

Correspondence of presaccadic activity in the monkey primary visual cortex with saccadic eye movements

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We continuously scan the visual world via rapid or saccadic eye movements. Such eye movements are guided by visual information, and thus the oculomotor structures that determine when and where to look need visual information to control the eye movements. To know whether visual areas contain activity that may contribute to the control of eye movements, we recorded neural responses in the visual cortex of monkeys engaged in a delayed figure-ground detection task and analyzed the activity during the period of oculomotor preparation. We show that ≈ 100 ms before the onset of visually and memory-guided saccades neural activity in V1 becomes stronger where the strongest presaccadic responses are found at the location of the saccade target. In addition, in memory-guided saccades the strength of presaccadic activity shows a correlation with the onset of the saccade. These findings indicate that the primary visual cortex contains saccade-related responses and participates in visually guided oculomotor behavior.

V1 | visuomotor integration | oculomotor behavior | neurophysiology | vision

For the analysis of the visual scene we constantly shift our eyes. These shifts of gaze or saccadic eye movements are not randomly directed but guided by visual information (1, 2). Neural responses that determine when and where to look are observed in the oculomotor structures (3–7). Typically such responses that control eye movement commands are observed immediately before the initiation of a saccade and correlate with the direction and onset of a saccade. During this presaccadic period the oculomotor areas thus integrate visual information. They may bias the gain of visual signals so that at the spatially corresponding saccade target location the visual signals are enhanced (8).

To know whether visual signals are enhanced during the presaccadic period we analyzed neural responses in the primary visual cortex of monkeys that were performing a delayed response task. We used both visually guided and memory-guided saccade trials. The results show that in the primary visual cortex neural activity starts to be enhanced just before the initiation of a saccade. Presaccadic activity is strongest at the target location of the saccade, and it predicts the onset of the memory-guided saccades. These results cannot be explained by e.g., small eye movements, arousal, or reward but instead indicate that the primary visual area contains activity that is related to the control of eye movements. We propose that the primary visual cortex integrates visual and saccade-related activity and may be included in the system that mediates visually guided oculomotor behavior.

Materials and Methods

Experimental Setup. Two monkeys (*Macaca mulatta*) were trained to fixate at the fixation point on the monitor. After 300 ms of fixation, a figure appeared and the animals maintained fixation for an additional 1,000 ms. After fixation point offset (cue time), animals were signaled to saccade toward the figure location. To study both visually and memory-guided saccades, the figure-ground texture was randomly replaced by either another differ-

ent figure-ground texture (visual trials) or a homogeneous texture (memory trials). In the former case, a figure of the same size as the first figure reappeared at the same location ($\approx 5,500$ trials), whereas in the latter case the figure disappeared ($\approx 3,500$ trials). The maximum time allowed for responding to the figure was 500 ms. Trials where the eye position left the electronic fixation window ($1^\circ \times 1^\circ$) during fixation, e.g., because of fixational saccades, or trials where the animals made incorrect responses were discarded. Eye movements were monitored by using scleral search coils with the modified double magnetic induction method and digitized at 400 Hz (9). From the eye position data, the moment of a correct target saccade was detected by using a vector velocity threshold of 50 degrees/s. For fixational saccades this was 10 degrees/s.

The stimulus screen with the figure-ground display consisted of a texture of a single particular orientation of line segments, except for a small square region (figure), where line segments had the orthogonal orientation. Stimuli were presented on a 21-in monitor screen driven by TIGA software. The display resolution was $1,024 \times 768$ pixels, and the refresh rate was 72.34 Hz. The monkey was seated in a primate chair and placed in a dark room 75 cm from the monitor screen. The screen subtended $28^\circ \times 21^\circ$ of visual angle. In each trial, a square of 3° was randomly presented at one of three possible locations at an eccentricity of 2.74 – 4.4° from the fixation point (a central red spot of 0.2°). Onset of figure-ground trials consisted of the abrupt transition from a texture of randomly oriented line segments into a texture of oriented line segments with a 90° orientation difference between figure and ground. This texture was replaced after 84 ms for monkey U and 280 ms for monkey T by another figure-ground texture for the visual trials and by homogeneous texture for the memory trials. Line segments were 16×1 pixels ($0.44^\circ \times 0.027^\circ$), and the density was five line segments per square degree. Line segments could have 135° or 45° orientation. Both orientations were used for both figure and background, resulting in complementary stimulus pairs. Responses to these pairs were averaged, so that local receptive field stimulation was identical for figure or background.

