Functional imaging of the intraparietal cortex during saccades to visual and memorized targets

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Introduction

The representation of perceived space and intended actions in the primate parietal cortex has been the subject of considerable debate. To address this issue, we used the quantitative 14C-deoxyglucose method to obtain maps of the activity pattern in the intraparietal cortex of rhesus monkeys executing saccades to visual and memorized targets. The principal effect induced by memory-guided saccades was found more caudally in the deepest part of the middle third of the lateral bank (within area LIPv) whereas that induced by visually guided saccades extended more rostrally and superficially in the anterior third of the bank (within area LIPd). The memory-saccade-related and the visual-saccade-related regions of activation overlapped only within area LIPv. Besides saccade execution, maximal activity in area LIPd required a visual stimulus. The region activated by visual fixation was located at the border of LIPv and LIPd, extending mainly within area LIPd, and occupying about one third of the neural space of the region activated by visually guided saccades. The lateral intraparietal cortex represents visual and motor space in segregated, albeit partially overlapping, regions.

The representation of perceived space and intended actions in the primate parietal cortex has been the subject of considerable debate. To address this issue, we used the quantitative 14C-deoxyglucose method to obtain maps of the activity pattern in the intraparietal cortex of rhesus monkeys executing saccades to visual and memorized targets. The principal effect induced by memory-guided saccades was found more caudally in the deepest part of the middle third of the lateral bank (within area LIPv) whereas that induced by visually guided saccades extended more rostrally and superficially in the anterior third of the bank (within area LIPd). The memory-saccade-related and the visual-saccade-related regions of activation overlapped only within area LIPv. Besides saccade execution, maximal activity in area LIPd required a visual stimulus. The region activated by visual fixation was located at the border of LIPv and LIPd, extending mainly within area LIPd, and occupying about one third of the neural space of the region activated by visual-saccades. We suggest that the lateral intraparietal cortex represents visual and motor space in segregated, albeit partially overlapping, regions.

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sessions on different days and in different animals. In contrast, the technique we employed allowed us to obtain high-resolution activity maps throughout the intraparietal cortex of rhesus monkeys engaged in visuo/oculomotor tasks. Our data demonstrate that visual space and eye movements are separately represented in partially overlapping regions of the lateral intraparietal cortex.

Methods

Six head-fixed adult female monkeys (Macaca mulatta) weighing between 3 and 5 kg were used in accordance with an experimental protocol approved by the Greek Veterinary authorities and the F.O.R.T.H. animal use committee, and complying with European Council Directive 86/609/EEC.

Surgical procedures in sterile conditions and under general anesthesia were performed for implanting a head-holding metal bolt and a scleral search coil as previously described (Moschovakis et al., 2001). Systemic antibiotics and analgesics were administered before and after the surgery, and the animals were allowed to recover for at least 3 weeks before training started. Eye position was sampled at a rate of 500 Hz using the Spike2 software (Cambridge Electronics Design, Cambridge, Massachusetts). On the day of the 14C-DG experiment, monkeys performed the tasks they had mastered for 45 min, and successful completion of each trial was rewarded with water.

Behavioral tasks

The behavioral apparatus was a video monitor placed 23 cm in front of the monkeys. Visual targets were red spots with a subtending angle of 1.5°. Monkeys executing visually guided saccades were required to hold eye position within a circular window of 5° diameter. Monkeys executing memory-guided saccades were required to hold eye position within a circular window of 10° diameter. All experimental procedures took place in complete darkness. Monkeys had their arms restrained on a primate chair (Christ Instrument Co.) for the duration of the 14C-DG experiment. Task parameters were chosen so as to ensure that the crucial variable, i.e., the total number of the stimulus-triggered saccades per minute, would obtain the same value in all animals.

The control monkey in the dark (Cd, Control-dark) was presented with auditory stimuli similar to the acoustic cues presented to the monkeys executing memory-guided saccades. Reward was delivered randomly in order to prevent association of the auditory stimuli with the reward expectancy. The monkey was alert during the whole 45 min of the 14C-DG experiment as illustrated 2D maps is 100 m/pixel) in the rostrocaudal extent and 135 m in amplitude and 135° in direction from the central starting position, within 0.6 s, and to maintain fixation on each target for 0.4–0.6 s. Intertrial intervals were between 0.3 and 0.5 s.

