccade accuracy, was defined as the first measure after saccade onset for which eye velocity fell below 50°/s. The highest velocity value during saccade execution was taken as the eye peak velocity. These three parameters were analyzed using a 5-factor ANOVA (monkey × target × hand × delay × vision).

Saccade-related neuronal activity was defined as any significant change of activity within a 200 ms interval (from 150 ms before to 50 ms after saccade onset) relative to set period. This window was adjusted for each neuron, depending on its firing pattern, for statistical analyses. The effects of saccade direction and hand position on the mean firing rate were then tested using a 2-factor ANOVA (target × hand) for the cells recorded under one condition only (hand visible or hand invisible), or a 3-factor ANOVA for those tested under both conditions (target × hand × vision). For all statistical tests, the significance level was set at 0.05.

*Behavior:* Saccade latencies varied with hand position. Analysis of saccade latencies on 4756 trials for monkey A and 3164 trials for monkey S revealed that eye–hand spatial configuration (i.e. congruent vs. non-congruent), did affect saccade latencies (configuration: $F_{1,7888} = 11.42, p = 0.001$). In both monkeys, the hand presence near the target could either hasten...
or retard saccade onset, although the precise conditions eliciting one or the other change differed in the two animals (monkey × configuration × target × delay interaction: $F_{1,7888} = 5.15, p = 0.02$). For example, shortened latencies for the congruent configuration were observed in monkey A for the right target and the 1000 ms delay ($250.5 \pm 9.2$ ms vs. $301.4 \pm 6.8$ ms; $t_{419} = 4.40, p < 0.001$), whereas they occurred for the left target and the 500 ms delay in monkey S ($263.2 \pm 2.2$ ms vs. $277.1 \pm 1.7$ ms; $t_{523} = 4.50, p < 0.0001$). The “hand invisible” condition attenuated the effect of eye–hand configuration on saccade latencies, but its effect did not reach significance (congruence × vision interaction: $F_{1,7888} = 3.17, p = 0.07$).

Previous studies have reported that hand movements can either decrease [16] or increase [3,19] saccade latencies in humans. The present results, together with those of Tipper et al. [31], suggest that the mere presence of the hand in the workspace is sufficient to affect saccade spatio-temporal characteristics, i.e. when the hand is resting, not performing a response toward the target. In addition, our findings that the effects on saccade latencies occur even when the hand was not visible are a strong argument for the idea that the oculomotor structures receive non-visual, proprioceptive signals from the arm motor system, as previously proposed in human studies [1,23,30,32]. These signals might play a key role in eye–hand coordination.

Modulation of saccadic activity by hand position. A total of 228 neurons were recorded in the two animals (Table 1), among which 130 (87 in monkey A, 43 in monkey S) changed their firing rate during the 200 ms interval around saccade onset. For most cells (93%), saccadic activity was direction selective, with a predominant preference for contralateral saccades (74%). Interestingly, we found that the activity of more than half of the

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Summary of cells properties</th>
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<tbody>
<tr>
<td></td>
<td>$n$ (%)</td>
</tr>
<tr>
<td>Recorded neurons</td>
<td>228</td>
</tr>
<tr>
<td>Saccadic neurons</td>
<td>130</td>
</tr>
<tr>
<td>Directionally selective neurons</td>
<td>121 (93%)</td>
</tr>
<tr>
<td>Hand modulated neurons</td>
<td>70 (54%)</td>
</tr>
<tr>
<td>Monkey A</td>
<td>44/87 (51%)</td>
</tr>
<tr>
<td>Monkey S</td>
<td>26/43 (60%)</td>
</tr>
<tr>
<td>Preferred “eye–hand” spatial configuration</td>
<td></td>
</tr>
<tr>
<td>Congruent</td>
<td>36 (51%)</td>
</tr>
<tr>
<td>Non-congruent</td>
<td>29 (41%)</td>
</tr>
<tr>
<td>Preferred “hand vision” condition</td>
<td></td>
</tr>
<tr>
<td>Hand vision</td>
<td>34/116 (29%)</td>
</tr>
<tr>
<td>No hand vision</td>
<td>40/93 (43%)</td>
</tr>
</tbody>
</table>

130 saccadic cells (70, 54%) varied significantly, for the same saccade, depending on hand position. This high proportion of hand modulated saccadic cells was found in the two animals (51%, monkey A; 60%, monkey S).

Most neurons whose activity was modulated by hand position were directionally selective (63/70, 90%; Figs. 2A and 3A), and the modulation occurred on activity associated with the preferred direction for the majority of them (53). This modulation took the form of an increase of the mean firing rate when the hand was close to (congruent condition; 36/70, 51%), or far from (non-congruent; 29/70, 41%) the saccade end point. Figs. 2B and 3B illustrate examples of these modulations when saccades are made in the neuron’s preferred direction. The remaining five neurons were active, and hand modulated, for

