Visuomotor Transformations for Reaching to Memorized Targets: A PET Study

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Positron emission tomography (PET) was used to identify cortical and subcortical regions involved in the control of reaching to visual targets. Regional cerebral blood flow (rCBF) was measured in eight healthy subjects using $H_2^{15}O$ PET during the performance of three different tasks. All tasks required central fixation while a 400-ms target was flashed every 5 s at a random location around a virtual circle centered on the fixation target. Additional instructions differed according to the task: (i) *visual detection* of the target without overt responses; (ii) *immediate pointing* to the most recent target in the sequence, and (iii) *pointing to the previous* target in the sequence. By design, the two motor tasks differed in the cognitive processing required. In each trial of *immediate pointing,* the spatial location of only the most recent target needed to be processed. In each trial of *pointing to the previous,* instead, while the most recent target was stored in memory for the movement of the next trial, the previous target had to be retrieved from memory to direct the current movement. Limb trajectories were comparable between the two motor tasks in terms of most spatiotemporal parameters examined. Significant rCBF increases were identified using analysis of covariance and *t* statistics. Compared with *visual detection* there was activation of primary sensorimotor cortex, ventrolateral precentral gyrus, inferior frontal gyrus in the opercular region, supramarginal gyrus, and middle occipital gyrus, all these sites in the hemisphere (left) contralateral to the moving limb, and cerebellar vermis, during both *immediate pointing* and *pointing to the previous.* During *immediate pointing* there was additional activation of left inferior parietal lobule close to the intraparietal sulcus, and when compared with *pointing to the previous,* dorsolateral prefrontal cortex bilaterally. During *pointing to the previous,* instead, there was additional activation of supplementary motor cortex, anterior and midcingulate, and inferior occipital gyrus in the left hemisphere; superior parietal lobule, supramarginal gyrus, and posterior hippocampus in the right hemisphere; lingual gyri and cerebellar hemispheres bilaterally; anterior thalamus; and pulvinar. The activation of two partially distinct cerebral networks in these two motor tasks reflects the different nature of signal processing involved. In particular, the specific activation of intraparietal sulcus and prefrontal cortex in *immediate pointing* appears characteristic of a network for visuospatial working memory. By contrast, the corticolimbic network engaged in *pointing to the previous* could mediate spatial attention and the sequence of encoding, recoding, and decoding of spatial memories required by a dual task with two competing targets. © 1997 Academic Press

INTRODUCTION

Reaching for a visual target involves a process of coordinate transformations (Flanders *et al.,* 1992; Lacquaniti, 1997). Psychophysical evidence in man (Flanders *et al.,* 1992) and electrophysiological data in the monkey (Lacquaniti *et al.,* 1995) indicate that, in the process of translating sensory information about target and limb position into motor commands, the brain codes spatial information for reaching in an egocentric frame of reference. The cortical networks that may underlie these coordinate transformations have begun to be elucidated in the monkey (cf. Jeannerod *et al.,* 1995), but are still poorly known in man. Clinical studies of brain-damaged patients provide one approach (Perenin and Vighetto, 1988). Functional neuroimaging provides an alternative approach, especially relevant to the study of healthy brain (Ungerleider, 1995). There have been a number of studies

reporting changes in rCBF during various limb movements under visual guidance. Kawashima *et al.* (1994) compared the changes in motor and premotor areas in preparation for reaching and actual reaching. A full description of the cortical networks activated has been provided for tracking a moving target with the finger (Grafton *et al.,* 1992), handwriting (Seitz *et al.,* 1994), keypress in response to visuospatial detection (Haxby *et al.,* 1994), preparation for reaching (Decety *et al.,* 1992), actual reaching (Grafton *et al.,* 1996), visuomotor learning (Kawashima *et al.,* 1995), and imaginary movements (Decety *et al.,* 1994; Stephan *et al.,* 1995). A number of regions of activation have been identified by these studies, delineating a basic network for visuospatial analysis and visuomotor transformations. This network is composed of areas along the dorsal stream of the visual corticocortical pathways (Ungerleider and Mishkin, 1982) feeding into motor and premotor areas.

A different but related issue concerns the networks involved in processing memorized information about the spatial location of a target seen previously. A number of studies have addressed this issue in the context of working memory paradigms (cf. Ungerleider, 1995). In monkeys, working memory has typically been studied in either delayed response or delayed matching-to-sample tasks (Goldman-Rakic, 1987). In both cases, a brief cue is given initially to be maintained in memory during a delay of a few seconds. At the end of the delay, the monkey must make a response based on the previous cue. Many neurons in dorsolateral prefrontal cortex exhibit a maintained discharge during the delay period (Fuster, 1988; Goldman-Rakic, 1988), discharge which is often related to the retinocentric location of the memorized target (Funahashi *et al.,* 1993). Participation of dorsolateral prefrontal cortex in visual working memory has been also verified in man by means of PET studies (Jonides *et al.,* 1993; Petrides *et al.,* 1993; Smith *et al.,* 1995) and functional MRI involving delay tasks (McCarthy *et al.,* 1994).

Simple delay paradigms, however, are not suitable to test alternative modes of functioning of spatial memory. When concurrent processing of multiple spatial locations is required by the task, memory may not be allocated to a single locus at a time. Consider the case of sequential actions, in which each segment of the sequence is contingent upon the accomplishment of the previous segment. Under such circumstances, vision is often used in an anticipatory fashion relative to the corresponding movement: vision explores the spatial locus for the next movement, while the current movement is directed to the spatial locus previously attended by vision and stored in memory. If the buffer of visuospatial working memory had to be shared to store the current target for the next movement and to retrieve simultaneously the previous target to direct the current movement, performance would be degraded because of the competition between the two targets, as it occurs in the interference or dual tasks of psychology (Brooks, 1967; Baddeley, 1992). A more efficient mechanism could consist, instead, in recoding the location of the current target in a cognitive representation of external space prior to memory storage and decoding the memorized location of the previous target to direct the next movement. This sequence of events may engage corticolimbic networks (Sakai and Miyashita, 1993).

The aim of the present study is to identify the cortical and subcortical regions which participate in the control of reaching to visual targets. In one task, subjects pointed to the most recent target in the sequence, whereas in the other task they pointed to the previous target in the sequence. Both tasks involved central fixation (to avoid eye movements), stimuli in randomized directions of the perifoveal field, comparable motor responses, and constant pacing of both stimuli and responses. In immediate pointing subjects must process only the most recent target. In pointing to the previous, instead, they must retrieve the previous target from memory to direct the current movement, but they also have to store the most recent target in memory for the movement of the next trial. The presentation of each new target represents a distractor for the retrieval of the previous target from memory, but cannot be ignored because it needs to be memorized for the movement of the next trial. Thus, the two targets compete between each other for engaging the buffer of working memory.

MATERIALS AND METHODS

Apparatus and General Procedures

Experimental protocols and procedures were approved by the H. S. Raffaele Hospital Ethics Committee and conformed with the Declaration of Helsinki on the use of human subjects in research. Eight normal right-handed subjects (seven males and one female; age, 30 ± 12 years) participated in the experiments. All had normal or corrected-to-normal visual acuity and reported good health. Handedness was assessed by a short questionnaire based on the Edinburgh scale. Written informed consent was obtained prior to participation.