The monkey performing the memory-guided horizontal saccade task (Hd, Horizontal-dark) was required to fixate straight ahead in total darkness following an auditory cue (90 Hz) and hold its gaze for 0.4–0.7 s, until a second auditory cue (180 Hz) signaled that a memorized saccade of 20° in the horizontal direction should be executed within 1 s, and fixation should be maintained for 0.4–0.7 s. Intertrial intervals ranged from 0.8–1.1 s. Following an auditory cue of 90 Hz, the monkey performing the memory-guided oblique saccade task (Od, Oblique-dark) had to keep its eyes straight ahead for 0.5–0.7 s, until a second auditory cue of 180 Hz commanded an up-left saccade of 25° in amplitude and 135° in direction within 1 s. The monkey held its gaze to the memorized target position for 0.5–0.7 s. Intertrial intervals were 0.5–0.7 s long. Auditory cues originated from a central speaker, placed in front of the monkey on top of the monitor. Each monkey executing memory-guided saccades was originally trained to fixate a central visual target during the presentation of the 90 Hz auditory cue, and to saccade to a visual target of specific amplitude (20–25 deg) and specific direction (either horizontal or oblique) during the 180 Hz auditory cue. Later on in its training, the visual targets were extinguished, and the monkey was rewarded for executing saccades to the target positions she had learned to associate with the respective sounds. Each monkey was required to execute saccades to a single memorized position. Because they were in complete darkness, monkeys executing memorized saccades were required to fixate both the central and the peripheral target within a window of 5°, in contrast to the monkeys executing visually guided saccades which were required to hold their gaze in a window of 2.5°.

Two-dimensional reconstructions and statistics

The 14C-DG experiments, brain sectioning, and quantitative autoradiography were performed as previously described (Gregor-iotu and Savaki, 2001). Local cerebral glucose utilization (LCGU) values (in μmol/100g/min) were calculated from the original operational equation of the method (Sokoloff et al., 1977) using the appropriate kinetic constants for the monkey (Kennedy et al., 1978). A total of about 550 serial horizontal sections of 20 μm thickness in each hemisphere were analyzed covering the full extent of the intraparietal sulcus (IPS). One section every 500 μm was stained with thionin for identification of cytoarchitectonic areas within the affected lateral bank of the IPs, according to the criteria of Medalla and Barbas (2006). Two-dimensional (2D) reconstructions of the spatial distribution of metabolic activity within the rostrocaudal and dorsoventral extent of each hemisphere were generated as previously described (Dalezios et al., 1996; Savaki et al., 1997). Briefly, for each horizontal brain section, a data array was obtained by sampling LCGU values (pixel by pixel, at a resolution of 45 μm/pixel) in the rostrocaudal extent of the IPs along a line parallel to the surface of the cortex which included all cortical layers. The intersection of the IPs with the parietooccipital sulcus (POS) was used for the alignment of adjacent data arrays. Given that the average of LCGU values was calculated in sets of five adjacent sections, the plotting resolution in the illustrated 2D maps is 100 μm. Thus, each 2D-reconstruction consists of 110 lines or sets of sections (550 sections divided by 5 sections/set) and each line represents the average of 5 adjacent
serial sections. Normalization of LCGU values was based on the average unaffected gray matter value pooled across all hemispheres of all monkeys.

The statistical significance of differences in LCGU values for the intraparietal regions in all monkeys was determined by the Student’s unpaired t test. Adopting a conservative criterion, only differences exceeding 7% were considered for statistical analysis given that homologous areas of the two hemispheres of a normal resting monkey can differ by up to 7% (Savaki et al., 1993).

**Geometrical normalization and activity plots**

Due to the inter- and intrahemispheric variability, and to allow for the direct comparison of the sites of activation, the individual 2D maps (functional-14C-DG, and anatomical-cytoarchitectonic) were further processed to match a reference map (geometrical normalization according to Gregoriou and Savaki (2003) and Gregoriou et al. (2005). In each horizontal section, the distances between the intersection of the IPs with the POs and the two crowns (anterior and posterior) of the IPs were averaged and used as landmarks to generate a reference surface map. The 2D functional and anatomical maps of each hemisphere were then transformed using linear transformations of the plane with custom designed routines in the Matlab software for numeric computations (The Mathworks, Inc.) to fit the reference surface landmark map.

