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Space Coding in Primate Posterior Parietal Cortex

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Neuropsychological studies of patients with lesions of right frontal (premotor) or posterior parietal cortex often show severe impairments of attentive sensorimotor behavior. Such patients frequently manifest symptoms like hemispatial neglect or extinction. Interestingly, these behavioral deficits occur across different sensory modalities and are often organized in head- or body-centered coordinates. These neuropsychological data provide evidence for the existence of a network of polymodal areas in (primate) premotor and inferior parietal cortex representing visual spatial information in a nonretinocentric frame of reference. In the monkey, a highly modular structural and functional specialization has been demonstrated especially within posterior parietal cortex. One such functionally specialized area is the ventral intraparietal area (VIP). This area is located in the fundus of the intraparietal sulcus and contains many neurons that show polymodal directionally selective discharges, i.e., these neurons respond to moving visual, tactile, vestibular, or auditory stimuli. Many of these neurons also encode sensory information from different modalities in a common, probably head-centered, frame of reference. Functional imaging data on humans reveal a network of cortical areas that respond to polymodal stimuli conveying motion information. One of these regions of activation is located in the depth of human intraparietal sulcus. Accordingly, it is suggested that this area constitutes the human equivalent of monkey area VIP. The functional role of area VIP for polymodal spatial perception in normals as well as the functional implications of lesions of area VIP in parietal patients needs to be established in further experiments. © 2001 Academic Press

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INTRODUCTION

The primate posterior parietal cortex (PPC) is related to the processing of spatial and motion information. As pointed out by Ungerleider and Mishkin (1982), damage to the ventral or WHAT pathway leads to disturbance of object recognition while damage to the WHERE or HOW pathway leads to behavioral deficits often referred to as *extinction* and *neglect* (typically after right hemispheric lesions, for reviews see Vallar, 1998; Mesulam, 1999) or *apraxia* (typically after left hemispheric lesions, see, e.g., Sirigu *et al.*, 1995). While neglect describes a phenomenon observed in patients who tend to ignore the part of space contralateral to their lesion, extinction is observed only if two attentionally competing sensory stimuli are presented simultaneously (Mattingley *et al.*, 1997; Driver and Mattingley, 1998; Ladavas *et al.*, 1998; Fink *et al.*, 2000). In such a case, only the stimulus which is more ipsilateral to the lesion site is perceived. Two specific functional aspects of neglect (and/or extinction) are essential for the description of this behavioral deficit and, importantly for this review, might be crucial for the understanding of how normal posterior parietal cortex operates. Firstly, the visual system of neglect patients up to the primary visual cortex is usually intact and these patients show exploratory eye movement behavior (Karnath *et al.*, 1998). Thus, although patients can look at points in space contralateral to their lesion site they do not perceive what is there. This implies that the observed behavioral deficit occurs not in retinally centered but rather in a head- or body centered frame of reference. Secondly, neglect not only occurs for visual but also for tactile and auditory stimuli, i.e., it is polymodal (Ladavas *et al.*, 1998; Kerkhoff, 1999).

Lesions of posterior parietal and frontal cortex lead to comparable behavioral deficits in humans and nonhuman primates (Lynch and McLaren, 1989; Gaffan and Hornak, 1997). It therefore appears appropriate to (i) consider the macaque monkey as an animal model for the better understanding of the normally working

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posterior parietal (and frontal) cortex and (ii) test for functional equivalencies between humans and macaques concerning specific cortical regions which have been described in detail for the macaque. This chapter reviews previous work on the macaque, describing polymodal responses in PPC and the reference frame in which sensory information is encoded. We then provide new evidence for functional equivalencies in the processing of polymodal motion information between humans and macaques that might be important for the further understanding of neglect.

NEUROPHYSIOLOGY: POLYMODAL MOTION INFORMATION RESPONSES IN MACAQUE POSTERIOR PARIETAL CORTEX

Recent neurophysiological studies in macaque monkeys revealed a number of functionally distinct subdivisions along and within the intraparietal sulcus (IPS). One of these areas is the ventral intraparietal area (VIP) located in the fundus of the IPS. Based on anatomical data (Maunsell and Van Essen, 1983; Ungerleider and Desimone, 1986), area VIP was originally defined as the MT projection zone in the intraparietal sulcus (IPS). These results suggested that neurons in area VIP might be responsive for the direction and speed of moving visual stimuli, a hypothesis confirmed in later physiological studies (Duhamel *et al.,* 1991; Colby *et al.,* 1993).