Visual stimuli were presented on a 14-in. color monitor (640×480 pixels, 60 Hz, P22 phosphor, HP Vectra 33 MHz). Subjects viewed the display binocularly in a darkened room and fixated a central spot that was constantly lit, at a 76-cm distance. A 400-ms-duration peripheral target was flashed every 5 s at a location that was randomly chosen among 24 possible locations equispaced around a 7-cm-radius virtual circle centered on the fixation target (Fig. 1). Identical target locations in two consecutive trials were not allowed by the randomization procedure. The peripheral targets had a constant eccentricity of 5.2° of visual angle but a
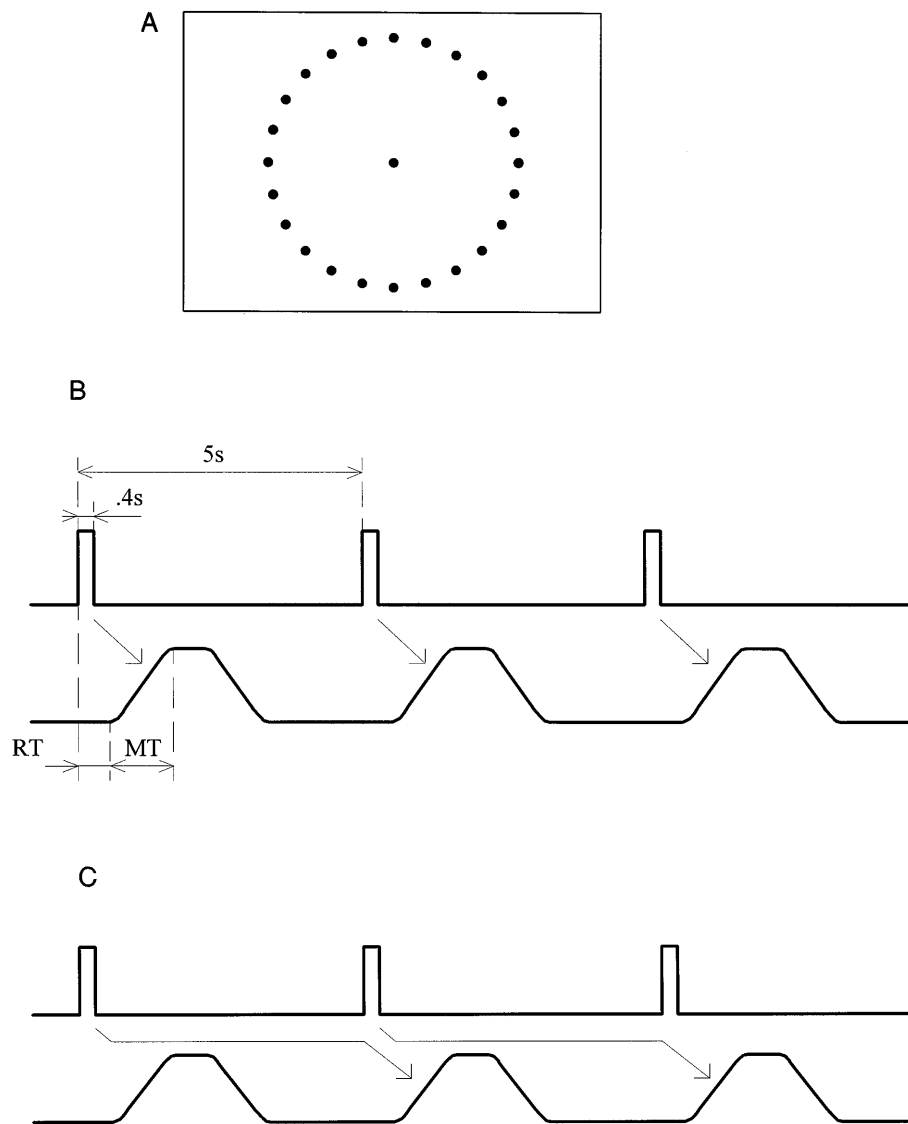
FIG. 1. Schematic of the experimental tasks. (A) Spatial arrangement of the visual stimuli. Targets were flashed randomly at one of 24 possible locations equispaced around a 7-cm-radius virtual circle centered on the fixation point. Target eccentricity was 5.2° and target direction was between 0 and 345° relative to the central point. (B and C) Temporal sequence of events. In all three tasks, subjects were instructed to maintain fixation on the central spot and to detect the location of 400-ms-duration targets flashed every 5 s. In *visual detection,* subjects did not respond overtly. In the two motor tasks, they were asked to move a hand-held cursor from the central spot to a peripheral target, to remain there briefly, and then return to the central spot. The target to be captured was the most recent target in the task of *immediate pointing* (B), whereas it was the previous target in the sequence in the task of *pointing to the previous* (C). Thus, in *immediate pointing,* subjects had to process only the most recent target, whereas in *pointing to the previous* they had to retrieve the previous target from memory, while they stored the most recent target in memory for the next trial. RT, reaction time defined as the time interval from target onset to movement onset. MT, movement time defined as the time interval from movement onset to the target-holding time.

variable direction between 0 and 345° relative to the central spot. Both the central spot and the peripheral targets were 0.35-cm-radius filled circles (subtending a visual angle of 0.5°) displayed on black background (3.9 cd/m² luminance, 0.36–0.33 xy coordinates): the central fixation spot was white (71.6 cd/m², 0.29–0.30), and the peripheral targets were yellow (67.9 cd/m², 0.41–0.50).

Subjects moved a stylus (closely resembling a ball-point pen) held by the right hand on an electromagnetic digitizing tablet (CalComp DrawingBoard II Model 33180; size, 30.5–45.7 cm) that was placed at a 90° angle, below and in front of the screen. The position of the pen's tip was sampled at 50 Hz with a 0.01-mm resolution and displayed on the screen as a cursor with the shape of an empty circle of 0.6-cm radius with a thin white contour. The scale of the cursor movement on the screen was the same as that of the pen movement on the tablet. Moving the cursor to the different targets involved rotations at both proximal joints (shoulder and elbow) and distal joints (wrist and fingers). The

central spot on the screen was set in correspondence with a fixed central point on the tablet. Central fixation was controlled by routine electro-oculography (EOG): horizontal eye movements were monitored by using bitemporal electrode placement and vertical eye movements by placing the electrodes above and below the right eye.

Subjects lay on the scanner bed, with an intravenous catheter inserted into the extended left arm to receive the injections of radioactive tracer. Their head was slightly raised above the bed by means of a head holder endowed with an individually molded bite-bar (Bettinardi *et al.,* 1991). They could look comfortably at the monitor that was rigidly suspended above their body at a 43° angle to the bed. The tablet was placed just above the chest of the subject. In this way shoulder and elbow joints of the right arm were supported by the tablet while the arm could slide freely along its surface. Room lights were off and cooling fans provided low-level background noise.

Tasks

In all three tasks, subjects were instructed to maintain fixation on the central spot and to detect the location of the peripheral target upon its appearance. In the baseline condition (*visual detection*), subjects did not respond overtly. In the two motor tasks, they were asked to move the screen cursor from the central spot to a peripheral target, to remain there briefly and then return to the central spot. The target to be reached for differed, however, between these two tasks: it was the most recent target in the task of *immediate pointing* (Fig. 1B), whereas it was the previous target in the sequence in the task of *pointing to the previous* (Fig. 1C). In both cases emphasis was on accuracy rather than speed. Moreover, subjects were instructed to always wait to move until the appearance of the visual cue.

The rationale behind this experimental design was the following. In all tasks, identical peripheral targets were presented at a constant cadence. Although *visual detection* did not involve overt responses, we verified that subjects did pay attention to target appearance by repeated verbal inquiries during the practice trials prior to PET scanning (see below). *Immediate pointing* and *pointing to the previous* involved similar limb movements. The main difference between these two tasks involved the cognitive processing required. In *immediate pointing,* subjects had to process only the most recent target. In *pointing to the previous,* instead, they had to retrieve the previous target from memory, while they stored the most recent target in memory for the next trial.

Subjects practiced a given task a few minutes prior to its execution during PET scanning. These practice trials were monitored by an experimenter to verify the correct execution of the task. The actual tasks were started 30 s prior to the administration of the radioisotope.

Motor Performance Analysis

Trajectories of the pen's tip were analyzed off-line. Movement onset was computed as the time when the position of the pen's tip deviated significantly from the starting point. Movement end corresponded to the time when the pen's tip first reached the final position and remained stationary for the subsequent 100 ms. *Reaction time* (RT) was defined as the time interval from target onset to movement onset, and *movement time* (MT) as the time interval from the onset to the end of the movement.

Pointing accuracy was measured by comparing the vector (**T**) of target position with the vector (**P**) of the position of the pen's tip at movement end, both **T** and **P** being defined relative to the central starting point. The difference between their arguments corresponded to the *directional error* ($\Delta\theta$), whereas the difference between their moduli corresponded to the *distance error* ($\Delta\rho$). Positive $\Delta\theta$s correspond to counterclockwise deviations from the target, and positive $\Delta\rho$s correspond to overshoots of the target. For both $\Delta\theta$ and $\Delta\rho$, the *constant error component* was computed as the mean value over all trials of each condition, and the *variable error component* as the corresponding SD.

Pairwise comparisons were carried out to assess the statistical significance of intercondition differences ($\alpha = 0.05$).

PET Scanning and Analysis

Subjects were positioned in the scanner with the head fixed in the head holder. The position of the apparatus (monitor and tablet) was adjusted relative to the subject so as to ensure a comfortable performance. Scans were obtained using a Siemens 931/04-12 (Siemens-CPS Knoxville, TN) whole-body scanner, allowing seven transaxial images to be obtained, 6.75 mm thick, parallel to the orbitomeatal line (Spinks *et al.,* 1988). The spatial resolution of the tomograph is 6.3 mm full width at half-maximum (FWHM) in the axial image plane. The bed of the scanner was shifted to cover a 94-mm axial field of view (Decety *et al.,* 1994). Radiation attenuation by the head and head holder was corrected using a transmission scan obtained during exposure of a ^{68}Ge external ring source prior to the activations. The corrected emission images were reconstructed using a Hanning filter with a cutoff frequency of 0.5 cycles/pixel. Each reconstructed image plane contained 128×128 pixels, with a pixel size of 2.05×2.05 mm.