Recordings and Data Analysis. Multiunit neural activity was recorded through platinum-iridium microwire electrodes (16 of ≈ 40 electrodes per animal, impedances 100–350 k Ω at 1,000 Hz) that were surgically implanted into the operculum of mainly upper layers of area V1. Sites were selected on the basis of the quality of the signal (signal-to-noise ratio) and their receptive field position. The obtained signals were amplified ($\times 40,000$), band-pass filtered (750–5,000 Hz), full-wave rectified, and then low-pass filtered (< 200 Hz). The resulting signal represents spiking activity (10), and such recordings are similar to single-unit recordings (11). Before the experiments, aggregate receptive field size and positions at each electrode were determined,

Abbreviations: To-RF, toward the receptive fields; Away-RF, away from the receptive fields.

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using moving bars. Receptive field sizes ranged from 0.4° to 1.0° , and eccentricity ranged from 1.25° to 5.7° . For each monkey, figure positions and electrodes were chosen such that the figure covered the receptive fields of the 16 electrodes simultaneously and therefore many recorded neurons had overlapping receptive fields (see ref. 12). In the other two figure locations, the receptive fields were covered by ground. In the former case saccades were directed toward the receptive fields of the recorded neurons (To-RF condition), whereas in the latter case they were directed away from the receptive fields (Away-RF condition). Data were obtained from 32 electrodes during 29 daily sessions.

We subtracted the dc component (average baseline activity from 0–30 ms after stimulus onset) from the responses. Thereafter, the average responses at each electrode were normalized; at each electrode, the responses were divided by a constant factor, which was the maximum response found for any of the conditions (i.e., To-RF, Away-RF, visual task, and memory task), obtained within a 1,000-ms recording period starting from stimulus onset (thus excluding saccade-induced responses). This way, each electrode contributed equally to the population average, yet relative differences between conditions were maintained despite the normalization.

The onset of the presaccadic activity was determined on the average activity per electrode by shifting windows analysis. The first sample of a sliding 20-ms time window was taken as the onset of presaccadic activity at the moment the average activity of that window was significantly ($P < 0.05$) stronger than the average activity of a previous window. Cue time was the starting point for this analysis. This method gave an accurate estimation of the onset of enhancement of the presaccadic activity when visually checked.

Results

We tested two monkeys in a delayed figure-ground detection task. Animals fixated on a small central red dot on a computer screen. After 300 ms of fixation, the stimulus screen appeared, containing a texture-defined figure, randomly positioned in one of three possible locations (Fig. 1). The figure-ground texture was randomly replaced by either a different figure-ground texture (visual trials) or a homogeneous texture (memory trials). In the former case, a figure reappeared at the same location, whereas in the latter case the figure disappeared. The replacements evoked transient neural responses (see Fig. 2A). The animals maintained fixation until cued to saccade toward the figure location. In this way, the pure visual responses are separated from possible presaccadic responses. Performance for both animals was 86% correct for the memory task and 91% correct for the visual task. While the animals were performing the delayed response task, we recorded multiunit activity of V1 neurons.

Presaccadic Enhancement of Neural Responses. The neural responses show the characteristically transient activity peaks (Fig. 2A) followed by a regular, sustained response at longer latency. These responses can decline below baseline activity (responses to the prestimulus screen; see refs. 13 and 14). To know whether presaccadic activity is included in these late responses, we aligned the neural responses on the moment of the gaze shift. The results show that ≈ 100 – 200 ms before the onset of a saccade V1 activity starts to increase monotonically over time until a saccade is initiated (Fig. 2B–E). The saccade itself causes a massive increase in activity (see arrow in Fig. 2C), which is evoked by sweeping the receptive fields over the visual field.

