in the figure legends). The stimuli were generated on a Mitsubishi colour monitor at 120 Hz by a computer-controlled framestore (Cambridge Research Systems VSG). Horizontal eye movements were monitored by an infra-red eye tracker (HVS Image Ltd), and actual delay of target presentation (with respect the saccade onset) were determined after each trial by computer. For the results shown in Figs 1–3, the bar was equiluminant with the background (as these stimuli are not suppressed during saccades[16]); the same pattern of results has been obtained with light or dark bars.

Vernier annulment. For the vernier annulment task, the top half of the bar was briefly displayed 75 ms before or after the bottom half, and physically misaligned. Observers reported whether the top half appeared displaced to the left or right. Adaptive routines adjusted the physical offsets at each display time, based on the previous responses. Final thresholds were estimated by fitting a cumulative gaussian to the probability-of-seeing curves, comprising 80–250 data points. The standard deviation of the gaussian which gives an estimate of error, was on average 0.7°, and did not vary systematically with display time.

Model. To simulate the data of Figs 1–4, we assume that apparent visual direction P of any point x in external space is given by:

$$P(x, t) = E(x, t) \times C(x, t) + O(t) \quad (1)$$

$E(x, t)$ is retinal eccentricity (the difference between physical external space and eye position); $C(x, t)$ is a compression function weighting the eccentricities; $O(t)$ is an 'extra-retinal' signal, that can be considered to set the origin of the internal representation of space, usually given by eye position (ignoring head movements for now). On each saccade, $O(t)$ changes gradually, following the sum of the fade-out and fade-in functions that weight the present and future eye position:

$$O(t) = F_0\left(1 - \int^{t} e^{-\frac{(\tau - \tau_0)^2}{2\sigma_0^2}} d\tau\right) + F_1 \int^{t} e^{-\frac{(\tau - \tau_1)^2}{2\sigma_1^2}} d\tau$$

The function $C(x, t)$ is given by

$$C(x, t) = e^{-k\left|E(x,t)[O(t) - Y(t)]/(F_0 - F_1)\right|^{\beta}}$$

where k is a constant and $Y(t)$ is eye position. $C(x, t)$ bears a similarity to the inverse of the cortical magnification function[22] (and may reflect a visual process designed to compensate for it). The free parameters in the equations were adjusted to achieve best fits to all the data for both subjects: $\sigma_0 = 30$ ms, $\sigma_1 = 38$ ms, $\tau_0 = 20$ ms, $\tau_1 = -40$ ms, $k = 1.48$, $\beta = 1.35$.

Received 7 June 1996; accepted 29 January 1997.

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Acknowledgements. This work was supported by the Australian ARC and the Italian CNR. We thank Stephen Peter for permission to use the photograph in Fig. 4.

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Perceived geometrical relationships affected by eye-movement signals

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To determine the location of visual objects relative to the observer, the visual system must take account not only of the location of the stimulus on the retina, but also of the direction of gaze[1]. In contrast, the perceived spatial relationship between visual stimuli is normally assumed to depend on retinal information alone, and not to require information about eye position. We now show, however, that the perceived alignment of three dots—tested by a vernier alignment task[2,3]—is systematically altered in the period immediately preceding a saccade. Thus, information about eye position can modify not only the perceived relationship of the entire retinal image to the observer, but also the relations between elements within the image. The processing of relative position and of egocentric (observer-centred) position may therefore be less distinct than previously believed[4–6].

Our perception of a stable visual world is achieved, in part, by computing the egocentric position of stimuli through summing their retinotopic location with an internal representation of the direction of the eye[6]. However, this process is not always perfect and can sometimes lead to mislocalization. Hence, if a flash is presented shortly before a saccade, owing to the large delay in the afferent visual pathway (up to 100 ms), the internal representation of the eye position may have already started to change in the saccade direction by the time the visual signal reaches the cortex. The spatial location of the visual stimulus would then be miscalculated[7]. Indeed, it is known that a single point of light flashed within a critical period (about 100 ms) before a saccade is perceived as displaced in the direction of the saccade (a phenomenon called presaccadic mislocalization)[7–10]. It has also been shown that a continuously lit spot of light, starting before the critical period and extinguished before saccade onset, is not mislocalized, presumably because its stable location has already been established[10].

