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Attentional modulation of visual motion processing in cortical areas MT and MST

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The visual system is constantly inundated with information received by the eyes, only a fraction of which seems to reach visual awareness. This selection process is one of the functions ascribed to visual attention[1–6]. Although many studies have investigated the role of attention in shaping neuronal representations in the visual cortex, few have focused on attentional modulation of neuronal signals related to visual motion. Here we report that the responses of direction-selective neurons in monkey visual cortex are greatly influenced by attention, and that this modulation occurs as early in the cortical hierarchy as the level of the middle temporal visual area (MT). Our finding demonstrates a stronger and earlier influence of attention on motion processing along the dorsal visual pathway than previously recognized.

Using standard extracellular techniques, we recorded from neurons in MT and the medial superior temporal area (MST) in the superior temporal sulcus of two behaving macaque monkeys. Both areas contain a high proportion of direction-selective cells[7–9], and their sensory response to moving stimuli has been extensively studied[10]. The animals were trained in a task that allowed us to compare the responses of individual neurons to identical visual stimuli under different attentional conditions. By comparing neural responses only between conditions of identical visual stimulation, and by strictly monitoring fixation with a scleral search coil, we ensured that the differences in neural response between the various attentional conditions were due solely to changes in the behavioural state of the animal.

The stimuli consisted of small bright dots presented on an otherwise dark computer monitor in front of the animal. Each trial began with the presentation of a small fixation cross on the screen (Fig. 1). After the monkey had fixated this cross, a stationary dot appeared somewhere on the screen, generally a few degrees to the left or right of the fixation point. The animal responded by depressing a lever which caused one (experiment 1) or two (experiment 2) other dots to appear. All dots immediately started to move back and forth along straight, non-crossing paths at the same speed (but not necessarily in the same direction). The animal's task was to track the dot that had appeared first (the 'target') (attentionally, rather than with the eyes) and to release the lever quickly when this dot changed speed. The other dots ('distractors') might also change speed, but the trial was terminated without reward if the animal responded to a speed change of

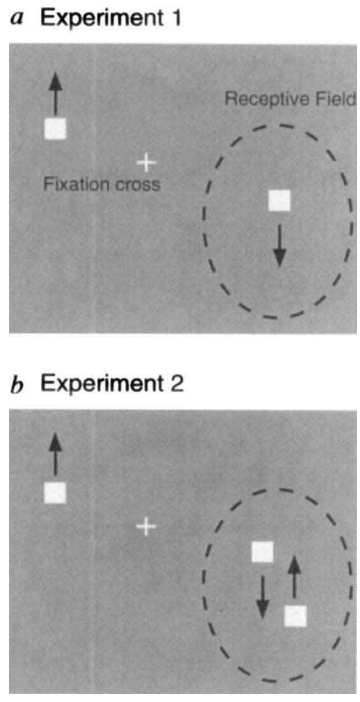

FIG. 1 Stimulus conditions for experiments 1 (*a*) and 2 (*b*). The dashed line is the circumference of the receptive field, plotted by hand using a freely movable dot or light bar while the animal fixated a small spot. The cross marks the fixation spot. *a*, One dot moved through the receptive field along the cell's preferred and null directions while the other dot moved (not necessarily parallel to the first dot) outside the receptive field. *b*, A further dot was added inside the receptive field, moving parallel to but in the opposite direction to the other dot. All dots ($\sim 0.5 \times 0.5^\circ$) travelled along straight paths at a constant speed (roughly matched to a cell's preferred speed) and their directions were reversed at the same time. The animal was instructed which dot to attend to by presenting it alone and stationary at the beginning of the trial. The animal had to depress the lever at this point which would make the other dot(s) appear and all dots would immediately start moving. The magnitude of the speed change was varied between cells roughly to match the performance of the animal for the given receptive field location, size and preferred speed. In experiment 1 the speed increases were about 30–55%. Excluding the trials that were aborted because of an eye movement the average rate of correct responses was 90% (5% target speed change missed; 5% responses to distractor dot or unknown reason). In experiment 2, the animal achieved about 70% correct responses even with speed increases of 40–70% (14% target speed change missed, 10% responses to speed change in a distractor dot, 6% unknown reason). Unless we lost the cell early the number of correct trials per trial type was about 10–20, although the total number varied. Motion trajectories were roughly matched to the size of the classical receptive field, except for the small receptive fields of the MT cells with small eccentricity. The separation of the two paths inside the receptive field in experiment 2 was generally about 0.5 to 2°. Eye positions were analysed to ensure that differences in neuronal responses could not be attributed to fixation differences. The median difference in fixation position between trial types was less than 0.15° for both experiments (receptive fields were rarely less than 6° across).