To plot graphically the spatial distribution of metabolic activity in the lateral bank of the IPs (area 7IP) in control and experimental monkeys, we first measured (every 100 μm) the local cerebral glucose utilization values (LCGU, in μmol/100 g/min) along lines parallel to the fundus of the IPs. The length of all these lines was then normalized to the average length of the 7IP (25 mm). The resulting arrays of LCGU values (which can be thought as vectors in a 250-D space) were then summed, and each value in the array of the resulting vector sum was divided by the total number of arrays to obtain line graphs which were plotted along with their 95% confidence intervals.

**Results**

We provide a broad overview of all eye movements that were executed by all 6 of our rhesus monkeys in directions opposite to the hemispheres we studied (Fig. 1). Because approximately 85% of the radiolabeled glucose is taken up by cells during the critical 10 first minutes of the 14C-DG experiment, within an oculomotor space 5 × 5° centered on the peripheral target. This corresponds to a density of 7.64 saccades/degree². In addition, the same animal executed small eye movements (<3°) mostly around the fixation window (density: 3.88 per degree²). Finally, saccades executed by Hl in other directions and amplitudes had a low average density (0.02 per degree²). The distribution of end points of the saccades and the small amplitude eye movements around the fixation point executed by this monkey during the critical 10 first minutes of the experiment are illustrated in Fig. 1C. The OI monkey executed a total of 138 saccades from the central to the peripheral visual target (density: 5.52 per degree²) during the critical 10 first minutes of the experiment (within the same 5 × 5° window centered on the peripheral target). Small eye movements (<3°) around the fixation point had a density of 3.4 per degree², while saccades of other amplitudes and directions had an average density of 0.08 per degree². It should be noted that because area LIP is known to represent the contralateral half of visual space (Blatt et al., 1990; Gnadt and Andersen, 1988), and its microstimulation to evoke contraversive saccades (Mushiake et al., 1999), we report only saccades contraversive to the reconstructed IPs. After the end of each trial and during the intertrial interval, the eyes made saccades in several directions before coming back to the central position in the beginning of the new trial. These widely scattered saccades had a small widespread effect on the activity of the opposite IPs and consequently they might be expected to have an even smaller, if any, effect on the IPs activity of the hemisphere considered. Indeed, subtraction of the IPs activity map of the control monkey in the dark (Fig. 3C), which made diffuse saccades in the entire oculomotor space (Fig. 1A), from the maps of the experimental monkeys (Figs. 3D–H) did not change the pattern of activations we observed (data not shown).

An extended region of the intraparietal cortex was activated in both monkeys executing visually guided saccades (Figs. 2C, 3E–F). To provide a more refined description of the location of the activated region, we divided the IPs into three parts (Fig. 3B), equidistant at all anteroposterior levels, the anterior one (IPA) including most of the cytoarchitectonically defined area LIPd, the...
Fig. 1. Three-dimensional histograms of the number of saccades (z axis) vs. horizontal (DH) and vertical (DV) eye displacements of all saccades executed by the monkeys during the critical first 10 minutes of the 14C-DG experiment. (A) Control-in-the-dark monkey. (B) Monkey fixating a centrally located visual target. (C, D) Histograms from monkeys executing visually guided saccades, 30° horizontal, and 20° up-left oblique, respectively. (E, F) Histograms from monkeys executing memory-guided saccades, 20° horizontal, and 25° up-left oblique, respectively.
middle one (IPm) covering most of the cytoarchitectonically delineated area LIPv, and the posterior one (IPp) including the caudalmost portion of area 7IP (most probably including LOP). Approximately, the middle and anterior thirds of the lateral bank were activated in these monkeys, covering parts of both areas LIPv and LIPd (Figs. 3E–F). A different pattern of activation was found in the control monkey which was rewarded for maintaining fixation of a visual target located straight ahead (Cf, Control-fixation). This monkey fixated the visual target for 75% of the time during the critical 10 first minutes of the 14C-DG experiment. During the same period in time, small movements (<3°) near the fixation point had a density of 7.2 per degree², whereas the average density of saccades executed outside the fixation window was very low (0.01 per degree²). The distribution of end points of eye movements executed by the Cf monkey during the critical 10 first minutes is illustrated in Fig. 1B. Cf demonstrated increased metabolic activity in the fixation-related region of the intraparietal cortex (Gregoriou and Savaki, 2001), which is located at the border of LIPd and LIPv and extends mainly in the anterior part of the lateral bank of the IPs (Fig. 3D).