To analyze the presaccadic enhancement of activity, we compared for each electrode the average neural responses of the 100-ms period before cue time with the average activity of the 100-ms period before the onset of the saccade. Of all of the electrodes ($n = 32$), 94% for the visual task and 97% for the

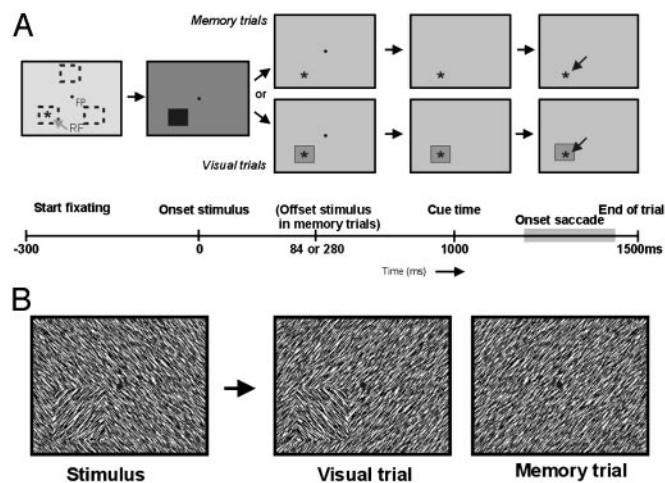


Fig. 1. Illustration of sequence of visual stimulation. (A) Animals had to fixate at a central point (FP) for 300 ms before the appearance of the stimulus. At stimulus onset, a texture appeared containing a figure. In 50% of the trials, the figure-ground texture was replaced by a homogeneous texture. The animals maintained fixation and had to make a saccade toward the figure location (arrows, Right) after offset of the fixation point (cue time). Two types of trials were used: visual and memory trials. In the former, the figure-ground texture was replaced by a different figure-ground texture with the figure at the same location. In the latter, a homogeneous texture replaced the figure-ground texture. The figure could appear in one of three possible locations (indicated by dotted squares, Left). The asterisk indicates the position of the receptive fields (RF). When the figure was overlying the receptive field responses to To-RF were recorded ($\approx 3,000$ trials). In the two other figure locations, Away-RF responses were obtained ($\approx 6,000$ trials). (B) Examples of complementary stimulus pairs so that the receptive field stimulus was identical for these conditions.

memory task showed activity that was stronger before the onset of a saccade than before cue time (Fig. 3A; $P < 0.005$ for both conditions separately, paired t test). Surprisingly, the increase of activity during the presaccadic period is very robust. Comparing the maxima of the presaccadic responses to the maxima of the visually evoked responses shows that the presaccadic responses are ≈ 0.7 times as strong as the visually evoked responses (maximum, 3.7, minimum, 0.01, median, 0.4; Figs. 2A and B and 3B). Thus, in the primary visual cortex neurons increase their activity just before the initiation of a visually or memory-guided saccade.

To exclude the possibility that these presaccadic-enhanced responses are artifacts of small anticipatory eye movements or fixational eye movements, or a consequence of flawed alignment on the saccade, we examined the eye positions (Fig. 4A). To control for fixation behavior, we first analyzed the accuracy of fixation by comparing the standard deviations of the x and y coordinates of the eye positions during the 100 ms before cue time with those of the 100 ms before saccade onset for each trial separately. The results show that during the fixation period the pattern of eye movements did not differ between these two periods ($P > 0.05$, ANOVA).

Next, we analyzed the rate, direction, and speed of fixational saccades that occurred in the period before cue time and in the period before the onset of the target saccade. For the detection of fixational saccades, we used a vector velocity threshold of 10 degrees/s. The results show no differences in fixational saccades between the two periods (Fig. 4B–D). Relatively large fixational saccades are not present because the animals are trained to fixate accurately, and trials with poor fixation were aborted. This finding may explain the low rate of fixational saccades (typically three to five per s) and an apparent lack of a drop in the rate before the onset of a target saccade. For each individual