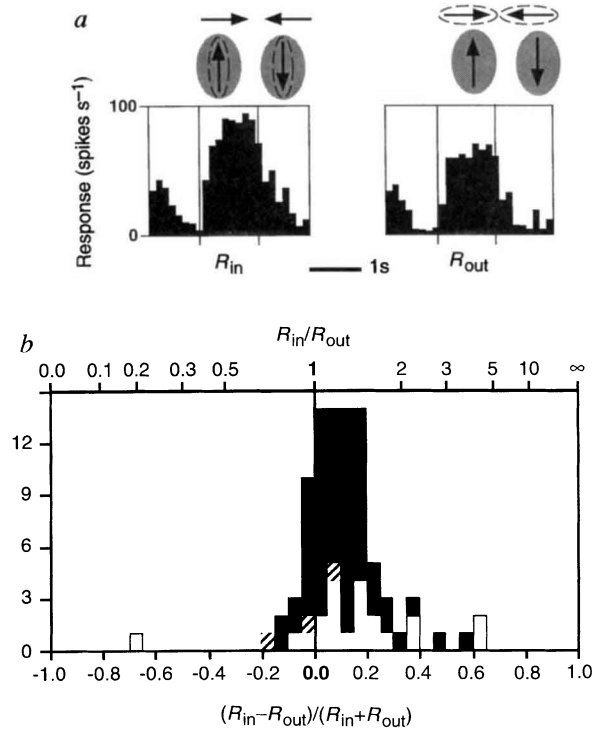

FIG. 2 Effects of attention on responses in experiment 1. *a*, Responses of an isolated neuron in MT, when attending either to the dot inside (left) or outside the receptive field (right). Stimulus motion is shown above, with the attended stimulus encircled by a dashed line and the shaded area symbolizing the receptive field. Vertical lines on the histograms mark the times when the dots reversed direction. The response from the second period, when the dot inside the receptive field was moving in the neuron's preferred direction, was used for the analysis. For this cell the response was about 30% stronger when the receptive-field stimulus was the target. *b*, Stacked histogram showing the strength of attentional modulation for all neurons tested in MT (black bars: 46 cells from animal S and 19 cells from animal D) and MST (grey bars: animal S, 6 cells; animal D, 15 cells) and for the three cells that were either in MT or MST (white bars: all from animal S). An attentional index was computed: $AI = (R_{in} - R_{out})/(R_{in} + R_{out})$, where R_{in} is the response to the preferred motion inside the receptive field when the target dot is the stimulus inside the receptive field and R_{out} is the response to the same visual stimulation when the target is the dot outside the receptive field. The upper *x*-axis shows corresponding ratios of responses (R_{in}/R_{out}). Testing the cells individually with a two-tailed *t*-test only 4 (24%) of the negative indices were significantly different from zero ($P = 0.05$) whereas 44 (61%) of the positive indices were significantly larger than zero. The median modulation was 19% for MT cells and 40% for MST cells. Because the index was on average larger for cells from animal D we tested for the inter-area difference for significance separately for the two animals (two-tailed *t*-test). The difference was significant in animal D. Because of the small number of MST cells from animal S, the difference did not reach significance.

a distractor. Throughout the trial, the animal had to maintain its gaze on the fixation cross. Only those portions of correctly completed trials, before any dot had changed speed, were analysed.