A limitation of the present study is that, because of the limited axial field of view of the tomograph, regions on the top of the brain (topmost part of the superior

parietal lobe and of the dorsal premotor areas) could not be scanned if the cerebellum was also to be imaged. All subjects were positioned in the scanner using standardized landmarks (corresponding to the orbitomeatal line) to cover approximately the same brain volume.

Prior to each scan, an iv bolus injection of 50 mCi (1850 MBq) $H_2^{15}O$ was given through the intravenous catheter. The integrated counts collected over a period of 90 s were used as an index of rCBF. Six sequential rCBF measurements were obtained at about 20 min intervals from each subject. The three tasks were presented in two blocks, and the bed was shifted between the first block and the second one, in randomized order across subjects.

Image analysis was performed in MATLAB 4.2 (Math Works, Natick, MA) using the software for statistical parametric mapping (SPM-1995). The original images were transformed by aligning them all with the first scan to correct for head movement between scans (Woods *et al.,* 1992) and by interpolating to 20 planes (4 mm apart) defined in standard stereotactic space (Talaraich and Tournoux, 1988), extending from −24 mm below to +52 mm above the intercommissural (AC-PC) line. Each image was smoothed with a low-pass Gaussian filter (20-mm FWHM) to compensate for intersubject anatomical variability and to suppress high-frequency noise, thus increasing the signal to noise ratio.

Differences in global blood flow within and between subjects were removed by an analysis of covariance with global flow as the confounding variable (Friston *et al.,* 1990). To this end, the data for each corresponding scan were pooled across all subjects. The task-related changes in regional blood flow (rCBF) represent relative increases or decreases of rCBF after normalization of global radioactive counts to a flow value of 50 ml/dl/min. For each voxel in stereotactic space, the analysis of covariance yields the mean equivalent values of rCBF across all subjects, together with the associated error variance. To compare the activity elicited in the brain by different tasks, the difference between the corresponding mean values of rCBF was evaluated for each pixel using the *t* statistic, transformed to the normal distribution (*Z* score).

The statistical threshold was set to a *Z* score > 3.09 ($P < 0.001$, without correction for multiple comparisons) in the comparisons of each motor task with the control (*visual detection*) and to a *Z* score > 2.32 ($P < 0.01$) in the direct comparison of the two motor tasks between each other. In the latter case, a lower threshold was justified because the number of foci explored (the number of interrogated pixels) was limited based on a priori hypotheses derived from the preceding comparisons. Significant pixels were displayed on coronal, sagittal and transverse views of the brain as projection maps. The location of maximum activation (corresponding to the 2-cm-diameter sphere centered on the pixel with highest significance) was identified in stereotactic coordinates with reference to the standard atlas of Talaraich and Tournoux (1988). To provide the reader with further localization cues, results will be reported making reference also to Brodmann areas (BA). These do not imply, however, cytoarchitectonic correlates, which are difficult to establish with the present resolution of the method.

RESULTS

Behavioral Performance

Central fixation was well maintained throughout the execution of all tasks, with fewer than three extraneous saccades off the central spot per subject. The task of *visual detection* did not involve overt responses, but we verified that subjects did pay attention to the appearance of the peripheral targets to detect their location by repeatedly inquiring during the practice trials (see Materials and Methods). An indication that attention was directed to the peripheral target was provided by the report of all subjects that they could not prevent moving the eyes to the target, despite the explicit instruction not to do so. In fact, these eye movements were illusory, as demonstrated by the continuous EOG monitoring (see above).

The trajectories described by the pen's tip in *immediate pointing* (Fig. 2A) were roughly similar to those directed to the corresponding targets in *pointing to the previous* (Fig. 2B). Motor performance during these two tasks was assessed quantitatively by computing a number of temporal and spatial parameters. Parameters averaged across all trials and subjects are reported in Table 1.
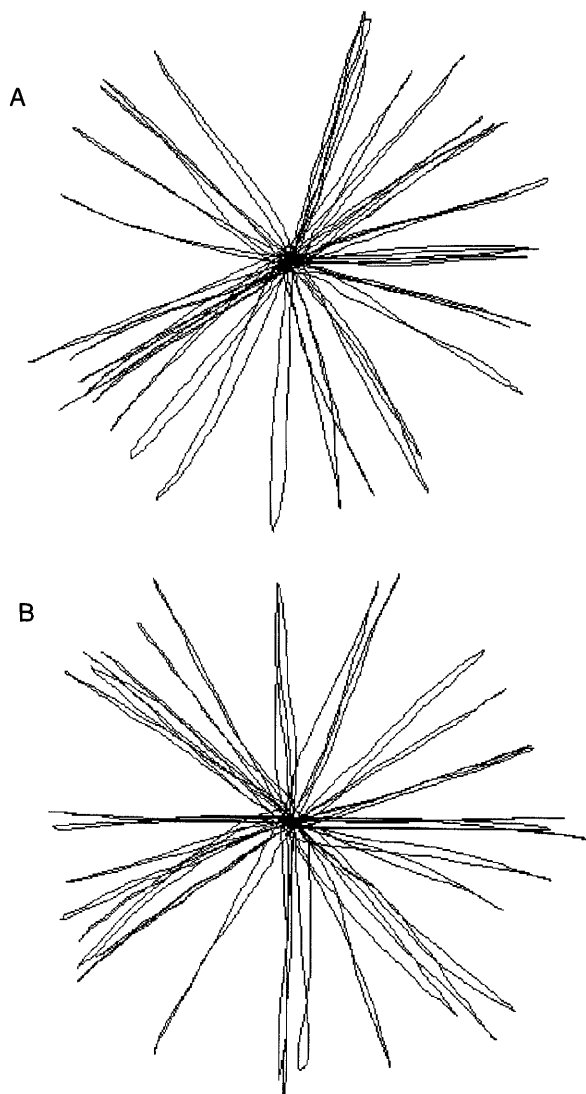
All subjects tended to overshoot the targets, as indicated by the positive value of the constant error in distance. This error, however, was small, amounting to less than 5 mm (7% of the movement amplitude). Constant errors in direction were limited to less than 2°. None of the temporal parameters (RT and MT) and spatial parameters (constant and variable errors) differed significantly between *immediate pointing* and *pointing to the previous,* except for the variable error in direction which was significantly ($P < 0.001$) greater in *pointing to the previous* than in *immediate pointing* (2.12 times greater).

PET Functional Anatomy

Immediate pointing versus visual detection (Fig. 3A and Table 2). Activations occurred in a number of cortical areas localized in the left hemisphere (contralateral to the moving arm): the primary sensorimotor cortex between +40 and +52 mm above the AC-PC line, the ventrolateral part of the precentral gyrus (BA 6), the inferior frontal gyrus in the opercular region (BA

44/45), the inferior parietal lobule close to the intraparietal sulcus (BA 40), the supramarginal gyrus (BA 40), and the middle occipital gyrus at the junction with the temporal lobe (BA 19/37). The cerebellar vermis was also significantly activated.

Pointing to the previous versus visual detection (Fig. 3B and Table 3). Foci of activation were found at locations comparable to those of the foci described for *immediate pointing:* primary sensorimotor cortex, ventrolateral precentral gyrus, inferior frontal gyrus, supramarginal gyrus, and middle occipital gyrus, all these

TABLE 1

Motor Performance

	Immediate pointing	*Pointing to the previous*
Reaction time (ms)	475 (75)	467 (142)
Movement time (ms)	1336 (424)	1436 (538)
Constant distance error (mm)	4.52 (1.31)	3.67 (1.57)
Variable distance error (mm)	6.45 (1.69)	6.33 (1.83)
Constant direction error (deg)	−0.04 (0.74)	1.59 (3.05)
Variable direction error (deg)	3.93 (2.03)	8.35 (2.37)*

Note. Mean values (±SD) computed over the data obtained during PET scanning in all subjects ($n = 8$). Asterisk denotes a statistically significant ($P < 0.001$) difference between the two tasks.

sites being lateralized to the left hemisphere, and cerebellar vermis. In addition, however, a number of other foci appeared specifically in this task. Most cortical regions were activated in the left hemisphere: the supplementary motor cortex (SMA) posterior to the AC line, two foci in the cingulate gyrus (a more anterior one, BA 23/33, and a more posterior one, BA 24/31), and the inferior occipital gyrus at the junction with the fusiform gyrus (BA 18/19). The superior parietal lobule (BA 7) and the upper part of the supramarginal gyrus (BA 40) were activated on the right side only. Posterior hippocampus and lingual gyrus were activated bilaterally. Additional subcortical foci were found in the anterior thalamus, pulvinar, and left caudate. Cerebellar hemispheres were activated bilaterally.