While, anatomically, located at the borderline between the visual and the somatosensory system, area VIP has not yet been assigned a specific behavioral function. Recent data suggested an involvement in the processing of self-motion information (Bremmer *et al.,* 1995, 1997; Schaafsma and Duysens, 1996; Schaafsma *et al.,* 1997). In these experiments, neurons were tested for their responsiveness to basic optic flow pattern like frontoparallel motion, or forward (expansion) or backward (contraction) motion. The great majority of neurons in area VIP respond selectively to such optic flow stimuli.

Like visual information, somatosensory signals can be used to encode motion information. Many neurons in area VIP respond also to tactile stimulation (Duhamel *et al.,* 1991, 1998; Colby *et al.,* 1993). Most VIP cells that have a somatosensory receptive field (RF) show a positive response to passive superficial stimulation of restricted portions of the head, with the upper and lower face areas being represented equally often. Somatic and visual RFs are organized in an orderly manner with tactile RFs showing a systematic relation to the main axes of the visual field. Critically, the matched tactile and visual RFs often demonstrate coaligned direction selectivity.

Another source of motion information may result from vestibular stimulation, i.e., rotational and/or translational self-motion. Accordingly, neurons in area VIP were tested with vestibular (vertical axis) stimulation (Bremmer *et al.,* 1995, 1997; Graf *et al.,* 1996). About one-third of the neurons responded with direction selective discharge during whole-body sinusoidal horizontal movement. All neurons with vestibular responses also show directionally selective visual responses. Interestingly, preferred directions for visual and for vestibular stimulation are codirectional, i.e., nonsynergistic, or noncomplementary. This response characteristic together with preliminary data on visual disparity sensitivity might be a hint as to the role of area VIP in the coding of motion especially in near-extra personal space (Bremmer *et al.,* 1997; Bremmer and Kubischik, 1999).

Finally, recent studies showed that many neurons in area VIP not only respond to visual, tactile, and vestibular, but also to auditory stimulation (Schlack *et al.,* 2000). In this study, using auditory stimuli in virtual space, it was demonstrated that many neurons in area VIP have spatially restricted auditory receptive fields. All of these neurons also have visual responses and, like in the tactile domain, these neurons tend to have spatially congruent visual and tactile RF locations.

This view of area VIP as a crucial node within a cortical network subserving the encoding of polymodal sensory signals arising either from object or self-motion, was complemented by an anatomical study showing direct connections between area VIP and an area within the ventral premotor cortex (PMv) which subserves head movements (Luppino *et al.,* 1999).

NEUROPHYSIOLOGY: REFERENCE FRAME FOR THE ENCODING OF POLYMODAL MOTION INFORMATION SIGNALS

The above-mentioned orderly arrangement of responsiveness across sensory modalities demands investigation of the reference frame used for the encoding of signals from all four sensory modalities. Vestibular signals as well as auditory signals are organized in head-centered coordinates per se. Tactile responses arising from stimulation of receptive fields on the head are organized in a head-centered frame of reference, too. Thus, the question arises whether visual signals might also be encoded in this very same frame of reference. Several theoretical studies have previously demonstrated that a combination of information about the position of a visual stimulus on the retina and information about the position of the eyes in the head can be used to compute the position of visual signals in nonretinocentric, probably head-centered coordinates (Zipser and Andersen, 1988). Yet the population of such eye position-influenced cells would need to fulfill certain prerequisites in order to allow such a nonretinocentric encoding. These conditions would be met if (i) the preferred directions, i.e., the gaze directions accompanied by the strongest discharge of the