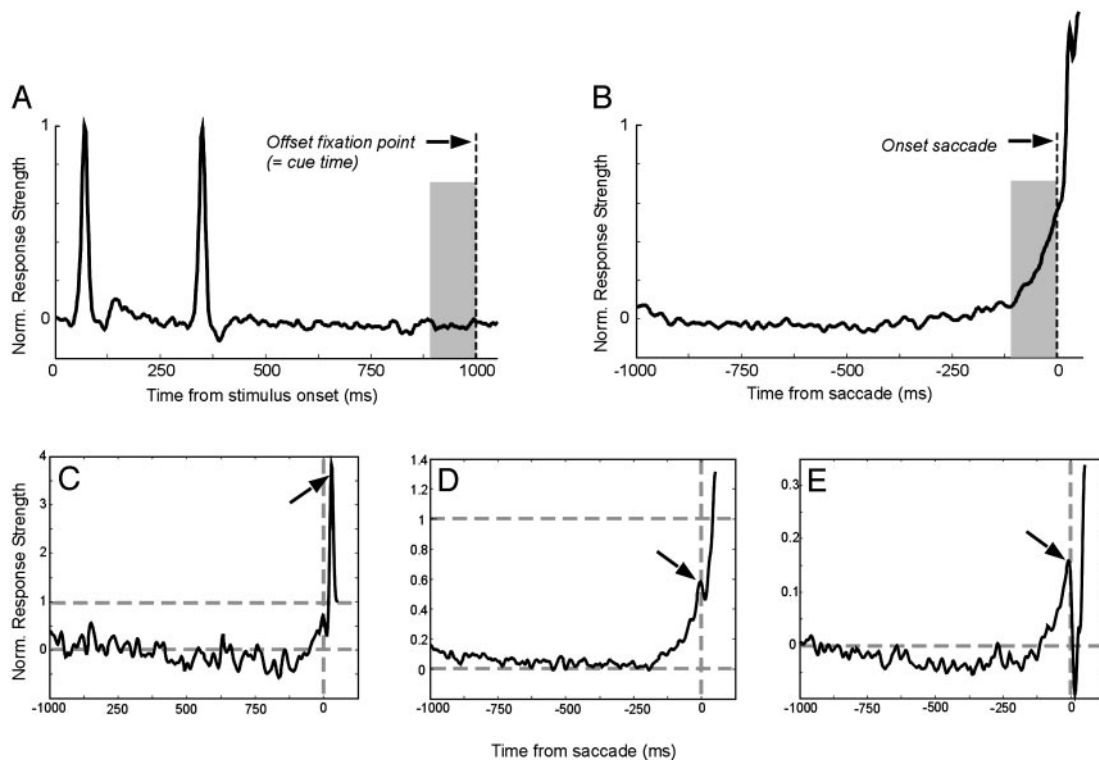


Fig. 2. Neural responses during visual stimulation. (A and B) Average normalized activity aligned on stimulus onset (A) and saccade onset (B). Note that the stimulus-evoked responses are not observable in the latter because of the reaction times. (C–E) Examples of presaccadic responses. After the initiation of the saccade first a decrease (arrows in D and E) and then an increase (arrow in C) of neural responses is observed.

electrode we also calculated the strength of correlations (Pearson) between eye velocity and neural response strength over time. For this calculation, 2D cross-correlograms with time versus lag on the x axis and correlation strength on the vertical axis (J-PSTHs) were calculated (see ref. 14 for details). The results show that V1 activity does not correlate with eye velocity until ≈ 40 ms (time that sensory information reaches V1) after initiation of the saccade (Fig. 4E; note that only the diagonal of the correlation matrix is shown here). In addition, we examined the influence of fixational saccades on the averaged neural activity during the period before cue time (Fig. 4F). Neural responses tend to show a small decrease in activity after such a saccade, which has been observed (15). Thus, we conclude

that the presaccadic enhancement of neural activity in the primary visual cortex is not the result of small eye movements during fixation or poor alignment of neural responses on the saccade.