It can be noted that two foci in the cingulate gyrus of the right hemisphere, roughly symmetrical to those on the left side, were apparent at a lower statistical threshold ($P < 0.01$).

Pointing to the previous versus immediate pointing (Fig. 3D and Table 4a). This comparison confirmed the differential activation of most of the foci that have been described above as selective of the task of *pointing to the previous:* in the left hemisphere, SMA, anterior cingulate (BA 32), posterior cingulate (BA 24/31), and fusiform gyrus; in the right hemisphere, superior parietal lobule (BA 7) and inferior parietal lobule (BA 40); in both hemispheres, posterior hippocampus and lingual gyrus; and in subcortical foci, anterior thalamus, cerebellar vermis, and hemispheres.

Immediate pointing versus pointing to the previous (Fig. 3C and Table 4b). This comparison revealed the activation of bilateral prefrontal foci (BA 8/9), left inferior parietal cortex (BA 40), and right superior temporal gyrus (BA 22).

DISCUSSION

Characteristics of the Tasks

The aim of this study is to describe the neural networks putatively involved in the visuomotor trans-

FIG. 2. Trajectories described by the pen's tip on the digitizing table during PET sessions of one subject. (A) *Immediate pointing.* (B) *Pointing to the previous.* Thirty-six trials are plotted for each condition, corresponding to 3 min of recording. For each trial, trajectories diverge first from the central, starting point toward the peripheral target to be reached for and return subsequently to the same central point. Because of the randomization procedure, not all 24 possible targets were lit during this recording session, but some targets were lit more than once.

formations for reaching to visual memorized targets. We examined three tasks that required central fixation and detection of the location of peripheral targets upon their appearance. These targets were briefly flashed at a constant eccentricity but variable direction in the perifoveal field, a retinal region of relatively high acuity (Wassle and Boycott, 1991). In the baseline condition of *visual detection* subjects did not respond overtly, but directed consistently their attention to the targets. This was indicated by the report of all subjects that they could not prevent moving the eyes toward the target, despite the instruction not to do so. In fact, continuous EOG monitoring proved that these eye movements were illusory.

In the motor tasks, the targets had to be captured by a hand-held cursor according to the general procedures previously investigated (Gordon *et al.,* 1994). By design, the two motor tasks differed in the cognitive processing required. In each trial of *immediate pointing,* subjects had to process only the most recent target to direct their movement. In each trial of *pointing to the previous,* instead, they had to retrieve the previous target from memory to direct the current movement, while they also had to store the most recent target in memory for the movement of the next trial. Thus, although one target at a time was presented, visuospatial attention could not be engaged to that target only during the delay, but had to be shifted to the previously memorized target to direct the movement.

Despite the very different cognitive requirements, the two tasks entailed similar behavioral responses. In particular, the movement trajectories described by the pen's tip in *immediate pointing* were similar to those directed to the corresponding targets in *pointing to the previous.* The mean values of RT, MT, constant error in distance, variable error in distance, and constant error in direction were not significantly different in the two tasks. Instead, the variable error in direction was significantly greater in *pointing to the previous* than in *immediate pointing,* indicating a greater amount of random variability in the neural processing of final position (Gordon *et al.,* 1994). This result is to be expected with increasing memory delay (Rossetti and Lacquaniti, unpublished observations).

Network for Immediate Pointing to Visual Targets

This network is coherent with the functional anatomy of the corticocortical pathways for visuomotor coordination and working memory described in primates and with that demonstrated in previous PET studies of arm movements under visual guidance (cf. Jeannerod *et al.,* 1995; Johnson *et al.,* 1996; Ungerleider, 1995). In humans, tracking a moving target with the finger (Grafton *et al.,* 1992), handwriting (Seitz *et al.,* 1994), keypress in response to visuospatial detection (Haxby *et al.,* 1994), preparation for reaching (Decety *et al.,*

1992), actual reaching (Kawashima *et al.,* 1995; Grafton *et al.,* 1996), and imaginary movements (Decety *et al.,* 1994; Stephan *et al.,* 1995), all involve prestriate areas along the dorsal stream of the visual corticocortical pathways, posterior parietal areas, and motor and premotor areas in the frontal lobe.

Visual occipital areas. Striate (V1) and prestriate (V2, V3a) areas remained occult in all pairwise comparisons, indicating that visual preprocessing involved similar changes in blood flow across all three tasks. By contrast, a region in the left middle occipital gyrus (BA 19/37), at the junction with the temporal lobe, was differentially activated in both visuomotor tasks compared with the *visual detection* task. This region corresponds closely with the visual motion area previously described in several studies (Corbetta *et al.,* 1991; Dupont *et al.,* 1994; Watson *et al.,* 1993; Decety *et al.,* 1994), corresponding to the MT/MST complex (V5) in the monkey. In the present study, the region was presumably activated by visual monitoring the cursor that moved back and forth between the central fixation spot and the peripheral targets. It must be noted that, due to its large ventrodorsal extent, the focus of activation in BA 19 might encompass, in addition to the MT/MST complex, also the dorsolateral occipital area described by Haxby *et al.* (1994) for visuospatial vision. This lateral occipital region could be the human homologue of area POd (V6A) in the monkey (De Jong *et al.,* 1994; Dupont *et al.,* 1994).

In the monkey, spatial visual information is preprocessed in V1, V2, and V3a and flows to MT/MST and PO (parieto-occipital area) (Felleman and Van Essen, 1991). Cells in MT/MST are broadly tuned to the direction and pattern of visual motion, whereas PO has a quasiuniform representation of the retina without foveal magnification. As one moves from V1, V2, and V3a to MT, MST, and PO, the receptive field size of individual neurons increases. Large receptive fields may contribute to localizing objects over retinal translation (as in the case of the moving cursor on the screen in the present task).