Fig. 2. Example of a congruent saccadic neuron. (A) The neuron’s preferred direction. Neuronal activity is shown in the form of conventional raster displays where each line represents data for one trial, and each dot represents the time of an action potential, and spike density function (SDF, spikes/s) computed on a trial by trial basis by convolving the spike train with a gaussian of standard deviation equal to 20 ms. Activity is aligned on the saccade onset (vertical dotted lines), and shown for saccades made to each of the two targets under the hand visible condition; the trials for the two hand positions were pooled together. Top: The large square represents the touchscreen, the small squares depict potential target locations, FP is the fixation point. Bottom: Horizontal (X) and vertical (Y) eye position is displayed beneath the raster displays. (B) Hand position effect on the activity for the preferred direction. Top: The location of the hand is near (solid line) or far from (dotted line) the saccade target. Bottom: The neuron’s activity is aligned on saccade onset (vertical line), and shown in the form of SDF functions computed on 10 trials each, for congruent (solid line) and non-congruent (dotted line) conditions. Middle: Mean and S.E.M. of saccade end points along the horizontal and vertical axes for saccades to the right target; the cross represents the center of the target; filled and open squares represent mean saccade end points for congruent and non-congruent configurations, respectively. Note that this neuron is more active when the visible hand (left panel) is close to the saccade endpoint (“congruent” configuration), and that hand position has no effect in the no hand vision condition (right panel).

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saccades to both targets. For each hand-modulated neuron, we compared the velocity peaks and end points of saccades across eye–hand configurations and hand vision conditions. There were no significant differences that could explain the effects of hand position on neuronal activity, whether at the single cell or at the population levels.

Fig. 4 illustrates the magnitude of activity changes due to hand position for the two populations of modulated cells. For the congruent cells, the amount of increase of average activity in the congruent configuration, relative to the non-congruent one, is 38%. For the non-congruent cells, the percentage change is 43%, in favor of the non-congruent configuration. A Student’s t-test confirms that the difference between the preferred and non-preferred eye–hand configurations is highly significant ($t = 4.33, p < 0.001$ for congruent cells; $t = 5.46, p < 0.001$, for non-congruent cells).

Among the 130 FEF cells with saccade-related activity, 116 were tested in the “hand visible” condition of the task and 93 were tested when hand vision was occluded. The results showed that visible hand position affected 29% of the cells (34/116) while 43% of them (40/93) were significantly modulated when monkeys could not see their hand during the task. In order to directly assess the relative contribution of vision and proprioception to hand modulation, 49 of the 70 modulated cells were studied under both hand visible and invisible conditions. It appeared that for a majority of cells (28/49, 57%), the hand modulation occurred specifically when the monkey could not see the hand (Fig. 3B). The remaining cells included 17 cells (35%) whose activity was modulated only when the hand was visible (Fig. 2B) and 4 (8%) which were modulated in both conditions. Thus, vision of the hand contributed to the observed modulation in 21 cells (17 + 4), whereas proprioception contributed in 32 (28 + 4) cells.

This study shows, for the first time, that hand position affects strongly saccadic activity of FEF neurons both with and without vision of the hand, suggesting that information on hand position can be gained through both visual and non-visual signals. The FEF is known to receive visual information from the dorsal visual pathway (e.g. [8]). When the hand is visible, information on hand position may simply be derived from retinal inputs and may explain the observed effects under the “hand visible” condition. By contrast, in the absence of hand vision, the observed effects must reflect non-visual signals, namely proprioception. These signals may come from several hand/arm related areas including the dorsal and ventral premotor areas, the supplementary motor area, the somatosensory cortex (SII, 3a), and from the parietal and parieto-occipital cortices [9,13,26,27,28].

These anatomical studies also show that FEF receives projections from cortical areas (PMv, VIP, 7a) and from the putamen, which are known to contain a multisensory representation of space surrounding the body. Neurons within this network have visuo-tactile properties with the visual receptive fields anchored to the body part (e.g. [11]). The present results might be interpreted in terms of multimodal integration of hand position signals for the generation of saccadic eye movements. In particular, it is likely that the hand biases the attentional and oculomotor processing of sensory information in near space.
This interpretation holds at least for cells whose activity was modulated by hand position preferentially when the hand was visible. In this condition, the visual saliency of the hand could attract attention to it location, thereby biasing sensory processing and oculomotor exploration of space. However, attentional bias is difficult to reconcile with hand modulation preferentially in the hand invisible condition, or with increased activity in the non-congruent eye–hand configuration. These findings suggest, rather, that proprioceptive signals from the hand are integrated by FEF cells for saccade generation, independently from attention. Overall, integration of hand position signals may allow FEF to play a key role in eye–hand coordination through multimodal integration.

Among previous studies that addressed the issue of eye hand interactions in the oculomotor areas [15,17,33], very few have investigated the effects of hand movement/position on saccadic activity [17]. In the later study, Mushiake et al. used a saccade/pointing task and reported that SEF, but not FEF, neurons vary their pre-saccadic activity depending on whether the saccade was made alone or together with a hand pointing movement. These findings suggest that SEF, but not FEF, would play a role in eye–hand coordination and may appear at odds with the present results. In fact, this discrepancy can be accounted for by important differences in the tasks used. In Mushiake et al.’s study, the hand moved from a single hold pad to the target of the saccade, or remained immobile during the saccade. Our results predict that, in order to observe hand modulation in FEF, it is necessary to vary the initial hand position. Alternatively, it is possible that the use of static hand position, varied in a systematic way within the work space, is more effective in modulating FEF cells than hand movements. In another, more recent study, Lawrence and Snyder [15] reported that FEF neurons are effector specific during the instructed delay period, as their activity reflects predominantly upcoming saccadic eye movements, rather than arm movements. Interestingly, FEF seems to be less effector specific than the lateral intraparietal area (LIP), a cortical field involved in saccadic eye movements which is reciprocally congruent to the lateral intraparietal area. J Neurosci 2006;26:8310–9.

References