The presaccadic enhancement could be a direct neural response to the removal of the fixation point (16). However, neural activity immediately after offset of the fixation point did not differ from activity immediately before offset (time windows of 200 ms; data not shown), which agrees with previous control experiments (17). In addition, the presaccadic enhancement starts on average 176 ± 54 ms (mean \pm SD) before the initiation of the saccade, whereas the average reaction time (the time between removal fixation point and initiation of the saccade) is 332 ± 70 ms (mean \pm SD). Thus, presaccadic activity starts to enhance ≈ 156 ms after the removal of the central fixation point. This period is much longer than the latency of a regular visual response and also longer than surround influences in V1 (18). Therefore, presaccadic activity is not a result of the removal of the fixation point (see below for further evidence).

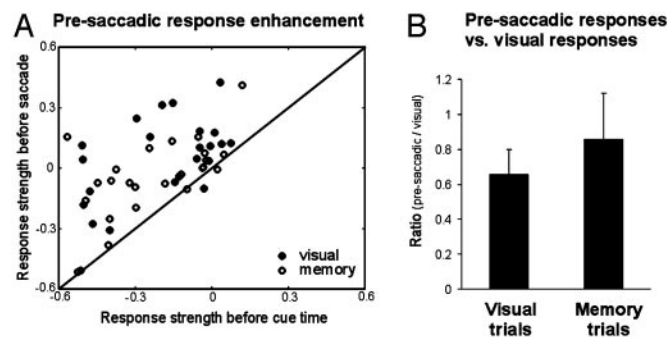


Fig. 3. Presaccadic response strength. (A) Average enhancement of neural responses for each individual recording site both for the visual and memory task. Enhancement is determined by calculating the difference in response strength before cue time and before saccade onset. See shaded boxes in Fig. 2 A and B. (B) The maximal response strength in the presaccadic period compared to the maximum of the visual response.

Presaccadic Activity and Saccade Target. We observed presaccadic activity for both To-RF and Away-RF trials. The To-RF trials are the trials where the direction of the saccade is toward the receptive fields of the recorded neurons, whereas Away-RF trials are the trials where the saccade is directed away from the receptive fields of the recorded neurons. Thus, presaccadic activity is observed irrespective of the saccade direction, indicating that it is not target specific. However, such nonspecific presaccadic activity is also observed in oculomotor structures like superior colliculus (7) and prefrontal cortex (19). Therefore to assess whether presaccadic activity in the primary visual cortex is selective for the saccade direction, we compared the strength of the presaccadic responses for the To-RF trials with that of the Away-RF trials.