Posterior parietal cortex. In the monkey, visual information is subsequently transmitted from MT/MST and PO to several areas lying in the intraparietal sulcus (MIP, VIP, and LIP) and in its proximity (7a, 7b) in the inferior parietal lobule. Many neurons in these regions are endowed with congruent visual and somatosensory receptive fields and code the location of external stimuli in body-centered coordinates. Moreover, bimodal visual/reaching neurons are frequent in these areas (Colby and Duhamel, 1991; Johnson *et al.,* 1996). Stimulus–response attributes are coded neurally with similar modalities during reaction-time movements under visual guidance and during delayed movements to memorized targets (Duhamel *et al.,* 1992; Gnadt and Andersen, 1988). MIP is connected with primary motor
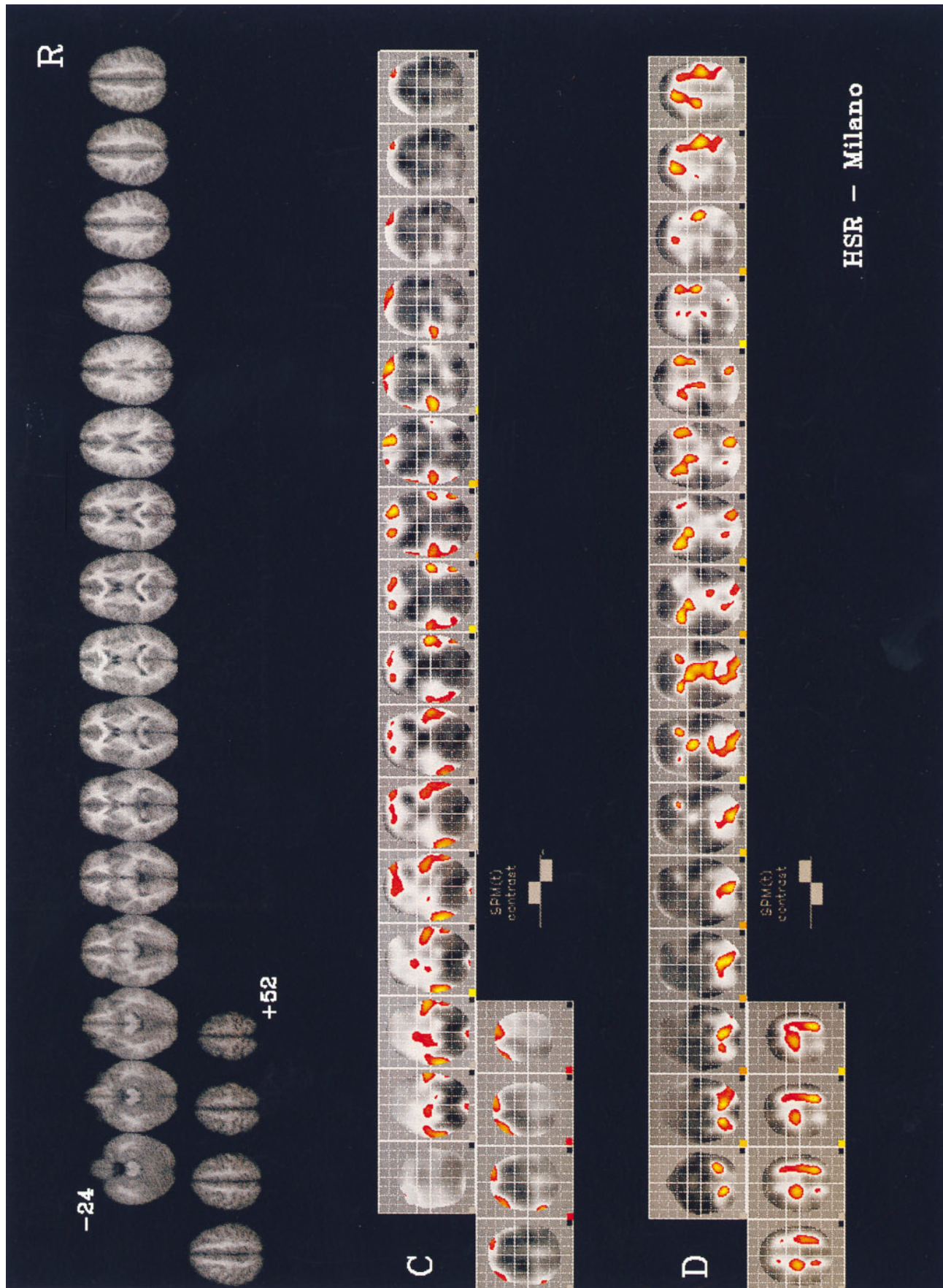
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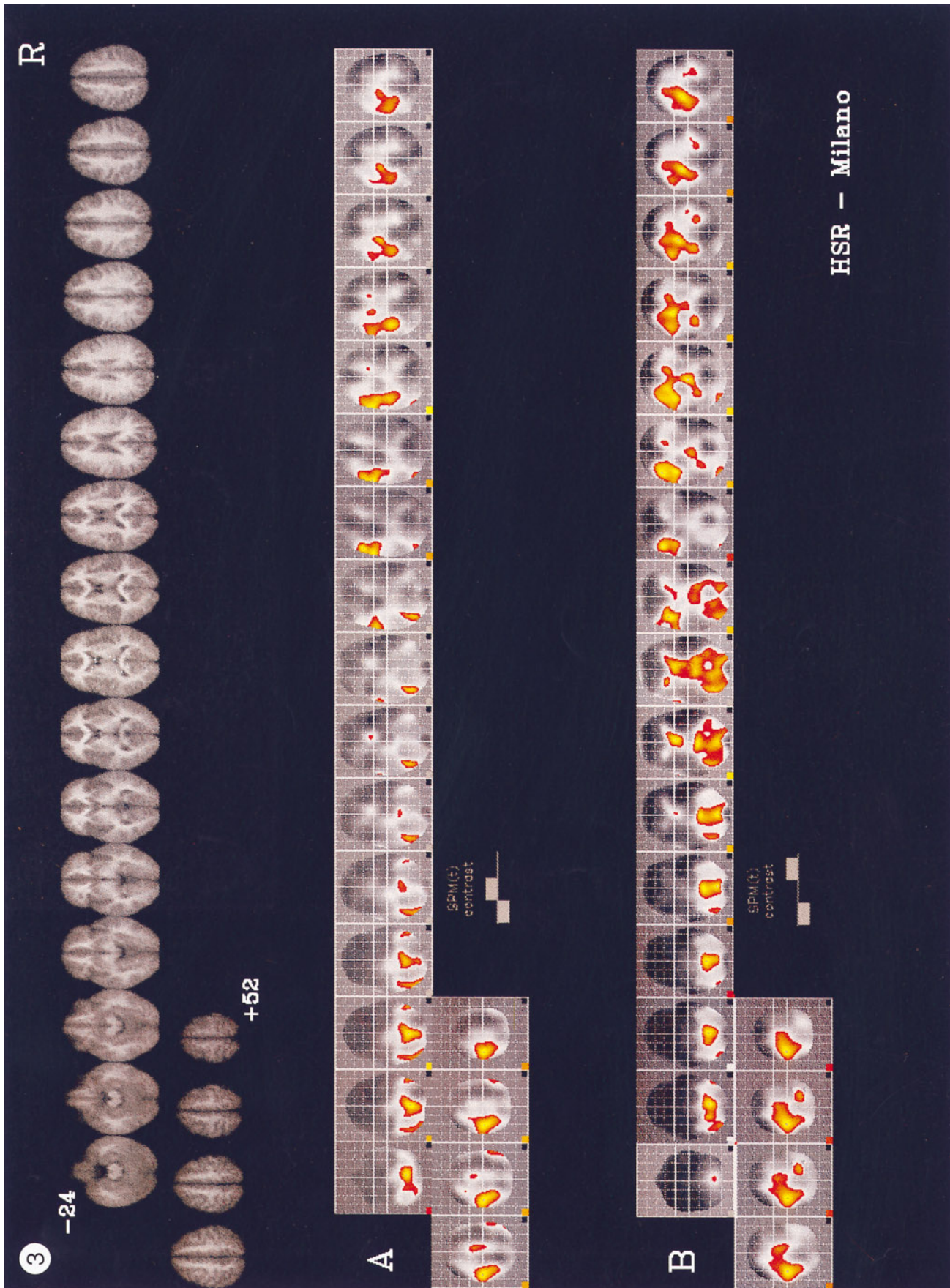
FIG. 3—Continued

cortex and dorsal premotor cortex (Johnson *et al.,* 1993). VIP and 7b are connected with ventral premotor cortex (Jeannerod *et al.,* 1995). VIP, LIP, and 7a are also interconnected with dorsolateral prefrontal cortex.

In the present study, the left supramarginal gyrus (BA 40) was activated in the visuomotor tasks. A similar activation has previously been reported in tasks involving directional movements of the arm (Colebatch *et al.,* 1991; Decety *et al.,* 1992). Eidelberg and Galaburda (1984) have proposed a homology between human BA 40 and area 7b in the monkey. The latter is located in the anterior part of the inferior parietal lobule and is extensively interconnected with the ventral premotor cortex (Jeannerod *et al.,* 1995). Area 7b neurons are endowed with spatially aligned visual and somatosensory receptive fields (Hyvärinen, 1981; Gentilucci *et al.,* 1988; Graziano *et al.,* 1994).

Immediate pointing activated another region in the inferior parietal lobule (BA 40) of the left hemisphere, located more dorsally relative to the supramarginal gyrus, in the proximity of the intraparietal sulcus. A similar activation has been reported in tasks involving executed or imagined arm movements (Decety *et al.,* 1994; Stephan *et al.,* 1995), visuospatial detection tasks (Haxby *et al.,* 1994), and visually guided hand movements (Grafton *et al.,* 1992; Seitz *et al.,* 1994). Neurological studies of patients affected by optic ataxia, a disturbance of visuomotor coordination, have indicated that the most common site of the lesion is centered around the intraparietal sulcus contralateral to the affected arm (Perenin and Vighetto, 1988).

Primary sensorimotor cortex. Activation was found in a region around the central sulcus, contralateral to the moving arm, encompassing both pre- and postrolandic areas. The Talaraich coordinates for this focus are close to those reported in previous studies that involved, as in the present study, whole arm movements with both proximal and distal components (Colebatch *et al.,* 1991; Sergent *et al.,* 1992; Matelli *et al.,* 1993; Paus *et al.,* 1993; Stephan *et al.,* 1995).