We investigated whether the perception of the relative position of nearby dots can be affected by the imminence of a saccade. We used a 3-dot vernier test in which the lower and upper dots were continuously lit until the presentation of the middle dot (for 4 ms), and then all three dots were extinguished together (Fig. 1, and see Methods). We carried out this test during the latency period of a visually evoked saccade (saccade trial) and compared the results with those obtained in the absence of an impending saccade (the

subject kept fixating). In each no-saccade trial, the positions and the timing of all visual stimuli duplicated those of a saccade trial (matched trials). The eye position was monitored by an infrared eye tracker. Only those saccade trials in which all visual stimuli were presented and extinguished before the eyes started to move were compared with no saccade trials. This ensured that the same visual stimuli were delivered onto identical retinal spots across conditions. Consequently, any difference of judgement must be of extraretinal origin.

When several visual stimuli are concurrently on the retina, the retinal information alone suffices to specify completely their relative positions and, as far as we know, in previous studies there has been no indication that extraretinal factors may be involved in such a situation. A distortion of vernier alignment by presaccadic mislocalization would indicate, however, that the perception of relative position is also dependent upon an extraretinal factor, even though the latter is in principle not needed.

Five human subjects (4 naive, 1 author) with normal or corrected vision were tested. For stimuli presented within 100 ms before a saccade, four of the five subjects showed large bias shifts in their vernier curves from the no-saccade positions (shifts ranging from 52′ to 59′ before 4° rightward saccades; Fig. 2). The fifth naive subject (A.K.) had a smaller shift (42′). The shift was such that the middle dot always appeared to be displaced in the direction of the saccade. Two of the subjects were tested further in a complementary situation, in which the display was to the left and 4° leftward saccades were made. Again, the middle dot was displaced in the same direction as the saccade (63′ and 45′). Thus, in all cases the direction of the shift was consistent with the direction of the presaccadic mislocalization observed previously[7–10] (except in a recent study conducted under very different experimental conditions[11]). Vernier acuity (slope) varied across subjects, but differed little between saccade and no-saccade conditions within the same subject.

Could the observed shifts be caused by saccadic suppression[12], rather than presaccadic mislocalization? This seems unlikely as saccadic suppression would predict shallower vernier curves but not a systematic directional shift in the curves. Another explanation would attribute our results to a covert attention shift before the saccade. If this were correct, the same shift would occur with or without an overt saccade[13]; however, our no-saccade condition, used as a baseline, has demonstrated the dependence of the shifts on the occurrence of overt saccades.

To verify further that the observed vernier shifts were caused by presaccadic mislocalization, we did two additional experiments. In the first, we flashed all three dots at the same time shortly before the saccade. If the observed vernier shift is indeed due to presaccadic mislocalization, it should now disappear, because all three dots should be mislocalized by the same amount. This prediction was tested in three subjects (Fig. 3a): for all three, the shift before saccade disappeared completely. In the second experiment, we exploited the finding that under our conditions the presaccadic mislocalization begins at ~100 ms before the saccade onset[8–10]. If the observed vernier shift is due to presaccadic mislocalization, the shift should not exist before this time. We tested this prediction in four subjects. The experiment was similar to that shown in Fig. 2, but instead of flashing the middle dot very close to saccade onset, it was flashed (and subsequently all three dots extinguished) more than 100 ms before saccade onset. As predicted, there was no systematic vernier curve shift between the saccade and no-saccade trials under this condition (Fig. 3b–d).

These two experiments showed that an impending saccade, by itself, is not sufficient to create a vernier curve shift. A specific set of stimulus characteristics and timing conditions, consistent with the

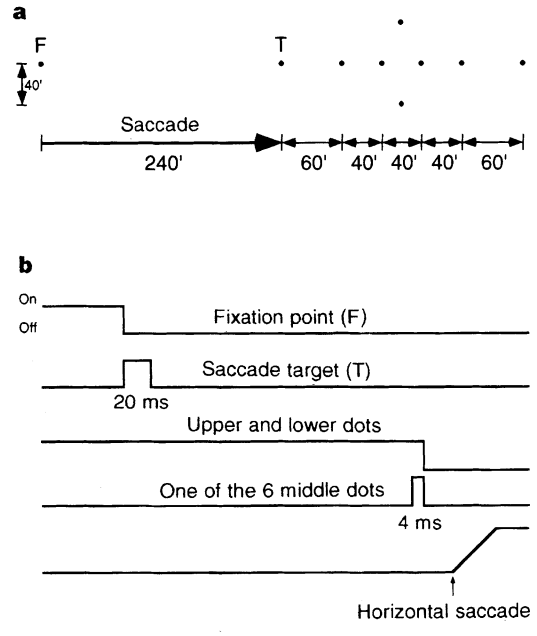

Figure 1 **a**, Stimulus locations drawn to scale (for all experiments). **b**, Stimulus timing (for Figs 2 and 3b, c).