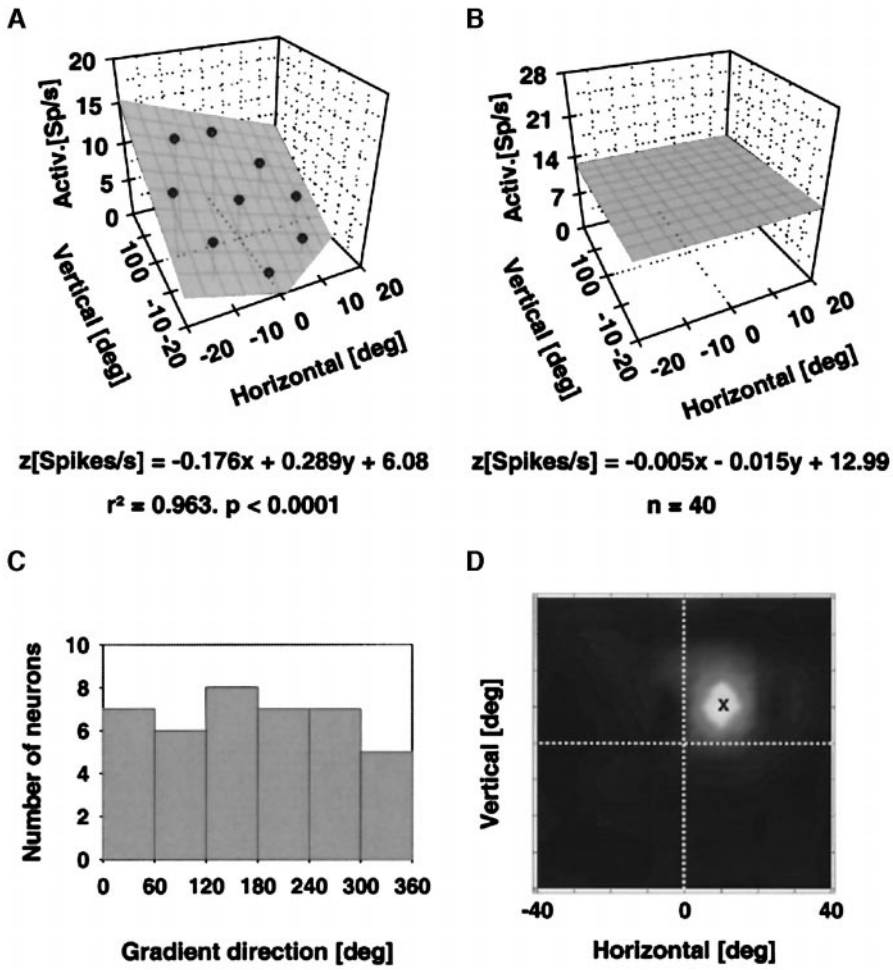

FIG. 1. Eye position effect during fixation in darkness. (A) Single cell level. The shaded plane represents the two-dimensional linear regression to the mean discharge values. Regression parameters are given below the 3-D panel. The *x–y* plane in this plot represents the central 40 by 40° of the tangent screen. The base point of each drop line depicts the fixation location on the screen, and the height of each line depicts the mean activity value during fixation at this location. (B) Population level. The mean population response plane was obtained by averaging all regression planes computed from individual neuronal discharges with a significant eye position effect. The resulting discharge plane proved to be flat. (C) Distribution of the gradients of the regression planes. Gradient directions were computed as arctan(*b*/*a*), with *a* and *b* the slopes of the regressions planes in horizontal and vertical direction, respectively. Statistical analysis proved the directions of the gradients to be uniformly distributed. (D) Retrieval of eye position from neuronal discharges. The position of the eyes in the orbit is computed by means of a population code termed isofrequency encoding (for details, see Boussaoud and Bremmer, 1999). The difference between the center of mass of the points of intersection of the isofrequency lines and the real eye position (*x*) is 2.75°.

cells, were uniformly distributed, and (ii) the eye position effect, observed at the single cell level, was balanced out at the population level (see Bremmer *et al.*, 1998). Accordingly, the activity of neurons in area VIP was tested for an influence of eye position during active fixation in darkness. Indeed, more than half the cells revealed such an eye position effect (Bremmer *et al.*, 1999). This modulatory effect of the position of the eyes was quantified using a two-dimensional linear regression analysis. An example is given in Fig. 1A. For this cell, discharges were strongest for fixation locations left and upward (ANOVA: $P < 0.0001$). Activity decreased for eye positions right and downward.

The eye position effect, which could be observed at the single cell level, was at equilibrium at the population level. Average discharge values of the population of neurons for the different fixation locations were not significantly different (ANOVA: $P > 0.9$; Fig. 1B). In other words, the average response of the ensemble of cells shows an invariance of discharges with respect to eye position.

This equilibrium of the population response does not necessarily result from a roughly equal distribution of eye position effects across all parts of the oculomotor range. Therefore, the distribution of the gradients (amount and direction of the steepest increase of activity with eye position) of the regression planes was analyzed too. The analysis indicated that the directions of the gradients were uniformly distributed (χ^2 test: $P > 0.9$; Fig. 1C). As mentioned above, the observed