Regions activated for memory-guided saccades

To obtain maps of the intraparietal regions activated for memory-guided saccades of amplitudes and directions similar to those of the visually guided saccades described above, one monkey (Hd) was rewarded for performing repeated acoustically triggered horizontal saccades to a memorized target location 20° away from straight ahead, and another monkey (Od) for performing acoustically triggered saccades to a memorized location 25° away from straight ahead in an oblique direction 45° up. The Hd monkey executed a total of 210 saccades from the central to the peripheral memorized location during the critical 10 first minutes of the experiment. The distribution of the end points of saccades and small amplitude eye movements around the fixation point executed by Hd during the critical 10 first minutes of the experiment are illustrated in Fig. 1E. As expected of saccades executed in the absence of targets, these were much more widely distributed than those of monkey Hl, and thus we had to increase the sampling window to an oculomotor space 10° centered on the peripheral memorized location (density: 2.1 saccades/degree²). Also as expected of saccades in the dark, these were slightly smaller than the visually guided saccades. However, any differences observed in the activation of their IPs are unlikely to be due to differences in the metrics of the saccades they executed, since both the memory-guided and the visually guided saccades were large in amplitude (20–30°) and the saccade amplitude-related tuning curves of area LIP neurons are broadly tuned (Barash et al., 1991b). Small eye movements (<3°), mainly around the fixation window, had a density of 0.24 per degree². Few saccades were performed outside these regions, at an average density of 0.09/degree². The Od monkey executed a total of 217 saccades from the central to the peripheral memorized location during the critical 10

Fig. 2. Quantitative color coded 14C-DG glucograms obtained from horizontal brain sections at the level of the intraparietal sulcus (IPs). (A) Lateral view of the right hemisphere of a monkey brain showing the dorsoventral location of the horizontal section through the IPs (illustrated below). The rectangle shows the region enlarged in the following glucograms (B–D). (B) Glucogram from the control monkey in the dark. Cytoarchitectonic borders between LIPd, LIPv, and area 7 are marked in the lateral bank of the IPs. Ls, lunate sulcus; STs, superior temporal sulcus. (C) Glucogram from the brain of a monkey executing horizontal visually guided saccades. (D) Glucogram from the brain of a monkey executing horizontal memory-guided saccades in the dark.
first minutes of the experiment, within an oculomotor space of similar size ($10 \times 10^2$) also centered on the peripheral memorized location (density: $2.17$ saccades/degree$^2$). Eye movements smaller than $3^\circ$ had a density of $0.64$ per degree$,^2$ and saccades performed elsewhere had an average density of $0.03$ per degree$.^2$ (Fig. 1F).

In contrast to the monkeys executing visually guided saccades, it is mainly LIPv in the middle third of the lateral bank of the IP$\acute{s}$ that was activated in both monkeys executing memory-guided saccades in the dark (Figs. 3G–H). Fig. 4 compares the main sequence relationship of visually guided saccades executed by one...
monkey (Fig. 4A) to that of the memory-guided saccades executed by another monkey (Fig. 4B) during the critical first 10 min of the experiment. As shown here, some of the memory-guided saccades were slower than expected from their amplitude (Fig. 4B). Otherwise, the saccades executed both in the light and in the dark by all our overtrained monkeys followed the same main sequence relationships. This indicates that any differences observed in the activation of their IPs are not due to differences in the kinematics of the saccades they executed.

To obtain the baseline metabolic activity of the IPs (Fig. 3C), a second control monkey was rewarded for remaining alert in the dark while listening to auditory stimuli similar to the acoustic cues delivered to the monkeys executing memory-guided saccades in the dark (Cd, Control-dark). This animal’s saccades were almost evenly distributed throughout its oculomotor space, with an average density equal to 0.04 per degree² in the central visual field and 0.03/degree² in the peripheral field (Fig. 1A).