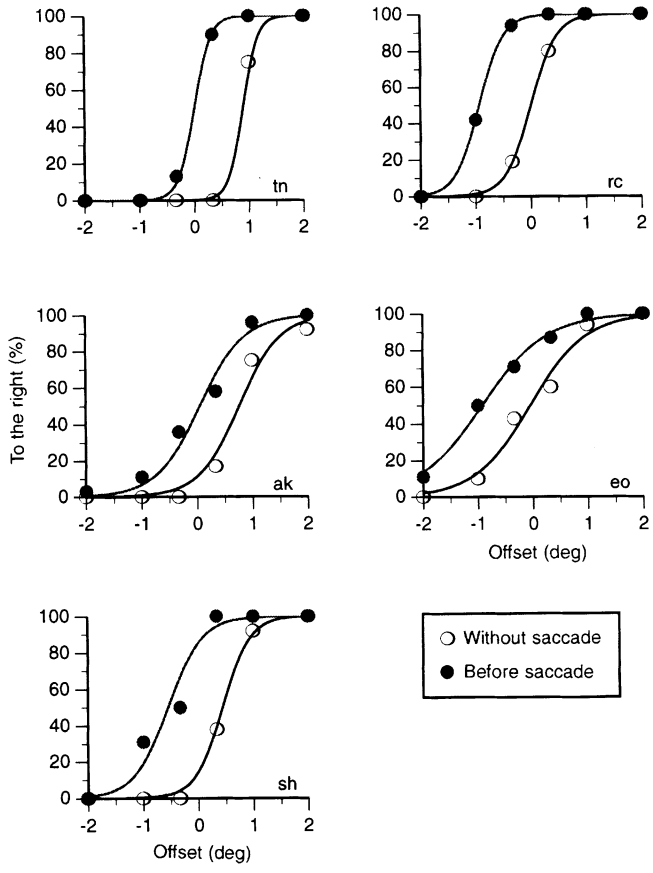

Figure 2 Shift of vernier curves within 100 ms before 4° rightward saccades for all five subjects. Abscissa: horizontal offset of the middle dot from the lower and upper dots (+ is to the right). Ordinate: percentage of seeing the middle dot to the right of the lower and upper dots. The lower and upper dots are lit from the beginning of the trial, the middle dot is flashed (Fig. 1b). The saccade curve is based on trials in which the middle dot flashed within 100 ms before the saccade onset. The saccade and the no-saccade curves are based on matched trials (see text). Constant errors (non-zero bias of no-saccade curves) exist in three subjects, as have been observed elsewhere[29]. The vernier curve shift is consistent across subjects, regardless of how much constant error each subject has.

mislocalization explanation, is also required for the shift to occur. These results also rule out the possibility that the vernier curve shift could be due to a motor response bias, conceivably created by imminent saccades always in the same direction.

Relative position judgement has been studied with both foveal[14,15] and extrafoveal stimuli[16,17]. In both cases, the subjects' performance has been explained by mechanisms operating at early stages of visual processing[16,17]. Most electrophysiological studies in this area have also been centred on the retinotopic neuronal responses in structures such as the primary visual cortex (V1) and the lateral geniculate nucleus[18–20]. The alignment of visual stimuli can be biased by other retinal cues, however, particularly those related to image motion[21,22]. Such results raise doubts about the exclusive dependence of vernier alignment upon the responses of striate neurons[22], but they agree with the idea that the perception of vernier alignment is entirely derived from the retinal input, because only visual variables were manipulated in these experiments. Here, by contrast, without any change in the visual input, we have shown that an extraretinal factor suffices to alter the perception of vernier alignment. To our knowledge, previous results never indicated that the perception of relative position could depend on neurons combining retinal and extraretinal signals. One possibility is that the calculation of vernier alignment is not completed—or at least the final decision not made—until a higher cortical area is reached, such as the parietal cortex, where a large percentage of visually responsive neurons are modulated by the eye position[23], and where the receptive fields of some neurons are shifted shortly before a saccade[24]. Alternatively, an extraretinal signal may enter early visual areas, altering the retinotopic responses of visual cells. Neurons modulated by eye position have been reported in V1 (refs 5 and 25) and V3A (ref. 4), and modelling studies have suggested that such early modulation can perform a spatial-processing function similar to that found in the parietal cortex[26,27]. Both of these possibilities suggest that the processing of relative position and the processing of egocentric position are more closely related than was previously thought[4–6]. □