Lateral frontal areas. Two distinct foci were activated in the left hemisphere. The first was located in the ventrolateral part of the precentral gyrus (BA 6). A similar activation has been found during different types of executed (Colebatch *et al.,* 1991; Stephan *et al.,* 1995) or imagined (Decety *et al.,* 1994; Stephan *et al.,* 1995) movements of the arm. The caudal part of the ventral premotor cortex in the monkey (area F4 of Gentilucci *et al.,* 1988) is connected with area 7b of

TABLE 2

Foci of Significant rCBF Increases in the Task of Immediate Pointing

Side	Region	Brodmann area	x	y	z	Z score
L	Pre/postcentral gyri	4/3/1/2	−34	−26	52	3.80
L	Precentral gyrus	6	−54	2	16	3.63
L	Inferior frontal gyrus	44/45	−46	18	12	3.67
L	Supramarginal gyrus	40	−38	−32	24	3.10
L	Inferior parietal lobule	40	−26	−36	40	3.61
L	Middle occipital gyrus	19/37	−38	−64	4	3.09
	Cerebellar vermis		4	−58	−24	4.51

posterior parietal cortex and is part of a cortical network for the control of grasping and reaching (Jeannerod *et al.,* 1995). Neurons in both F4 and 7b have congruent visual and tactile receptive fields (Gentilucci *et al.,* 1988; Graziano *et al.,* 1994), and encode the location of external stimuli in peripersonal space in head-centred or arm-centred coordinates.

A second focus was located anteriorly to the previous one, in the inferior frontal gyrus. This region overlaps partially with Broca's area. Its activation could depend on a possible internal verbalization during movement execution (Zatorre *et al.,* 1992; Kapur *et al.,* 1994). Internal verbalization could arise in relation to the construction of an iconic representation of the spatial location of the targets. Thus, targets located around a circle could be mentally represented as hours and minutes on a virtual clock face. A more likely explanation for the activation of this area resides in the specific processing required by visuomanual coordination (Jeannerod *et al.,* 1995). This region has recently been found to be activated also during passive observation of grasping movements (Rizzolatti *et al.,* 1996), and analogies have been drawn with area F5 of the monkey (Gallese *et al.,* 1996). F5 forms the rostral part of inferior area 6 and is connected with the hand fields of primary motor cortex, being similarly related to distal movements (Muakassa and Strick, 1979; Rizzolatti and Gentilucci, 1988). F5 neurons participate in planning specific patterns of wrist and finger movements (Rizzolatti and Gentilucci, 1988).

Prefrontal cortex. Bilateral activation of BA 8 and BA 9 in the superior and middle frontal gyri was observed in the comparison of *immediate pointing* versus *pointing to the previous.* It has been suggested

FIG. 3. Brain areas activated during different tasks displayed on transverse planes in the stereotactic space of Talaraich and Tournoux (1988). (A) *Immediate pointing* minus *visual detection.* (B) *Pointing to the previous* minus *visual detection.* (C) *Immediate pointing* minus *pointing to the previous.* (D) *Pointing to the previous* minus *immediate pointing.* Significant rCBF increases are shown as statistical parametric maps, with Z scores displayed on a linear color scale. Threshold for significance: Z score > 3.09 in A and B and Z score > 2.32 in C and D. In each panel, left to right, top to bottom: sections (4 mm apart) extending from −24 mm below to +52 mm above the intercommissural (AC-PC) line. MRI images are displayed above the corresponding transverse planes of PET data for better anatomical localization.

TABLE 3

Foci of Significant rCBF Increases in the Task
of Pointing to the Previous

Side	Region	Brodmann area	x	y	z	Z score
L	Pre/postcentral gyri	4/3/1/2	−30	−22	52	4.52
L	Precentral gyrus	6	−36	0	12	3.82
L	SMA	6	−12	−8	44	3.19
L	Inferior frontal gyrus	44/45	−40	20	12	4.44
L	Supramarginal gyrus	40	−28	−34	24	3.45
R	Inferior parietal lobule	40	24	−38	32	3.22
R	Superior parietal lobule	7	22	−52	52	3.26
L	Cingulate gyrus	24/31	−18	−14	36	3.97
L	Cingulate gyrus	23/33	−14	2	24	3.49
L	Hippocampus		−2	−42	0	3.28
R	Hippocampus		12	−38	4	3.13
	Anterior thalamus		4	−2	0	3.28
L	Pulvinar		−4	−24	20	3.30
L	Middle occipital gyrus	19/37	−38	−82	12	3.12
L	Inf. occip./fusiform gyri	19/37	−34	−80	−20	3.93
L	Lingual gyrus	18	−8	−72	4	3.09
R	Lingual gyrus	18	4	−76	−8	3.86
L	Caudate		−20	12	20	3.12
	Cerebellar vermis		2	−60	−16	5.12
L	Cerebellar hemisphere		−16	−64	−24	4.85
R	Cerebellar hemisphere		46	−66	−20	3.55

that these regions are involved in working memory both in man and monkey (see Fuster, 1988; Goldman-Rakic, 1988; Ungerleider, 1995). In monkeys, working memory has typically been studied in either delayed response or delayed matching-to-sample tasks. In both cases, a brief cue is given initially to be maintained in memory during a delay of a few seconds. At the end of the delay, the monkey must make a response based on the previous cue. Many neurons in dorsolateral prefrontal cortex exhibit a maintained discharge during the delay period (Fuster, 1988; Goldman-Rakic, 1988), discharge which is often related to the retinocentric location of the memorized target (Funahashi *et al.,* 1993). There are two main kinds of cells activated during the delay (Quintana and Fuster, 1992). Cells of the first type (*cue-coupled*) are excited at a maximum during the cue to be remembered, and as the delay progresses their firing decreases gradually. Cells of the second type (*motor-coupled*) behave in the opposite way: their firing is attuned to the forthcoming response and accelerates as the latter approaches.

Participation of dorsolateral prefrontal cortex in visual working memory has been also verified in man by means of PET studies (Goldberg *et al.,* 1996; Jonides *et al.,* 1993; Petrides *et al.,* 1993; Smith *et al.,* 1995) and functional MRI (McCarthy *et al.,* 1994). In addition, the dorsolateral prefrontal cortex is activated in PET studies involving willed actions (Frith *et al.,* 1991; Squire *et al.,* 1992; Decety *et al.,* 1994; Jenkins *et al.,* 1994), and suppression of eye movements for central fixation (Anderson *et al.,* 1994).

The present findings of a prefrontal activation in *immediate pointing* could be explained as follows. Central fixation was common to all three tasks, and thus it is an unlikely determinant of this differential activation. Differential activation could result, instead, because in each trial of *immediate pointing,* subjects directed their attention to the most recent target based on retinal error and relied on afterimages and retinocentric working memory after target extinction. Thus, the memory buffer could be allocated exclusively to the spatial location of the last target. The differential activation of prefrontal regions in the comparison of *immediate pointing* versus *pointing to the previous* could also depend on a selective decrease of the net rCBF in the latter task. In fact, as we argue in the next section, a different functioning mode of memory was presumably engaged by the task of *pointing to the previous.*

Cerebellum. Cerebellar vermis was activated in *immediate pointing.* A similar activation has been reported in simple arm movements (Colebatch *et al.,* 1991), in visual tracking (Grafton *et al.,* 1993) and drawing movements (Seitz *et al.,* 1994), movement observation (Decety *et al.,* 1994), and visual motion detection (Dupont *et al.,* 1994).

Network for Pointing to the Previous Target

This network overlaps in part that just described for *immediate pointing.* Thus, all regions discussed above

TABLE 4

Comparison of Pointing to the Previous
with Immediate Pointing

Side	Region	Brodmann area	x	y	z	Z score
	(a) *Pointing to the previous* vs *immediate pointing*					
L	SMA	6	−6	−14	52	2.50
R	Inferior parietal lobule	40	40	−20	28	2.61
R	Superior parietal lobule	7	20	−48	52	2.50
L	Cingulate gyrus	24/31	−18	−16	40	2.33
L	Cingulate gyrus	32	−4	24	32	2.35
L	Hippocampus	30	0	−42	0	2.49
R	Hippocampus	30	12	−38	4	2.56
	Anterior thalamus		−8	0	8	2.59
L	Inf. occip./fusiform gyri	19/37	−36	−82	−16	3.69
L	Lingual gyrus	18	−10	−66	4	2.42
R	Lingual gyrus	18	6	−78	−8	2.83
	Cerebellar vermis		6	−64	−16	2.94
L	Cerebellar hemisphere		−20	−62	−20	2.60
R	Cerebellar hemisphere		28	−52	−24	2.35
	(b) *Immediate pointing* vs *pointing to the previous*					
L	Sup./mid. frontal gyri	8/9	−38	20	48	2.52
R	Sup./mid. frontal gyri	8/9	14	36	48	2.49
L	Inferior parietal lobule	40	−48	−50	44	2.97
R	Sup. temporal gyrus	22	52	−24	8	2.79

for that task were also activated in *pointing to the previous,* except for the left intraparietal sulcus and the dorsolateral prefrontal regions. These latter regions were not activated in this task, presumably because pointing was not guided by the visuospatial processing involved in working memory. Instead, several cortical and subcortical regions presumably involved in spatial attention and in recoding/decoding of spatial memories were specific of this task. The attentional network was activated by the process of selection–competition between the previous target and the current one. This network may tentatively include the right superior parietal lobule, the pulvinar, and the anterior cingulate gyrus (BA 32). Orienting and engaging attention to each new target is presumably subserved by the pulvinar, whereas disengaging attention to direct it to another target depends on the right superior parietal lobule (Petersen *et al.,* 1989; Posner and Petersen, 1990). Anterior cingulate would play a role as both a high-level attentional center (Posner and Petersen, 1990) and as a component of the response selection system that is recruited when the underlying processing proceeds in a controlled manner, as opposed to automatically (Corbetta *et al.,* 1991, 1993). The putative network engaged by spatial memory was composed of prestriate visual areas, medial temporal areas (hippocampus/parahippocampal region), anterior thalamus, and right posterior parietal cortex. In the following, we discuss the regions differentially activated in *pointing to the previous* relative to *immediate pointing.*