We recorded from 96 direction-selective neurons in the superior temporal sulcus. Histological reconstruction from myelin-stained sections showed that 65 of these cells were in MT, 21 in the lateral or dorsal subdivisions of MST, and 3 in either MT or MST. The remaining 7 cells were excluded form the analysis as they were near the MT/V4 border and could not be assigned to MT with certainty.

When a neuron was isolated, one (experiment 1) or two (experiment 2) dots were positioned to move back-and-forth within its receptive field, with their axis of motion aligned to the cell's preferred direction. Experiment 1 was designed to test the effect of directing attention either inside or outside the receptive field of the cell, while maintaining identical visual stimulation. Figure 2*a* shows the response of a neuron in MT to the back-and-forth motion of the dot within its receptive field, under these two conditions. The left panel is a histogram of the cell's response during trials where the animal was instructed to attend to the dot inside the receptive field (with the distractor outside), and the right panel shows the response when the target was the dot outside the receptive field (with the distractor inside). The visual stimulation was thus kept identical. Like most cells we encountered, this neuron responded more strongly when the stimulus inside its receptive field was the target. The median value for this enhancement was 19% for cells in MT, and 40% for cells in MST. The strength of attentional modulation for all sampled MT and MST cells is summarized in Fig. 2*b*.

In the second experiment an additional dot was presented inside the receptive field, moving parallel to the other dot, but always in the opposite direction. On a given trial, any one of the three dots could be the target. The responses of most neurons depended greatly on which of the dots was the target. The responses of one MT cell are shown in Fig. 3*a*. When the animal was instructed to attend to either of the dots in the receptive field, the neuron responded most strongly when that dot moved in the cell's preferred direction (upwards). When the other dot in the receptive field was the target, the phase of the response changed, so that the neuron now responded most strongly when that other dot was moving in the preferred direction. Thus, the neuron encoded the movement of the target, even if a more powerful sensory stimulus was present in the receptive field. When the animal was cued to attend to the dot outside the receptive field, the neuron maintained a relatively steady level of activity, between the level of responses to the preferred and null motion direction alone, as observed in the first experiment, when the animal attended to the dot outside the receptive field. This intermediate level of activity reflects the previously observed response suppression in MT using transparent stimuli[11]. When the target moved in the null direction inside the receptive field the response of the neuron was depressed below that evoked when the target was outside the receptive field.

We quantified the strength of the attentional modulation in experiment 2 by comparing for each neuron the response during the second phase of motion, while one or the other receptive field dot was the target. The index distributions in Fig. 3*b* show that almost all MT and MST neurons responded most strongly when the attended dot was travelling in the preferred direction. The median enhancement was 86% for MT and 113% for MST, that is, the neural response was roughly doubled when the stimulus moving in the preferred direction was the target dot.

These results demonstrate a powerful effect of attention on the processing of visual motion information. The responses of neurons in MT and MST are reduced when attention is directed to a stimulus outside their receptive fields. When one of two dots moving inside the receptive field is the target, the responses of the cells depend primarily on the movement of that stimulus. The influence of the distractor dot is much reduced, even if it is a more powerful sensory stimulus. Earlier reports have described extraretinal effects in areas in the dorsal pathway beyond MT (MST, Areas 7 and 7a (refs 12–16); and in positron emission tomography (PET) studies of human parietal cortex[17,18], but previous single-unit studies failed to find evidence for appreciable systematic extraretinal effects in MT[14,19,20]. In contrast, we found robust attentional effects in most of the neurons we encountered in this area. It is likely that this difference is due to differences in the tasks employed. In particular, our first experiment, which uses a design similar to many previous studies, shows a much smaller