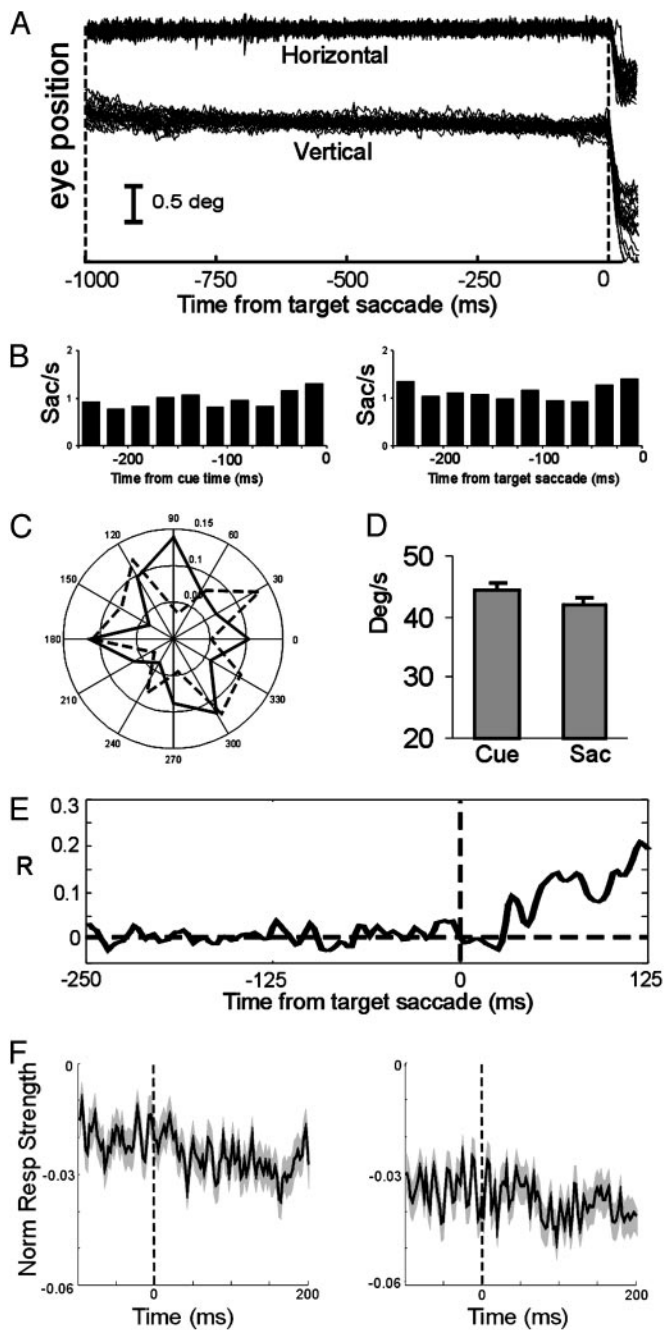


Fig. 4. Eye positions and fixational saccades during visual stimulation. (A) Example of 25 randomly taken trials of the horizontal and vertical eye positions during the fixation period. (B) Frequency of fixational saccades. (C and D) Probability density function of saccade direction (C) and peak velocity (D) of fixational saccades before cue time (thick line, Cue) and before onset target saccade (dashed line, Sac). No differences were found between the two conditions (saccade direction, $P = 0.9$, Kolmogorov–Smirnov test; saccade velocity, $P = 0.13$, t test). (E) Correlation (Pearson) strengths over time between eye velocity and V1 activity. Note that the correlations become positive ≈ 40 ms after saccade onset. (F) Averaged response strength relative to the onset of fixational saccades (dashed vertical lines) during the period before cue time for visual (Left) and memory (Right) trials. Shaded areas represent SEM.

We calculated on a single-trial basis the distribution of the average response strength of the 100-ms period before the onset of the saccade. These results show that 81% (26/32) of the electrodes for the visual task and 63% (20/32) of the electrodes

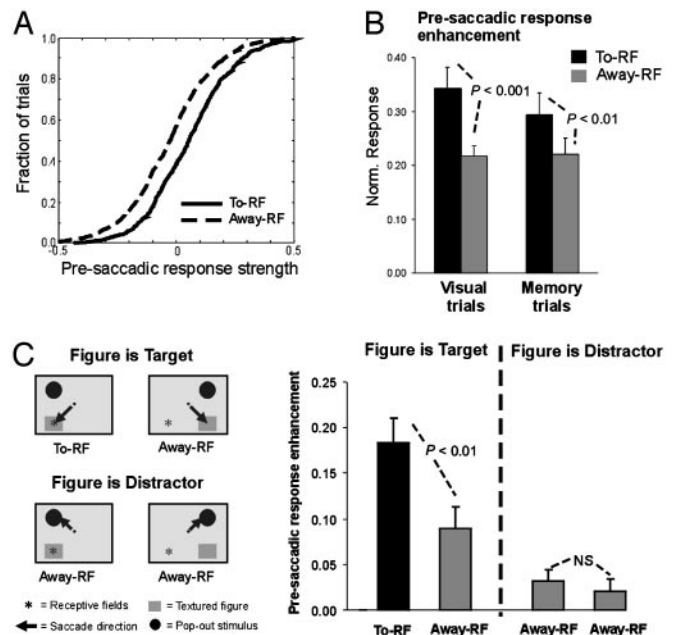


Fig. 5. Presaccadic response strength and enhancement and task configuration. (A) An example of the distribution of presaccadic responses calculated per individual trial. Responses are sorted in ascending order for To-RF and Away-RF trials. (B) Population data of the presaccadic response enhancements for To-RF and Away-RF trials. (C) A blocked task design where the different tasks were done on different days. In each trial two stimuli appeared: a textured figure (gray square) and a red circle (black dot). (Upper Left) In the first set of trials, the textured figure was the target (figure = target condition). (Lower Left) In the second set of trials, the circle was the target (figure = distractor condition). (Right) The corresponding enhancements of the presaccadic responses for the different task designs and conditions.

for the memory task gave significantly stronger presaccadic responses in the To-RF condition than in the Away-RF condition (Fig. 5A; for each individual electrode $P < 0.05$, Wilcoxon rank sum test). The remaining sites showed no significant differences. The stronger presaccadic response in the To-RF condition may be a result of the maintained enhanced figure (To-RF) responses compared to the ground (Away-RF) responses (13), i.e., the continuation of the figure-ground signal until the saccade.