Visual occipital areas. Two different regions were specifically activated in *pointing to the previous.* The first was located in the left inferior occipital gyrus at the junction with the fusiform gyrus (BA 19/37), more ventral than MT. This region could correspond to that recently identified in studies on visual motion perception (De Jong *et al.,* 1994; Dupont *et al.,* 1994). Dupont *et al.* (1994) suggested that it could correspond to anterior STP in the monkey, a region known to contain motion-sensitive, form-insensitive neurons (Oram *et al.,* 1993). STP projects to perirhinal (BA 35,36) and entorhinal (BA 28) cortices, which in turn project to the hippocampus. A recent study reported the activation of the fusiform gyrus (BA 19/37) during long-term retrieval of spatial locations of memorized visual stimuli (Moscovitch *et al.,* 1995).

The lingual gyrus (BA 18) was also activated bilaterally in *pointing to the previous.* Activations in this region have previously been reported for both foveal and peripheral stimulations involving different visual attributes that pertain to both spatial and object (shape, color) processing (Petersen *et al.,* 1988; Corbetta *et al.,* 1991, 1993; Decety *et al.,* 1994).

Posterior parietal cortex. Two different areas of the posterior parietal cortex of the right hemisphere were differentially activated in *pointing to the previous.* One

focus was located in the upper part of the supramarginal gyrus (BA 40). Ipsilateral activation of BA 40 has been reported in tasks that require learning a sequence of keypresses (Jenkins *et al.,* 1994) and somatosensory discrimination (O'Sullivan *et al.,* 1994). In the study of Jenkins *et al.* (1994) learning a new sequence but not rehearsal of a prelearnt sequence activated this region. In the present task of *pointing to the previous,* the complex requirements of visuospatial attention (shifting between the previous target and the most recent one) might demand an enhanced somatomotor control of the ongoing limb movement, as contrasted to the more direct reliance on visual information in *immediate pointing.* This view is consistent with the hypothesis that processing of somatospatial information for the guidance of limb movement is largely lateralized to the right inferior parietal lobule (Heilman *et al.,* 1987; Kolb and Wishaw, 1990). The present focus of activity is close to, though not coincident with, that described in a previous PET study of visuospatial working memory (Jonides *et al.,* 1993).

On the whole, the involvement of right posterior parietal cortex in spatial attention and memory is consistent with classical neuropsychological data, indicating that these functions can be impaired in patients with right-hemisphere lesions encompassing the parietal lobe. Spatial hemineglect is frequently associated with lesions of the right supramarginal gyrus (see Vallar, 1993). The anatomical correlates of spatial short-term memory deficits, although less precisely defined, are centered around posteroinferior parietal regions (see Vallar and Papagno, 1995).

The other focus activated in *pointing to the previous* was located in the right superior parietal lobule (SPL, BA 7). A similar activation has been found during automatic and voluntary shifting of visuospatial attention (Corbetta *et al.,* 1993, 1995), spatial vision (Haxby *et al.,* 1994), and visual imagery (Kosslyn *et al.,* 1993). Neurons in the SPL of the monkey take part in the process of visuomotor coordinate transformations by encoding reaching movements in a body-centered frame of reference (Lacquaniti *et al.,* 1995). Activation of the SPL during *pointing to the previous* may then reflect at the same time the complex demands on visuospatial attention and the use of a body-centered frame of reference to guide the reaching movement in the absence of visual feedback about target location. It is also interesting to note that area 7a of the monkey, whose human homologue possibly resides in SPL, is densely interconnected with limbic regions (parahippocampal gyrus, cingulate cortex) that were coactivated with SPL in this task. By contrast, area 7b (putatively associated to the human supramarginal gyrus) receives few limbic projections in the monkey.

Supplementary motor area. The paracentral lobule contralateral to the moving arm, posterior to the AC

line, was activated during *pointing to the previous.* Similar foci have been reported during the execution of different types of arm movements, with and without visual guidance (Colebatch *et al.,* 1991; Grafton *et al.,* 1993; Matelli *et al.,* 1993; Jenkins *et al.,* 1994; Seitz *et al.,* 1994; Stephan *et al.,* 1995). It has been proposed that this area corresponds to Vogts' area 6aα, the homologue of area F3 in the monkey (Matelli *et al.,* 1991, 1993). It is not clear why this region was significantly activated during *pointing to the previous,* but not during *immediate pointing.* However, SMA lesions disrupt preplanned actions more severely than relatively automatic responses guided by external cues (Laplane *et al.,* 1977). Moreover, it has recently been shown that SMA plays a specific role in planning delayed movements (Tanji and Shima, 1994).

Cingulate cortex. Two distinct foci of activation could be recognized in the left hemisphere (although two symmetrical foci in the right hemisphere were apparent at a lower statistical threshold). One focus, encompassing BA 24 and 31, was located in the midportion of the cingulate gyrus, just ventrally to the focus in the SMA (see above). Activity in this area has been described for the execution of simple whole arm movements (Grafton *et al.,* 1993; Matelli *et al.,* 1993; Stephan *et al.,* 1995). It is considered a secondary motor area, whose homologue in the monkey corresponds to area 24d (Luppino *et al.,* 1991; Shima *et al.,* 1991). Interestingly, both these cingulate areas and the SMA project not only to the arm field in primary motor cortex, but also directly to the spinal cord in the monkey (Dum and Strick, 1991).

The second focus we found in cingulate cortex was located more anteriorly and ventrally with respect to the first one. In the comparison of *pointing to the previous* versus *immediate pointing,* this focus coincided with BA 32, an area that has been related to the attentional demands of response selection (Pardo *et al.,* 1990; Playford *et al.,* 1992; Paus *et al.,* 1993; Corbetta *et al.,* 1993). In fact, *pointing to the previous* requires spatial attention to both the previous stimulus and the current one and the selection between a correct response directed to the former and an incorrect response directed to the latter. This externally instructed process of selection competition is also present in the Stroop test used by Pardo *et al.* (1990) and in the anti-stimulus task of Paus *et al.* (1993), both of which activated a similar anterior cingulate region. Area BA 32, however, is also active in memory tasks, such as in the acquisition and retrieval of verbal episodic memory (Shallice *et al.,* 1994), subspan and supraspan auditory–verbal memory (Grasby *et al.,* 1993, 1994), and self-ordered visual sorting of abstract designs in a working memory test (Petrides *et al.,* 1993). On the whole, the high demands inherent in the task of *pointing to the*

previous may well explain the activation of these cingulate areas.

Prefrontal cortex. As noted above, prefrontal regions were activated in *immediate pointing,* but not in *pointing to the previous.* This differential activation could depend on the fact that different functioning modes of memory were engaged in these two tasks. In contrast with *immediate pointing* in which the memory buffer could be allocated exclusively to the spatial location of the most recent target, in *pointing to the previous* the two last targets competed between each other for the memory buffer. When the most recent target was stored in memory for the movement of the next trial, the previous target had to be retrieved from memory to direct the current movement. One might speculate that subjects could not rely solely on the retinocentric code of the target, but had to recode the stimulus in a spatial frame to free the visual frame for the next target. It is possible then that prefrontal cue-coupled cells fired briefly during this task during the initial encoding of the stimulus, but that the sustained discharge was lacking in prefrontal neurons during the delay interval because the stimulus had been recoded in other regions of the memory network (see below). This hypothesis would explain why the net rCBF in prefrontal cortex, integrated over the PET acquisition period, would be lower in *pointing to the previous* than in the other tasks.