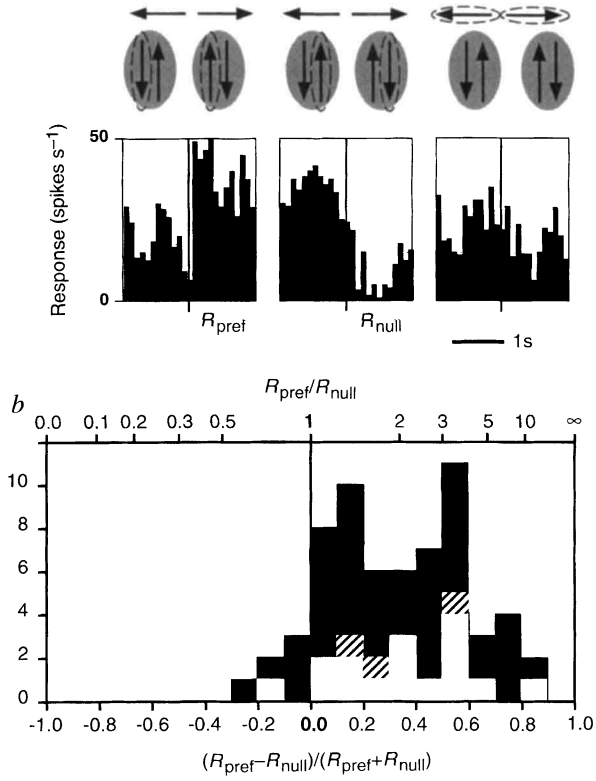

FIG. 3 Responses with two dots inside the receptive field. *a*, Responses of a neuron in MT during experiment 2, when three dots were presented. The left and central histograms show responses when the animal had been instructed to attend to either of the two dots in the receptive field, the right histogram plots responses when the target was the dot outside the receptive field. The axis of motion of the dot outside the receptive field relative to the axis of motion of the dots inside varied from cell to cell. When the target dot was inside the receptive field, the response of the neuron was strong whenever that dot (circled) moved in the preferred direction. The activity was relatively unmodulated at an intermediate level when the animal was attending to the dot outside the receptive field (shown for reference only, and not used for analysis). *b*, Stack histogram of the attention index for the subset of cells (44MT cells; 16MST cells) from experiment 2 (labels as in Fig. 2). Each index is computed using the average rate of firing, when the target dot was moving in the preferred direction (marked R_{pref}) inside the receptive field, compared with the response when the animal was attending to the dot moving in the null direction (marked R_{null}) inside the receptive field. The median modulation was 86% for MT cells and 113% for MST cells. This difference in modulation was significantly different between these two cell types in animal D, while it was not significant in animals because of the small MST sample. Testing the cells individually with a two-tailed *t*-test, only 1 (17%) of the negative indices was significantly different from zero $P < 0.05$ whereas 47 (82%) of the positive indices were significantly larger than zero.

attentional effect in MT than experiment 2, which uses differential attention within the receptive field. Our results are in agreement with a functional magnetic resonance imaging study showing attentional modulation located in a region believed to contain the human homologues of areas MT and MST[21] during a motion attention task. Modulations of responses to colours or oriented bars have also been described in the early stages of the ventral pathway in visual cortex[22–24], although differences between attention inside and outside the receptive field, are not seen in all cases[23].

The stronger attentional modulation that we found in MST compared with MT indicates that extraretinal influences may increase in successive levels of cortical processing, such that there is a progression from the purely sensory representations in the first stages of the retinocortical pathway to representations in later extrastriate cortex in which extraretinal factors have a powerful, perhaps even dominating, influence. At the same time, our demonstration of robust attentional effects in MT–an area which receives direct input from primary visual cortical area V1 (refs 25, 26)—suggests that responses of neurons throughout much of the extrastriate cortex are substantially influenced by behavioural state, and that an understanding of visual information processing even in early extrastriate cortex requires approaches that do not concentrate solely on the sensory qualities of the visual input. □

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Reversal of apoptosis by the leukaemia-associated E2A–HLF chimaeric transcription factor

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THE *E2A–HLF* (for hepatic leukaemia factor) fusion gene, formed by action of the t(17;19) (q22;p13) chromosomal translocation, drives the leukaemic transformation of early B-cell precursors[1–4], but the mechanism of this activity remains unknown. Here we report that human leukaemia cells carrying the translocation t(17;19) rapidly died by apoptosis when programmed to express a dominant-negative suppressor of the fusion protein E2A–HLF, indicating that the chimaeric oncoprotein probably affects cell survival rather than cell growth. Moreover, when introduced into murine pro-B lymphocytes, the oncogenic E2A–HLF fusion