To know whether the enhancement of presaccadic response differs between To-RF trials and Away-RF trials, we subtracted for each electrode the average neural responses of the 100-ms period before the cue time from the average activity of the 100-ms period before the onset of the saccade. This process estimates the strength of the presaccadic response increase. Of all of the electrodes, 91% (29/32) for the visual task and 69% (22/32) for the memory task show a stronger presaccadic response enhancement for To-RF trials than for Away-RF trials ($P < 10^{-4}$ for both conditions separately, paired t test). This result is consistent with the average population data (Fig. 5B). Thus, in the primary visual cortex presaccadic activity is spatially specific, i.e., the responses and the enhancement of the responses are strongest at the saccade target. These findings seem to contrast with previous observations showing no or only weak target selectivity of the responses in the primary visual cortex (17, 20). However, the latter study did not separate sensory responses from saccade-related responses, and their analysis was concentrated on the strength of the visually evoked responses and not on the activity before the start of the saccade. In this respect, their results agree with our findings showing no target selectivity of visually evoked responses. The former study did show saccade-related responses but failed to analyze the spatial selectivity of these responses.

The paradigm we used, however, may provide an explanation for the occurrence of presaccadic responses in Away-RF trials where the saccade is directed away from the receptive fields of the recorded neurons. For example, differences in the design of a detection task can lead to a difference in neural responses within the oculomotor system (21, 22). In our task, the figure appeared randomly in one of three possible locations. These locations were always the same, which may have led to nonspecific resurgent neural interactions caused by stimulus repetition. To test this, we used a blocked, delayed saccade task where the textured figure was either the target or the distractor (Fig. 5C). In the first part of the experiment, the textured figure was the target and a red circle (5–6° eccentricity, 1.50 radius) was the distractor, whereas in the second part, the textured figure was the distractor and the red circle was the target. In the former task, the saccade is always directed toward the textured figure location (To-RF and Away-RF trials), and in the latter case it is always directed away from the figure location.

We calculated the presaccadic response enhancement by measuring the response difference between the activity before cue time and the activity before saccade onset (as described before). The results from the figure = target condition confirm the earlier data in that the presaccadic response enhancement is stronger at the saccade target location (To-RF trials) than at the nontarget location (Away-RF trials), and that in this latter condition the presaccadic responses are nevertheless present. However, in the task where the figure is always the distractor (and thus the saccade is never directed to the receptive fields of the recorded neurons) presaccadic response enhancements are weak. Thus, presaccadic responses in the primary visual cortex are strongest at the saccade target location and are therefore spatially selective.

Furthermore, the stronger presaccadic enhancement of activity for To-RF than for Away-RF trials supports the notion that the presaccadic responses cannot be a general effect of the removal of the fixation point or of eye movements and excludes the possibility that the presaccadic responses are a general effect of arousal or reward, which should also give an equally strong response for these two conditions.

Presaccadic Activity and Reaction Time. To further analyze the possible link between the presaccadic responses in V1 and saccadic behavior, we analyzed the relation between presaccadic activity and the moment of saccade initiation. We divided the visual and memory data into six consecutive reaction time groups of 25-ms bin size each and calculated for all of the reaction time groups the averaged strength of the 10-ms period of the presaccadic activity before the onset of the saccade. This estimates the level of the threshold for initiating a saccade (3). Next, we fitted a linear regression line through these six data points, which reveals whether a relation exists between presaccadic responses and reaction time. For the visually guided saccades, we observed no clear relationship between the threshold activity and reaction time ($R^2 = 0.007$; Fig. 6A), which agrees with previous findings (3). However, for the memory-guided saccades we observed a clear correlation between presaccadic activity and reaction time ($R^2 = 0.89$; Fig. 6B). Thus, here presaccadic responses predict the moment of the saccade where stronger responses result in shorter reaction times.

