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Polymodal Motion Processing in Posterior Parietal and Premotor Cortex: A Human fMRI Study Strongly Implies Equivalencies between Humans and Monkeys

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Summary

In monkeys, posterior parietal and premotor cortex play an important integrative role in polymodal motion processing. In contrast, our understanding of the convergence of senses in humans is only at its beginning. To test for equivalencies between macaque and human polymodal motion processing, we used functional MRI in normals while presenting moving visual, tactile, or auditory stimuli. Increased neural activity evoked by all three stimulus modalities was found in the depth of the intraparietal sulcus (IPS), ventral premotor, and lateral inferior postcentral cortex. The observed activations strongly suggest that polymodal motion processing in humans and monkeys is supported by equivalent areas. The activations in the depth of IPS imply that this area constitutes the human equivalent of macaque area VIP.

Introduction

The neural circuits underlying normal spatial vision and attentive sensorimotor behavior of primates have been most intensively studied in macaque monkeys. Both electrophysiological (Colby and Duhamel, 1996; Andersen et al., 1997) and anatomical (Rizzolatti et al., 1997) studies have highlighted the importance of the posterior parietal and premotor cortices for the integration of neural signals from different sensory modalities and their use for guiding and controlling action in space. In the monkey, a highly modular structural and functional specialization has been demonstrated within these areas. One such functionally specialized area in the macaque posterior parietal cortex is the ventral intraparietal area (VIP) located in the fundus of the intraparietal sulcus (IPS). Area VIP contains many neurons that show polymodal directionally selective discharges (i.e., these neurons respond to moving visual, tactile, vestibular, and auditory stimuli) (Colby et al., 1993; Bremmer et al., 1997a, 2000; Duhamel et al., 1998; Schlack et al., 2000). A considerable proportion of these neurons encodes this polymodal information in a common, probably head-centered, frame of reference (Duhamel et al., 1997). Finally, direct anatomical connections between area VIP and an area within the ventral premotor cortex (PMv) that subserves head movements have been reported recently (Luppino et al., 1999).

In ventral premotor cortex, the majority of neurons are either unimodal (somatosensory, visual, or auditory) or bimodal (i.e., they respond to visual and tactile or visual and auditory stimuli) (Graziano et al., 1997). However, in a recent study, a polymodal zone has been identified at the dorsal rim of the ventral premotor cortex with most neurons responding to visual, tactile, and auditory stimulation (Graziano and Gandhi, 2000). If not identical, this polysensory zone overlaps at least in part with the projection zone of area VIP (Luppino et al., 1999). Again, many of the sensory responses depicted in this area are organized in head- or body-centered coordinates (Fogassi et al., 1992; Graziano et al., 1997).

Although many specific human behaviors necessitate the convergence and integration of information conveyed through anatomically distinct sensory pathways, to date little is known about polymodal motion information processing and integration in humans. Functional imaging studies successfully delineated networks of cortical areas associated with visual and visuospatial motion processing (Corbetta et al., 1991; Zeki et al., 1991; Dupont et al., 1994; Cheng et al., 1995; Orban et al., 1995, 1999; Tootell et al., 1995, 1997; Beauchamp and Cox, 1997; Sunaert et al., 1999), auditory processing (Griffiths et al., 1994), vestibular processing (Dieterich and Brandt, 2000), and tactile processing (Maldjian et al., 1999; Downar et al., 2000). Many of these studies have implicated parietal or premotor areas, in particular, whenever human attentive sensorimotor behavior concerned with guiding and controlling action has been studied (Griffiths et al., 1996, 1998; Baumgart et al., 1999; Iacoboni et al., 1999; Lewis et al., 2000).

The functional imaging data obtained in humans is supported by neuropsychological studies of patients with posterior parietal or frontal (premotor) cortex lesions. These studies reveal a variety of impaired attentive sensorimotor behaviors such as hemispatial neglect or apraxia (Driver and Mattingley, 1998; Vallar, 1998; Mesulam, 1999). Interestingly, these behavioral deficits can occur both within and across different sensory modalities (Ladavas et al., 1998) and are often organized in head- or body-centered coordinates (Vallar, 1998). Taken together, neuropsychological and functional imaging studies implicate the existence of a human polymodal network of posterior and frontal areas for the representation of spatial information in a nonretinocentric frame of reference, which may well be organized both structurally and functionally in a very similar way to the macaque.

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As none of the above studies specifically tested for the potential existence of equivalencies of polymodal signal processing in monkeys and humans, we here aim at identifying the neural mechanisms underlying human polymodal motion information processing. Based on the literature on the functional aspects of cortical areas in the macaque, we expected the involvement of (at least) two cortical areas in polymodal motion information processing: PMv and an area in the intraparietal sulcus (as the equivalent of macaque area VIP). Neurophysiological data from the macaque also implicate the superior temporal polysensory area (STP) in polymodal processing; however, neurons in this area seem not to be involved specifically in motion information processing.