**Comparison of regions activated for visually and memory-guided saccades**

To better compare the effects induced by memory-guided saccades in the dark (without any visual stimulus) to those induced by visually guided saccades, we generated two average maps of the IPs map obtained after averaging the two hemispheres of monkey LIPv of the middle third of area 7IP, which was produced after averaging the corresponding maps of the two monkeys performing saccades to memorized target locations. Comparison of these two average quantitative glucograms indicates that the region activated for visually-guided saccades (Fig. 5A) extends more rostrally and superficially (close to the crown) in the lateral bank of the IPs whereas that activated for memory-guided saccades (Fig. 5B) is restricted to a region more posterior and deep in the lateral bank (close to the fundus). The differences in saccade metrics within each group (visually or memory-guided) were much bigger than the difference between the two groups. Thus, differences in saccade metrics cannot account for the shift of activity to relatively more posterior-ventral positions in our memory-saccade monkeys. The geometrical normalization of the IPs cannot account for this difference either. Because the IPs of the memory-saccade monkeys were shorter than that of the visual-saccade monkeys (23 vs. 27 mm on the average), normalization would push the memory-saccade-related regions rostrally (given the caudal origin of our anteroposterior axis). In fact, the opposite was true, in that the memory-saccade-related region extended further caudally than the visual-saccade-related region.

To better define quantitatively the anteroposterior location and extent of the 7IP regions activated for visually and memory-guided saccades, we plotted the local cerebral glucose utilization values (LCGU, in μmol/100g/min) every 100 μm along the rostrocaudal extent of the lateral bank of the IPs (area 7IP) with 95% confidence intervals (Fig. 5C). The line graph obtained from the Cd control monkey (Fig. 5C, light gray) is the average of the two lateral banks of the IPs in its two hemispheres and indicates the baseline activity of area 7IP. By comparison to it, the peak value of the line graph obtained from the two monkeys engaged in memory-guided saccades (Hd + Od) is higher by approximately 15%, and is located in the middle third of the lateral bank of the IPs (Fig. 5C, dark gray). Again by comparison to Cd, the peak value of the line graph obtained from the two monkeys engaged in visually guided saccades (Hd + Od) is similarly increased by approximately 15% as far as the middle third of their area 7IP is concerned (Fig. 5C, intermediate gray). However, the peak value of this line graph is considerably higher (by approximately 35%) and is located in the anterior third of area 7IP in the lateral bank of IPs.

To illustrate the spatial distribution of the LCGU differences between experimental and control monkeys, we subtracted the average metabolic maps of different groups from each other. The IPs map obtained after averaging the two hemispheres of monkey Cd was subtracted from the map obtained after averaging the IPs maps of monkeys Hl and Ol which executed visually guided saccades (Hd + Od) is similarly increased by approximately 15% as far as the middle third of their area 7IP is concerned (Fig. 5C, intermediate gray). However, the peak value of this line graph is considerably higher (by approximately 35%) and is located in the anterior third of area 7IP in the lateral bank of IPs.

Fig. 4. Scatterplots of radial mean velocity (ordinate) vs. radial size (abscissa) for all saccades executed during the critical first 10 min of the 14C-DG experiment by a monkey performing visually guided (A) and a monkey performing memory-guided (B) saccades.
markedly (by an average of 35% as compared to the Cd) for visually guided saccades and much less for memory-guided saccades (10% higher than the Cd). To elucidate the IPs region responsible for visuo-spatial saccade-related processing, we subtracted the average Hd + Od map from the average Hl + Ol map. The resulting image (Fig. 6B) indicates that this visuo-spatial saccade-related region is confined to a portion of the anterior third of the lateral bank of the IPs, it remains superficial within the bank and covers mainly area LIPd.

Fig. 7 illustrates the spatial relationship of 7IP regions activated for distinct facets of oculomotor behavior. Firstly, the geometrically normalized IPs metabolic maps of both hemispheres of the monkey executing visual fixation were averaged, and all pixels in area 7IP with LCGU values higher (by 10% or more) than those of the Cd were color coded green. The resulting map (Fig. 7A) was superimposed on the average IPs map of the two monkeys executing saccades to visual targets, which was generated with the same 10% threshold and was color coded red. The region of overlap (green + red = yellow) indicates that about one third of the neural space of area 7IP devoted to visually guided saccades also participates in visual fixation (Fig. 7B). In a similar manner, we explored the spatial relationship of the intraparietal regions devoted to visually and memory-guided saccades. To this end, the average metabolic IPs map of the two monkeys executing saccades to visual targets (whose activated regions were color coded red) were placed on top of the corresponding map of the two monkeys executing saccades to memorized target locations whose activated regions were color coded blue. Clearly, the region of overlap (Fig. 7C, blue + red = violet) indicates that most of the 7IP area activated by saccades to memorized target locations, in the absence of any visual stimulus, extends through the caudalmost and deepest portion of the region activated for saccades to visual targets, and is confined to area LIPv. In addition, there is a widespread activation related exclusively to the visually guided saccades (Fig. 7C, red) within area LIPv, and a small region in the depth of the sulcus (close to the fundus of the IPs) which is activated exclusively by memory-guided saccades (Fig. 7C, blue). In view of the large extent of the fixation-related area of 7IP (Fig. 7A, green), the fact that the region activated for visually guided saccades (Fig. 7C, red + violet) is more widespread and significantly more intense (Table 1) than that activated for memory-guided saccades (Fig. 7C, blue + violet) must be partly due to the fact that monkeys executing visually guided saccades devoted some of their time into fixating visual targets. It should be noted that the fixation of visual targets implies not only exposure to more intense sensory stimulation but also more marked oculomotoricity, as demonstrated by numerous small eye movements executed around the fixation target (Fig. 1B). Fig. 7D summarizes the 7IP regions activated for the distinct facets of oculomotor behavior we explored. Besides those shown in green,
Values represent the mean normalized glucose utilization (LCGU) in \( \mu \text{mol}/100\text{g/min} \).