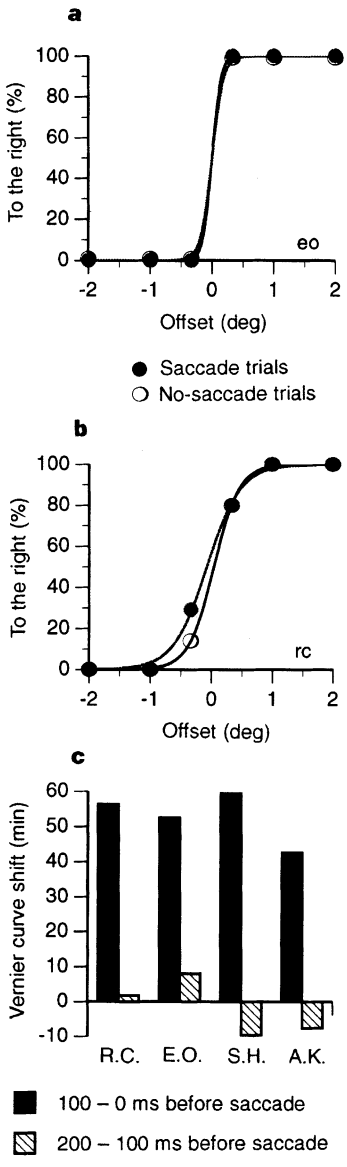

Figure 3 a, Lack of vernier curve shift when all three dots simultaneously flashed within 100 ms before 4° rightward saccades (two curves overlap). One subject's data are shown here (all three subjects' data similar). The vernier curve is steeper than that in Fig. 2. This is consistent with the finding that the highest vernier acuity is achieved with synchronous stimulus onset and offset[28]. (The precise slope is beyond the resolution limit of our display apparatus.) **b**, Vernier curve shifted little when the middle dot flashed between 200 and 100 ms before saccade onset (subject R.C.). **c**, Amount of vernier curve shift (shift in point of subjective equality) in early and late latency period for all four subjects tested. Same experimental conditions as for Fig. 2.

Methods

The subject sat in total darkness with the head immobilized by a bite plate, 130 cm away from the visual display. The eye movements were recorded with an Ober2 infrared eye-orbit scanner. The viewing was monocular (right eye). All visual stimuli were small green light-emitting diodes (LEDs) ($r = 0.06$ deg). The top and bottom dots were vertically aligned and served as reference points; the middle dot took one of six possible horizontal positions (Fig. 1). The luminance of the outer dots was 100 cd m^{-2}, and the middle dot (flashed) was adjusted to have the same subjective brightness. At the beginning of a saccade trial, a central fixation point (straight ahead) and the upper and lower reference dots (at 6° to the right) were turned on. After the computer determined that the eyes had been steadily on the fixation point for a duration that was randomly varied between 700 and 1,800 ms (to prevent anticipatory saccades), the fixation point was turned off and the saccade target was flashed for 20 ms at 4° to the right. The subject was to saccade towards this target as soon as possible (average saccade latency was ~200 ms). The saccade onset time was predicted from the average saccade latency of the past 4 trials. Some time before this predicted onset (20–30 ms for Figs 2 and 3a; 100–200 ms for Fig. 3b–d), the middle dot was flashed for 4 ms. All three dots were then extinguished at the same time. This method produced an average 88.2% of saccade trials in which all visual stimuli were presented before the saccade onset (Fig. 2). After the saccade, the subject reported, by pressing one of the two buttons, whether the middle dot appeared to the left or right of the upper and lower dots. In no-saccade trials, the exact same sequence of visual stimuli was displayed while the subject was instructed to keep fixating. Saccade and no-saccade trials were run in separate blocks of 200 trials per block. Only one block was run on a given day to prevent fatigue.