Accordingly, we measured changes in neural activity in healthy volunteers using functional magnetic resonance imaging (fMRI), while moving visual, tactile, or auditory stimuli were presented. Stimuli were chosen in accordance with those used in previous macaque experiments on polymodal motion information processing (Bremmer et al., 2000). For visual stimulation, we used a random dot pattern moving coherently in the frontoparallel plane. For visual control, a stationary random dot pattern was presented for the following reason: recent studies that identified macaque area VIP as a parietal cortical site with converging polymodal sensory responses contrasted "moving visual stimulus" with "stationary visual stimulus" to differentiate area VIP from its neighboring areas within the intraparietal sulcus that also respond to visual stimulation (Colby et al., 1993; Bremmer et al., 1997a, 2000). For tactile stimulation, we employed room air flowing continuously across the subject's forehead; for tactile control, a no airflow condition was introduced, as neurophysiological macaque studies have demonstrated that a considerable number of neurons in area VIP respond not only to moving stimuli but also to stationary tactile stimuli (Colby et al., 1993; Duhamel et al., 1998). For auditory stimulation, "binaural beats" (Griffiths et al., 1994) producing an illusion of sound movement in the azimuthal plane were used. For auditory control, no additional auditory stimulation over and above the scanner noise, which is present during all conditions, was presented.

Note, this experiment was designed specifically to reveal neural activity common to all three stimulus modalities. Although the above design allows the assessment of increases in neural activity associated with processing of each of the unimodal motion information (relative to its individual control condition), the design of the experiment primarily aims at revealing the areas activated by all three stimulus types by means of a conjunction analysis (Price and Friston, 1997); cognitive conjunction experiments are designed such that two or more distinct task pairs each share a common processing difference (in our case, the motion information processing). The neural correlates of the process of interest are then associated with the common areas of activation for each task pair. Here we exploit this approach by making use of the two main advantages of the cognitive conjunction relative to the cognitive subtraction approach typically employed in functional imaging experiments: (1) the greater latitude for the control tasks (as the control tasks do not have to control for all but the component of interest as in cognitive subtraction experiments) and (2) the independence of cognitive conjunction experiments from the assumption that the addition of an extra processing component (specifically here, motion) has no effect on the implementation of processes that are also engaged by the baseline task (Price and Friston, 1997).

Results

Group Results

Modality-Specific Neural Activations: Simple Main Effects

Significant ($n = 8$; $p < 0.05$, corrected for multiple comparisons) modality-associated (i.e., visual, tactile, auditory) activations (assessed using statistical parametric mapping [SPM99]; Wellcome Department of Cognitive Neurology, http://www.fil.ion.ucl.ac.uk) in the respective primary, secondary, and associated "higher order" cortices were observed in all stimulus conditions relative to the modality-specific baselines.

Visual motion information (relative to the visual control condition) increased neural activity in the primary and secondary visual cortex, the lateral temporooccipital region (corresponding to human MT/V5$^+$ [Watson et al., 1993]), posterior parietal cortex, lateral inferior postcentral cortex, and lateral premotor cortex bilaterally (Figure 1A).

Tactile motion information (relative to the tactile control condition) showed increased neural activity in the primary and secondary somatosensory cortex bilaterally, posterior parietal cortex bilaterally, and right lateral premotor cortex (Figure 1B).

Auditory motion stimulation (relative to the auditory control condition) led to increased neural activity in primary and secondary auditory cortex, posterior parietal cortex, lateral premotor cortex bilaterally, and left cerebellar hemisphere (Figure 1C).

Neural Activity Common to All Three Modalities When Conveying Motion Information: Conjunction Analysis

A conjunction analysis (Price and Friston, 1997) revealed significant activations ($n = 8$; $p < 0.05$, corrected for multiple comparisons) common to all three modalities (i.e., vision, somatosensation, and audition) when conveying motion information (relative to the respective no motion information–conveying control conditions) in three cortical regions: posterior parietal cortex bilaterally, right ventral premotor cortex, and lateral inferior postcentral cortex (upper bank of the sylvian fissure) bilaterally (Table 1; Figure 2).

The bilateral activation observed in posterior parietal cortex was centered on the IPS (see Figure 2A, area 1; Table 1). Superposition of functional and anatomical (mean MR) images of the same group of subjects normalized to the same standard stereotaxic reference space (Talairach and Tournoux, 1988; Friston et al., 1995b) revealed that the local maximum within this area of activation lay in the depth of IPS (Figure 2B, area 1).