Discussion

The present report is the first to provide high-resolution quantitative functional images of the location and extent of lateral intraparietal cortical regions engaged in saccades to visual targets and saccades to memorized target locations in the dark. Also, this is the first study to assign functional roles to the cytoarchitectonically defined areas LIPd and LIPv. We demonstrate that area LIPv is activated for both visually guided and memory-guided saccades whereas LIPd is activated only for visually guided saccades. We provide evidence that topographically distinct thal palm partially overlapping neuronal populations process visuo-spatial and memory-related oculomotor signals.

Our data indicate that the rostromedial extent and the location of the 7IP region activated for visually guided saccades and fixation differ from those of the traditionally defined area LIP. The latter has been variously described as occupying the middle-posterior fourth (Fig. 1 in Gnadt and Andersen, 1988; Fig. 1 in Barash et al., 1991a), the posterior two-thirds (Fig. 2 in Andersen et al., 1990), the middle third (Fig. 2 in Colby, 1998), and the middle two-fourths (Fig. 8 in Ben Hamed et al., 2001, Fig. 11 in Lewis and Van Essen, 2000) of the lateral bank of the IPs. In contrast, our high-resolution quantitative images demonstrate that the 7IP region activated for visually guided saccades extends more rostrally than previously reported, occupying approximately the anterior and middle two thirds of the lateral bank of the IPs, occupying both LIPv and LIPd. Finally, our data can help reconcile the long standing debate between two alternative hypotheses concerning the principal role of area LIP. On the one hand, area LIP has been thought to participate in selective spatial attention and to embody a salience map of the visible world (Colby and Duhamel, 1996; Goldberg et al., 1990; Gottlieb and Goldberg, 1999; Gottlieb et al., 1998; Kisunoki et al., 2000) and on the other, to directly represent saccade-related movement plans (Barash et al., 1991b; Gnadt and Andersen, 1988; Mazzoni et al., 1996; Snyder et al., 1998). Both hypotheses are supported by our data which indicate the existence of two segregated regions in the lateral bank of the IPs, each entrusted with a different role. A rostral one located superficially (close to the crown) within area LIPd is mainly associated with visuo-spatial processing, and a caudal one deeper in the bank (close to the fundus) within area LIPv is primarily associated with motor control.

Table 1
Metabolic effects in the intraparietal cortical regions

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Values represent the mean normalized glucose utilization (LCGU) in \( \mu \text{mol}/100\text{g/min} \). Cd, average of distinct IPs regions in the two hemispheres of the control monkey in the dark. Hd, Od, values from the monkeys executing horizontal and oblique memory-guided saccades, respectively. Cf, average of the IPs regions in the two hemispheres of the fixating monkey. HI, OI, values from the monkeys executing horizontal and oblique visually guided saccades, respectively. n, number of sets of five adjacent horizontal sections used to obtain the mean LCGU values for each region in each hemisphere. %Cd, %Cf, percent difference between the experimental and the Cd, Cf monkeys, calculated as (experimental − Cd) / Cd * 100 and (experimental − Cf) / Cf * 100, respectively. Values in bold indicate statistically significant differences by the Student's unpaired \( t \) test at the level of \( P < 0.001 \). 5IPa, 5IPm, 7IPp, anterior, middle, posterior part of the medial bank of the IPs, respectively.
Consistent with previous reports (Barash et al., 1991b; Colby et al., 1996; Gnadt and Andersen, 1988), our quantitative results demonstrate that area 7IP is significantly activated in association with both visual fixation and visually guided saccades. The region activated for the fixation of visual targets is smaller than that activated for visually guided saccades, is located at the border of LIPv and LIPd, and extends mainly rostrally through LIPd. Such an anterior location of the intraparietal fixation-related area is consistent with previous electrophysiological descriptions (Murata et al., 2000). Also, the herein documented relatively large size of the intraparietal-fixation region is consistent with the reported overrepresentation of the central visual field (Ben Hamed and Duhamel, 2002; Ben Hamed et al., 2001) and may be due to the enlargement of the neural space allocated to central vision during fixation (Ben Hamed et al., 2002). Finally, the fact that horizontal 30° and oblique 20° visually guided saccades induced roughly similar patterns of activation within 7IP may be due to the coarse visual field topography of area LIP (Ben Hamed et al., 2001; Blatt et al., 1990) and to the broad tuning of LIP neurons (Barash et al., 1991b).