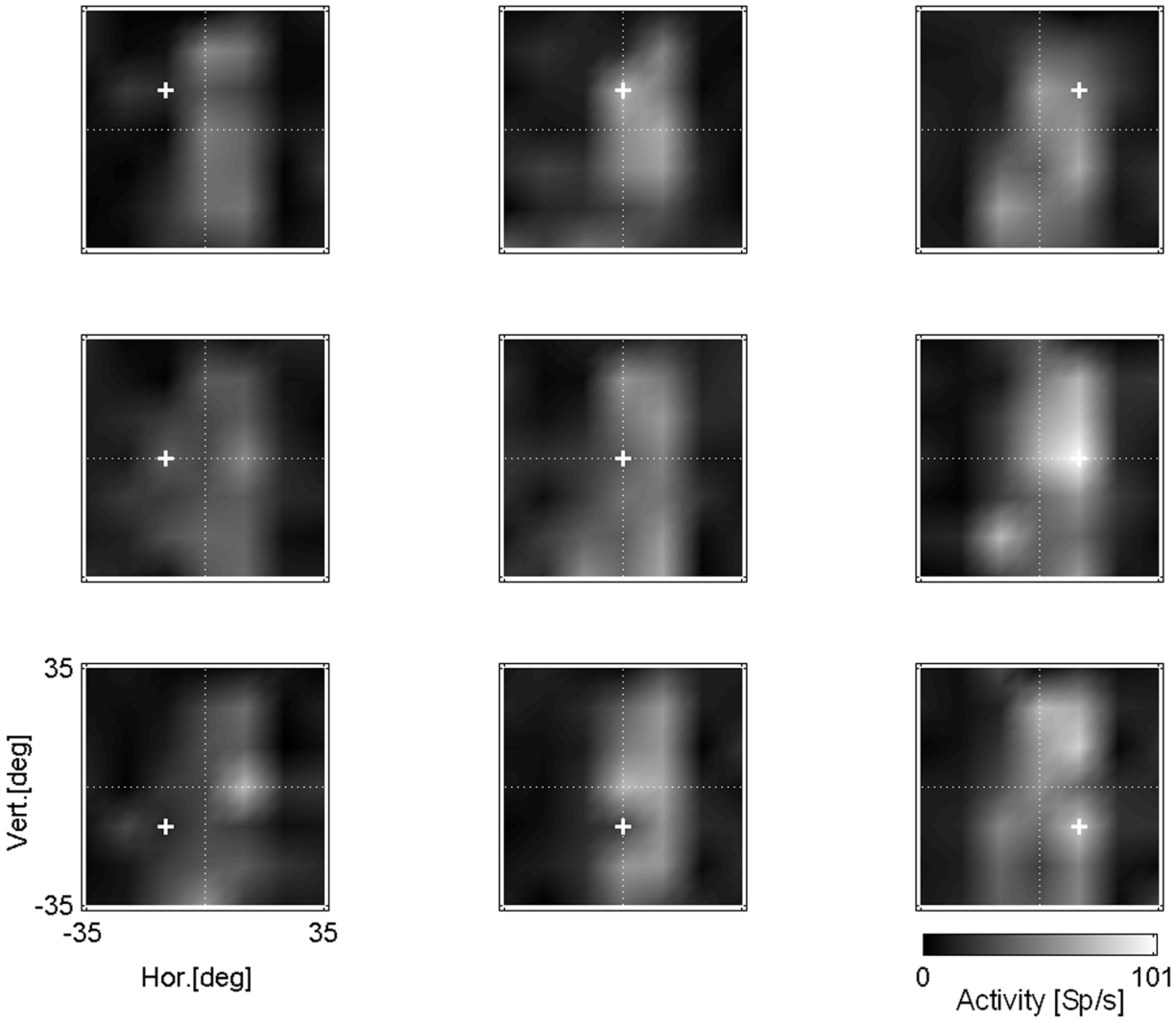

FIG. 2. Single neuron data for visual receptive field mappings when the RF remains in the same spatial location irrespective of eye position. The RF was mapped with a white bar moving at 100°/s for brief intervals in the neuron's preferred direction. Gray shaded maps of the RF were constructed for each fixation position. Maps are displayed in screen coordinates. The small black crosses correspond to eye position during visual stimulation and the intersection of the light horizontal and vertical lines correspond to the straight-ahead direction in space.

distribution of eye position effects at the single cell and at the population level can be considered prerequisites for a population encoding of the current eye position. This prediction was verified by employing a previously introduced algorithm termed isofrequency encoding (Boussaoud and Bremmer, 1999). The result is shown in Fig. 1D. The color coded map indicates the distribution of the points of intersection of the isofrequency lines, while the "*x*"-symbol indicates the true eye position. The error between the center of mass of this distribution and the real eye position is 2.75°. The average error for all nine tested eye positions is 2.92°.