Hippocampus. The region corresponding to posterior hippocampus and parahippocampal gyrus was activated in *pointing to the previous.* One focus was clearly lateralized to the right hemisphere, whereas the other focus was close to the midline, making its attribution to one or the other hemisphere uncertain.

We hypothesize that the activation in these regions depends on the following sequence of events: the location of the most recent target initially encoded in visual space was subsequently recoded in a cognitive, exocentric representation of external space prior to storage in memory, while the memorized location of the previous target was retrieved and decoded in a body-centered frame to direct the current movement (Sakai and Miyashita, 1993).

The hippocampal formation has been implicated in memory functions by a considerable body of evidence from both animal brain lesions and neuropsychological studies of amnesic patients (see Fazio *et al.,* 1992; Perani *et al.,* 1993; Zola-Morgan and Squire, 1993). Amnesic patients with medial temporal lobe lesions are typically impaired in long-term explicit memory (see Zola-Morgan and Squire, 1993). However, PET-activation studies that have tested declarative memory have often failed to detect significant rCBF changes in the hippocampal region (Kapur *et al.,* 1994; Shallice *et al.,* 1994; Tulving *et al.,* 1994; Buckner *et al.,* 1995). Instead, activation in this region has been described in a

visual imagery task (Kosslyn *et al.,* 1993), visual selective discrimination tasks (Corbetta *et al.,* 1991), subspan and supraspan auditory–verbal memory (Grasby *et al.,* 1993), and tactile learning and recognition during a working memory task involving somatosensory discrimination (Seitz *et al.,* 1991).

According to current views on memory, the hippocampus and the parahippocampal cortex are involved in the encoding, recoding, and decoding processes as information flows between the sensory analyzers, the memory storehouse, and the motor controllers, but these medial temporal structures do not represent the memory storage itself (Sakai and Miyashita, 1993; Zola-Morgan and Squire, 1993). In the initial steps of long-term memory formation, the hippocampus would be involved in binding together the multiple neocortical areas that subserve perception and short-term memory (Zola-Morgan and Squire, 1993). Gradually, the neocortex would support long-term memory storage independently of the medial temporal lobe and diencephalon (Zola-Morgan and Squire, 1993).

Imagery would be also implemented by the decoding mechanisms which enable retrieval of stored information and would similarly involve medial temporal lobe structures (Kosslyn *et al.,* 1993; Sakai and Miyashita, 1993).

In addition, animal work has led to the hypothesis that the hippocampus is endowed with an allocentric representation of space based on multimodal sensory information (O'Keefe and Nadel, 1978; O'Keefe, 1979; McNaughton *et al.,* 1991), representation which could be used for both spatial navigation and spatial memory (Rolls, 1989, 1991). In humans and other primates, lesions to the hippocampus or fornix may impair spatial tasks, such as memory of where in space an object has been seen before, use of spatial cues to determine which object to select for reward in spatial memory tasks, and learning where to make a spatial response (Corkin, 1965; Smith and Milner, 1981, 1989; Gaffan and Saunders, 1985; Petrides, 1985; Parkinson *et al.,* 1988; Gaffan and Harrison, 1988; Rolls, 1990; for a critique of a specific role of hippocampus in spatial memory see, however, Squire, 1992). In man, pure topographic amnesia and disorientation is consistently correlated with lesions of medial temporal regions of the right hemisphere, particularly at the level of posterior parahippocampal gyrus (Habib and Sirigu, 1987).

The bulk of these deficits could be correlated with the neuronal properties of primate hippocampal neurons (Rolls *et al.,* 1989; O'Mara *et al.,* 1994). The hippocampus receives vestibular and visual information from the parietal cortex (mostly PIVC) via the subiculum and entorhinal cortex, and visual information may also reach the hippocampus from the inferior temporal cortex via the entorhinal cortex (Felleman and Van Essen, 1991). Pyramidal cells in the hippocampus

(CA1) are active when the animal occupies specific places in the environment (*place coding*) or when his body has specific orientations in space (O'Keefe, 1979; McNaughton *et al.,* 1991; O'Mara *et al.,* 1994). Visual stimuli appear also to be encoded in allocentric coordinates in several cells (Feigenbaum and Rolls, 1991). The responses of these units do not change when the stimuli remain in the same laboratory position but the animal is rotated or displaced to a different position. A proportion of hippocampal units respond according to the direction of the stimulus, independently of the stimulus type (visual, acoustic, etc.; Tamura *et al.,* 1992).

Thalamus. Anterior thalamus was activated in *pointing to the previous.* Spatial attention (Corbetta *et al.,* 1993), auditory/verbal memory (Grasby *et al.,* 1993), and visual imagery tasks (Kosslyn *et al.,* 1993) activate this region. Anatomical interconnections of anterior thalamus with the hippocampus, in particular the subiculum and presubiculum, are well known (cf. Amaral, 1987). Also, lesions of the mammillothalamic tract and anterior thalamus result in severe memory impairments (Graff-Radford *et al.,* 1990).

The activation of the pulvinar, in conjunction with that of the right superior parietal lobule, can be related to the specific visual attentional requirements involved in this task. It has been proposed that the role of the pulvinar is to orient and engage attention to a new target, whereas the right superior parietal lobule would be involved in disengaging attention to direct it to another target (Petersen *et al.,* 1989; Posner and Petersen, 1990). Neurons in posterior parietal cortex and the interconnected lateral pulvinar nucleus of the monkey exhibit a spatially selective enhancement of a visual response when the animal is covertly attending to a stimulus location (Petersen *et al.,* 1985). This could correspond to the case of *pointing to the previous,* when subjects attend the location of the most recent target while performing a movement in a different direction (to the previous target).

Basal ganglia. The activation of caudate nucleus was inconsistent, as it occurred in the comparison of *pointing to the previous* with *visual detection,* but not in the direct comparison of *pointing to the previous* with *immediate pointing.*

Cerebellum. Cerebellar vermis and hemispheres were activated in *pointing to the previous.* Activation of cerebellar hemispheres has been reported in visual drawing (Seitz *et al.,* 1994) and tracking movements (Grafton *et al.,* 1993), as well as in verbal memory (Paulesu *et al.,* 1993).

In sum, a hypothetical sequence of events in *pointing to the previous* would involve feature analysis and initial encoding of the most recent target in visual space; subsequent recoding in a cognitive, allocentric representation of external space prior to storage in

memory; and final retrieval of this memorized location decoded in a body-centered frame to direct the movement. Feature analysis could occur in prestriate visual areas (i.e., fusiform gyrus and lingual gyrus), recoding the allocentric spatial representations could involve medial temporal lobe areas, memory storage, and decoding in body-centered coordinates could occur in the right posterior parietal cortex. The memory network could be interconnected with the attentional network at the level of the posterior parietal cortex and at the level of the anterior cingulate cortex via the anterior thalamus. In addition, secondary motor areas in the paracentral lobule (BA 6aα or SMA-proper) and midcingulate gyrus (BA 24d) could participate in decoding the representation of the memorized target to direct the movement.

The differential activation of the dorsolateral prefrontal cortex in *immediate pointing* and of the hippocampus in *pointing to the previous* is also in agreement with the notion that short-term memories in these two structures may have a different nature (Guigon and Burnod, 1995). Dorsolateral prefrontal cortex might be specialized in learning delayed responses within fixed environmental conditions, leading to inflexible representations. The hippocampus, by contrast, would create flexible representations, which can be expressed independent of the environmental context in which the information was initially acquired. Thus, the direction of limb movement was rigidly associated to that of the most recent target in *immediate pointing,* whereas movement direction was independent of that of the most recent target in *pointing to the previous.*

Conclusions

The present results are consistent with current views about the multicomponent structure of memory systems (see Baddeley, 1992; Squire, 1987). The nature of the signal processing involved is probably more important than the time range of the memory delay for engaging one or another network for memory. Thus, both *immediate pointing* and *pointing to the previous* involved memory processing in the range of few seconds. However, the buffer of working memory could be allocated exclusively to the spatial location of the most recent target in the former task only. In the latter task, instead, the memory buffer could not be allocated to one target only, because of the competition between the two last targets: when the most recent target was stored in memory for the movement of the next trial, the previous target had to be retrieved from memory to direct the current movement. The different nature of signal processing was reflected in the corresponding activation of two partially distinct cerebral networks: a parietofrontal network for visuomotor working memory in *immediate pointing* and a corticolimbic network

more characteristic of spatial memory in *pointing to the previous.*

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