Our quantitative functional results also demonstrate that a considerable part of area 7IP, confined to area LIPv, is activated for both visually guided and memory-guided saccades. The demonstration that the middle third of area 7IP is markedly activated for saccades executed to memorized locations in the absence of visual stimuli is consistent with the fact that LIP neurons discharge for delayed saccades to a recently extinguished target (Colby et al., 1996; Gnadt and Andersen, 1988) and for saccades to memorized locations in the absence of visual stimuli (Colby et al., 1996). The much weaker activation we observed in the anterior third of area 7IP is compatible with the weak oculomotor signals carried by relatively rostral 7IP neurons (Ben Hamed and Duhamel, 2002). The present report is the first to demonstrate that the extent of the region activated for memory-guided saccades is smaller, and the intensity of its activation weaker than that of the entire region activated for visually guided saccades of similar direction and amplitude. The fainter activation accompanying memory-guided saccades is consistent with the fact that to discharge maximally LIP neurons require both the presence of visual stimuli and the execution of saccades towards them (Colby and Duhamel, 1996; Colby and Goldberg, 1999; Kusunoki et al., 2000; Paré and Wurtz, 1997). Unexpectedly, the region activated for memory-guided saccades extends to the fundus of the IPs into some of the traditional area VIP (Colby et al., 1993). Nevertheless, this finding confirms a previous report indicating that the saccade-related part of the IPs extends beyond the traditional LIP, rostral and ventral to it, into area VIP (Thier and Andersen, 1998).

In contrast to the region activated for memory-guided saccades, which was located fairly deeply in the middle third of the lateral bank of the IPs and which was confined to LIPv, the region activated for saccades to visual targets occupied both deeper and superficial territories of both its anterior and middle thirds and

![Fig. 7. Qualitative imaging of the functional parcellation of area 7IP.](image-url)
extended through both the LIPv and the LIPd. The activation in LIPd displayed the most dramatic effects we observed in this study. The level of activation in LIPv was the same in the monkeys executing visually guided saccades and the monkeys performing memory-guided saccades, in both cases displaying about 17% higher glucose consumption than that of the Cd monkey. The activation induced by visually guided saccades which extended to LIPd was even higher (by about 35%) as compared to the Cd monkey. Apparently, LIPd requires visual stimulation in addition to saccades to be maximally activated. To recapitulate, our data demonstrate that the saccade-related region of area 7IP can be divided into three portions: (a) one activated for all saccades, both visually and memory-guided, occupying the middle third of the lateral bank close to the fundus, and lying within LIPv, (b) one which is activated mainly for visually guided saccades and/or visual stimuli and extends further rostrally and closer to the crown, and which lies within both LIPv and LIPd, (c) a much smaller one extending further caudally and deeply (closer to the fundus) preferentially activated for memory-guided saccades and/or memorized spatial target representations, and lying within LIPv and probably area VIP. Such a functional parcellation of the lateral IPs is consistent with known anatomy and neurophysiology. Firstly, the posterior part of the lateral bank of the IPs projects to the frontal eye field (FEF) and contains a high proportion of neurons related to memory-guided saccades (Blatt et al., 1990) whereas a more anterior part contains a representation of the visual field (Ben Hamed et al., 2001). Also, LIPv, close to the fundus of IPs, is strongly connected with the core FEF and the superior colliculi whereas LIPd, close to the crown, is not (Blatt et al., 1990; Lynch et al., 1985; Schall et al., 1995). Moreover, LIPv receives projections mostly from dorsal stream areas whereas LIPd from both the dorsal and ventral streams (Andersen et al., 1990; Blatt et al., 1990; Boussaoud et al., 1990; Stanton et al., 1995; Ungerleider and Desimone, 1986).