Discussion

The present results show that neurons in the primary visual cortex start to enhance their activity 100–200 ms before the onset of a visually or memory-guided saccade. Neurons that have their receptive fields on the target location of the saccade show the strongest presaccadic responses. For memory-guided saccades, but not for visually guided saccades, presaccadic activity also predicts the moment of the eye movement where stronger

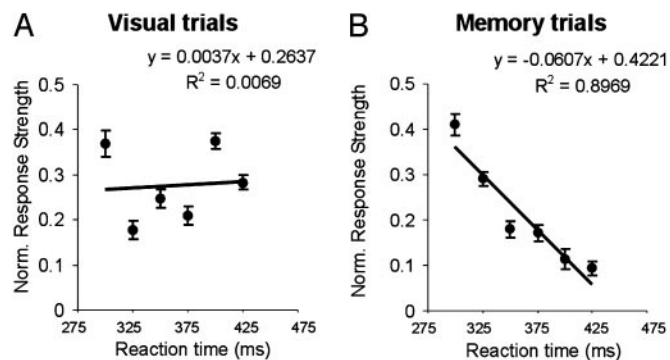


Fig. 6. Strength of the presaccadic activity grouped into six reaction time groups in a visual task (A) and a memory task (B). The line is the regression line, and error bars are SEM.

presaccadic responses lead to faster reaction times. This relation between neural activity and reaction time may reflect attentional modulation, which can differ between visual and memory trials and may change over time (23). For example, in the visual task the visual information remains present, whereas in the memory task it declines over time (13). Thus, presaccadic activity in the primary visual cortex shows a correspondence with the saccade target location and the moment of the eye movement.

The source of the observed presaccadic activity in the primary visual cortex is unknown. However, the spatial specificity, the task dependency, the correlation with reaction time, and the difference between visually and memory-guided saccades herein, rule out that the presaccadic responses can be explained solely by reward, expectancy, arousal, fixation point offset, or small eye movements. Instead the presaccadic responses are similar to the presaccadic responses observed in oculomotor structures during motor preparation. In these structures saccade-related responses emerge ≈ 100 – 200 ms before the onset of a saccade and predict the saccade direction and timing. The observed presaccadic responses in V1 may therefore reflect an efferent copy or a corollary discharge about movement planning in the oculomotor structures (24). However, the enhanced visual responses may also be related to the enhanced visual representation that occurs before saccading (25, 26) and/or represent a shift of attention preceding gaze shift (27–29). Even the enhanced visual signals may be related to phenomena such as visual masking or transsaccadic integration that have been hypothesized to eliminate retinal smear as a consequence of saccading and to produce a stable percept (30). Thus, although the function and the underlying neural mechanisms remain to be investigated, the presaccadic responses in the primary visual cortex appear to be closely related to saccadic behavior.

Previous observations suggest a distinction between the mechanisms that initiate a saccade and the mechanisms that guide a saccade (5, 19, 31–34). At the subcortical level, the superior colliculus is a key structure controlling the oculomotor commands, where the visual analysis and the motor commands are represented in different layers and neurons (6, 32, 35, 36). The superficial layers of the superior colliculus, which contain visual neurons, receive direct projections from the primary visual cortex by means of the large pyramidal neurons of layer 5 (see ref. 35) but the function of this connection has always remained somewhat mysterious.

Findings from earlier studies show that neural activity in the primary visual cortex can be associated with perception (12, 13) and saccade behavior (17, 37–39). Moreover, lesions to the primary visual cortex result in altered saccade metrics (40–42). These and the present findings thus indicate that the primary visual cortex participates in visually guided oculomotor behav-

ior. A possible role of V1 in visuomotor integration is to provide the motor structures with the visual information (1, 2) during motor planning. This notion agrees with studies suggesting that microstimulating the primary visual cortex interferes with saccade processing by disrupting visual processing (43, 44) and is

supported by the recent finding of a relationship between the strength of perceptual activity in V1 and reaction time (45).

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