These data indicate that a relatively small number of cells sampled throughout area VIP is sufficient to obtain the required population response allowing a precise encoding of eye position. This in turn indicates the capability of the existing network to construct head-centered cells by combining the information about the position of the eyes with information about the position of the stimulus on the retina. Accordingly, area VIP was tested for the existence of such cells by measuring the location of visual RFs for different fixation locations (Duhamel *et al.*, 1997). A wide range of RF types was found. Some neurons had an RF that moved rigidly with the eyes, while other neurons encoded the same location in space irrespective of eye position. The plots in Fig. 2 show, for a single VIP neuron, the distribution of neural activity over the stimulated screen area for nine different eye fixation positions. In each map, the most active region is located around the central part of the screen. The fact that the cell's RF remains fixed relative to the stimulation screen indi-

cates that it does not encode visual information in an eye-centered, but rather a head-centered frame of reference. This type of encoding was found for about one third of the cells in area VIP.

fMRI IN HUMANS

Taken together, the most prominent functional characteristics of macaque area VIP are (i) polymodal sensory responses and (ii) the encoding of sensory information from different modalities in a common frame of reference. As mentioned before, it is exactly this type of system that, when lesioned, would result in polymodal neglect or extinction organized in a head- or body-centered spatial frame of reference. This is the impairment that most often and most reliably results from lesions centered on the posterior parietal cortex (Vallar, 1998). From the aforementioned, it becomes obvious that the question that needs to be explored is, whether or not in humans an equivalent area to macaque area VIP exists which may consistently be damaged in patients with parietal lesions suffering from neglect and/or extinction. Previous functional imaging studies have repeatedly demonstrated neural activations in posterior parietal cortex and in the depth of the intraparietal sulcus associated with object- and space-based attention (Fink *et al.*, 1997), visuo-spatial judgments (Fink *et al.*, 2000), and spatial orienting (Corbetta, 1998), strongly implying that this region is implicated in visuo-spatial cognition. However, none of these studies so far has tested specifically for the existence of an area in human IPS that may correspond functionally and anatomically to macaque area VIP. Thus, the possibility of a functionally equivalent area in human posterior parietal cortex needed to be explored.

Accordingly, the test for the existence of 'human area VIP' was based on one of its most prominent response features in the macaque, i.e., sensory responses to polymodal motion stimuli (Bremmer *et al.*, 2001). In this functional MRI experiment, subjects experienced either a visual (large random dot pattern), tactile (air flow) or auditory (binaural beats) motion stimulus or a stationary control. Spatially circumscribed, significant cortical activation ($P < 0.05$, corrected) was observed for each individual stimulus condition. Conjunction analysis revealed cortical structures activated by all three modalities, i.e., vision, touch, and audition. Bilateral activation was found in three circumscribed cortical regions, one of which was located in parietal cortex. By superimposing the functional images on the average anatomical brain originating from the eight subjects it was possible to identify the activated region as lying in the depth of the intraparietal sulcus (Fig. 3).

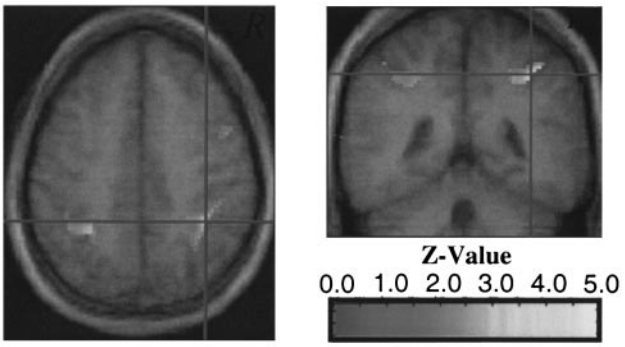

FIG. 3. Conjunction analysis revealed significant activations ($P < 0.05$, corrected) by visual, tactile, and auditory stimulation bilaterally in the depth of the intraparietal sulcus. The activated region is shown in a coronal section (right panel) and a horizontal section (left panel). "R" indicates the right hemisphere in each image. The horizontal line in the coronal (horizontal) image indicates the *z*-coordinate (*y*-coordinate) of the horizontal (coronal) image. Significance of activation is gray shaded, with light gray corresponding to highest significance values. Anatomical images are average anatomical MRIs from the eight subjects.

CONCLUDING REMARKS

Cross-modal stimulation revealed a cortical area within the human parietal cortex responding to motion stimuli originating from vision, touch and audition. Neurophysiological studies in the macaque had employed comparable stimuli to define functionally area VIP located in the fundus of the IP. The activated human cortical region found by means of fMRI was also located in the depth of the IP. These findings thus strongly imply the existence of the human equivalent of macaque area VIP. More complementary studies in which monkey single cell recordings and functional imaging are combined are needed in order to further establish the functional role of area VIP for polymodal spatial perception in normals as well as the functional implications of lesions of area VIP in parietal patients and its putative role in disturbed visuospatial behavior such as visuo-spatial neglect.

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