Such a functional parcellation of area LIP into subregions related to memory and visually guided saccades can help reconcile certain apparently conflicting results regarding the response properties of its neurons and the deficits resulting from its lesions. For example, almost all LIP neurons were shown to respond to visual stimuli in one study (Colby et al., 1996). In contrast, only about half of the LIP neurons were shown to respond to visual stimuli in another two studies (49% in Gnadt and Andersen, 1988 and 63% in Barash et al., 1991a). Our data could help explain this discrepancy if the three studies focused on different subregions of area LIP, namely if the neurons studied in the former one were located more rostrally than the neurons studied in the latter two. Unfortunately, no map of the recording sites was provided by Colby et al. (1996). However, in a later publication of this group (Colby, 1998), recording sites are indeed reported to occupy more anterior locations than those of Gnadt (Gnadt and Andersen, 1988) and Barash (Barash et al., 1991a). Moreover, the recording sites of Gnadt (Gnadt and Andersen, 1988) and Barash (Barash et al., 1991a) are also more rostral than their descriptions lead one to expect, and roughly correspond to the middle third of our study, because (i) the location of their electrode tracks was projected onto the parasagittal plane (a procedure which underestimates the length of segments normal to the horizontal plane, such as the caudal part of the IPs) whereas we unfolded the entire IPs, and (ii) our reconstructed 2D maps extend more caudally, up to the intersection of the IPs with the parietooccipital and the lunate sulci. Similarly conflicting are the results from lesion studies. Visual perception deficits rather than saccade execution deficits were reported following reversible inactivation of area LIP in one study (Wardak et al., 2002) whereas memory-guided saccades (but not visually guided ones) were compromised in another (Li et al., 1999). Again, our data can help reconcile these conflicting results if the lesion was more severe in the middle third and in the depth of the lateral bank of IPs in the latter study (thus impairing the region we found activated for memory-guided saccades), and in the rostral third and more superficially within the bank in the former study (thus impairing a region more intensely activated for visually guided saccades).

All in all, our findings illustrate that the lateral bank of the IPs is a mosaic of the following segregated, albeit partially overlapping, regions: (i) A centrally placed fixation-related region at the border of LIPv and LIPd (Fig. 7A, green). (ii) This is surrounded by a widespread region extending in both LIPv and LIPd, which is activated for visually guided saccades and possibly encodes visuospatial and saccade-related parameters (Fig. 7B, red). (iii) A more caudal region confined to LIPv, which is activated for memory-guided saccades and possibly encodes the remembered locations of saccade targets and/or saccade metrics. The area of overlap between regions ii and iii (Fig. 7C, violet) lying in LIPv may correspond to the representation of oculomotor space in area 7IP, while the area of overlap between all three regions (fixation, visual- and memory-saccade-related) lying in the middle of the bank around the border of LIPv and LIPd may correspond to the representation of the central part of oculomotor space in area 7IP (Fig. 7D, white). To the regions of area 7IP that we found activated for visually and memory-guided saccades in the present study, one should add the regions activated for visually guided arm-reaching described in previous studies of our laboratory. Besides occupying a large part of area 5IP in the medial bank of the IPs, the region activated for visually guided arm-reaching also extended within area 7IP in the lateral bank of the IPs (Gregoriou and Savaki, 2001, 2003). Consistent with previous reports (Snyder et al., 1998, 2000), our present and previous data demonstrate that there is minimal overlap between the saccade-related and arm-reach-related regions of area 7IP; and this is largely confined to a portion of the saccade-related region of the present study in the depth of the sulcus. This supports the notion that LIP neurons process effector-specific signals, responding more strongly to visual stimuli serving as targets for eye movements than to visual stimuli targeted by arm movements.

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References

Andersen, R.A., Asanuma, C., Cowan, W.M., 1985. Callosal and prefrontal associational projecting cell populations in area 7a of the
Snyder, L.H., Batista, A.P., Andersen, R.A., 1998. Change in motor plan,
without a change in the spatial locus of attention, modulates activity in posterior parietal cortex. J. Neurophysiol. 79, 2814–2819.