The vernier display was not placed at the site of fixation because the subjects found it very difficult to pay attention to the foveal vernier test, while at the same time attempting to move the eyes quickly toward a peripheral saccade target. Thus, the vernier display was placed close to the saccade target. The larger the saccade, the greater the magnitude of mislocalization. But as the vernier display needs to be placed close to the saccade target, a larger saccade would also mean a more peripheral vernier display, and hence poorer vernier acuity. After repeated trials, we found that placing the display at 6° best satisfied the requirements of the experiment. The optimum dot separation depends on eccentricity[16] and we found 40′ to be a good choice for our specific test conditions.

Received 3 March; accepted 14 March 1997

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Acknowledgements. We thank D. Bavelier and J. Thomas for their comments and valuable help. This work is supported by the US National Eye Institute.

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Temporal dynamics of brain activation during a working memory task

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Working memory is responsible for the short-term storage and online manipulation of information necessary for higher cognitive functions, such as language, planning and problem-solving[1,2]. Traditionally, working memory has been divided into two types of processes: executive control (governing the encoding manipulation and retrieval of information in working memory) and active maintenance (keeping information available 'online'). It has also been proposed that these two types of processes may be subserved by distinct cortical structures, with the prefrontal cortex housing the executive control processes, and more posterior regions housing the content-specific buffers (for example verbal versus visuospatial) responsible for active maintenance[3,4]. However, studies in non-human primates suggest that dorsolateral regions of the prefrontal cortex may also be involved in active maintenance[5–8]. We have used functional magnetic resonance imaging to examine brain activation in human subjects during performance of a working memory task. We used the temporal resolution of this technique to examine the dynamics of regional activation, and to show that prefrontal cortex along with parietal cortex appears to play a role in active maintenance.

Neurologically normal subjects (5 males, 5 females; ages 18–34) were scanned while performing a sequential-letter memory task (Fig. 1). This task has reliably produced activation of cortical regions that are believed to be involved in working memory.[9,10] Memory load was varied parametrically to identify these regions sensitively[11]. In addition, the rate of stimulus presentation was slowed in order to acquire multiple scans during each trial, and thereby track the dynamics of activation (Fig. 2). We reasoned that temporal information, together with the manipulation of memory load, would provide new information permitting a finer analysis of the cognitive functions associated with activated regions than has previously been possible. Specifically, we predicted that sensory and motor processes (ones not involved in working memory) would exhibit transient increases in activation associated with stimulus presentation and response execution (peaking after a delay of about 5 s, as a result of the well-characterized lag in haemodynamic response[12–14]), but should not vary as a function of memory load. We predicted that the areas involved in working memory would vary as a function of memory load, with greater activation at higher levels of load. Furthermore, we predicted that such load-sensitive areas would dissociate into two types: those involved in active maintenance would exhibit sustained activation throughout the trial, whereas those involved in other working memory functions (assumed to be time-limited, such as updating working memory contents, decision processes and so on) would exhibit transient activation (such as sensory and motor processes) but would peak higher (or last longer) at higher levels of load. Thus these areas would show an interaction between the effects of time and load.

Our findings, from pooled data for 10 right-handed subjects, reveal each of the patterns predicted above (Fig. 3). As expected, regions within visual, motor and somatosensory cortex all exhibit strong effects of time, but no effect of memory load (see Table 1 and Fig. 3a). Motor and somatosensory regions are left-lateralized, consistent with right-handed response. The time course of activation in all of these regions concurs with other studies focusing specifically on these systems[12,13] and validates our ability to track the dynamics of activation using this method.

The distribution of regions showing sensitivity to memory load corresponds well with previous observations using this task[10,11] and with structures thought to be involved in working memory. These include dorsolateral prefrontal cortex (PFC), more posterior and inferior regions of frontal cortex (including Broca's area), and posterior parietal cortex. As predicted, however, two different temporal patterns are evident among these regions. Within anterior frontal cortex, including dorsolateral PFC (BA46/9), only regions showing an effect of load are observed but none showing an interaction with time (Table 1 and Fig. 3b). Such regions are also observed within more posterior structures, including Broca's area (BA44) and posterior parietal cortex (BA40), but in posterior areas they co-occur with (and sometimes are directly adjacent to) other regions that show an interaction between load and time (Fig. 3c).

The pattern of activation observed within dorsolateral PFC (greater with higher levels of load, and sustained throughout the trial) is consistent with a role in the active maintenance of information in working memory. This suggests that PFC is not exclusively