The most anterior activation was found in right ventral premotor cortex, as identified following superimposition of the $SPM_{\{z\}}$ map and the group mean magnetic resonance image (Figures 2A and 2B, area 2; Table 1).

This activation pattern of posterior parietal cortex acti-

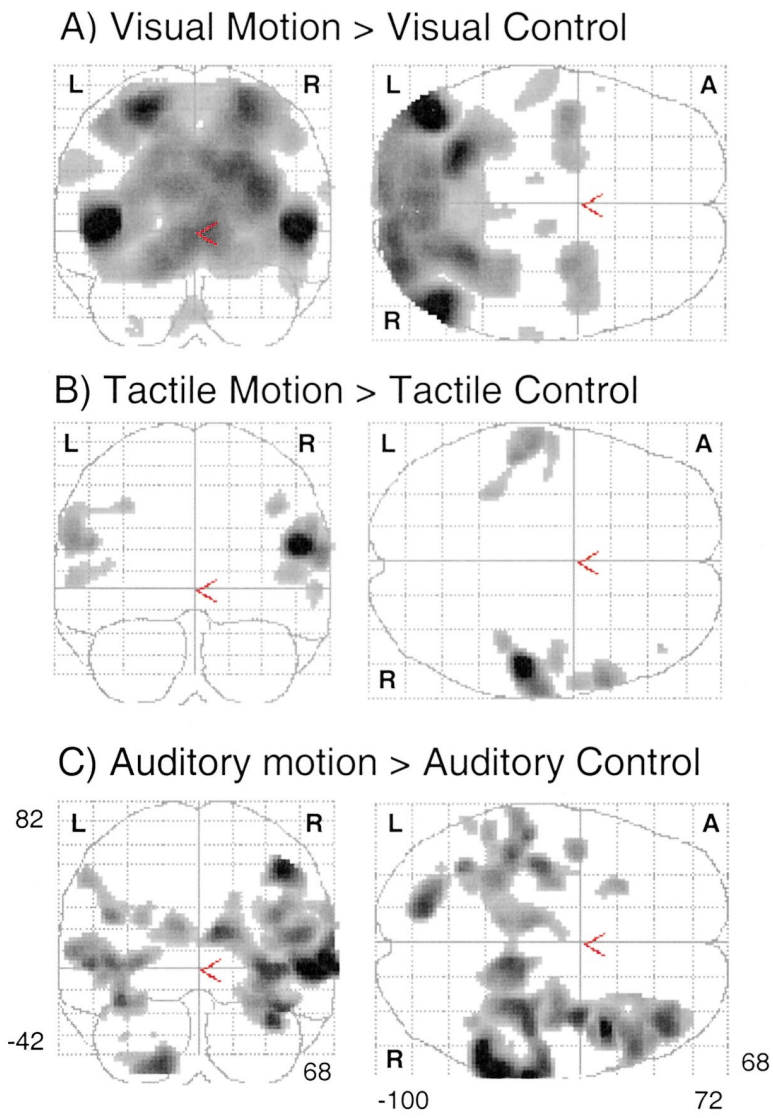

Figure 1. Modality-Specific Activation Pattern

(A–C) The activation patterns (motion stimulus response minus no motion control response) for visual (A), tactile (B), and auditory (C) stimulation.

vation in the intraparietal sulcus and ventral premotor cortex was hypothesized on the basis of macaque electrophysiological and anatomical data. In addition to these two predicted cortical regions, another area of activation that responded to all three stimulus types conveying motion information was observed; this activa-

Table 1. Spatial Coordinates of the Local Maxima within the Regions of Activations

Area	Side	X	Y	Z	Z Score
Ventral intraparietal cortex	L	−40	−40	42	4.90
(1)	R	38	−44	46	6.31
Ventral premotor cortex	R	52	10	30	7.58
(2)					
Lateral inferior postcentral cortex	L	−64	−18	30	7.74
(3)	R	66	−18	30	>7.74

Two regions are activated bilaterally (numbers 1 and 3), while the premotor region is activated predominantly in the right hemisphere (number 2). Coordinates are in standard stereotaxic space (Talairach and Tournoux, 1988) and refer to maximally activated foci, as indicated by the highest Z score within an area of activation associated with the neural activations evoked by all three stimulus modalities (relative to the modality-specific controls). X is the distance in millimeters to the right (+) or left (−) of the midsagittal (interhemispheric) line, Y is the distance anterior (+) or posterior (−) to the vertical plane through the anterior commissure, and Z is the distance above (+) or below (−) the intercommissural line. The anatomical description is based on the localization of the local maximum within an area of activation superimposed on the group mean MR image. R, right; L, left. Numbers in parentheses refer to the labels in Figure 1.

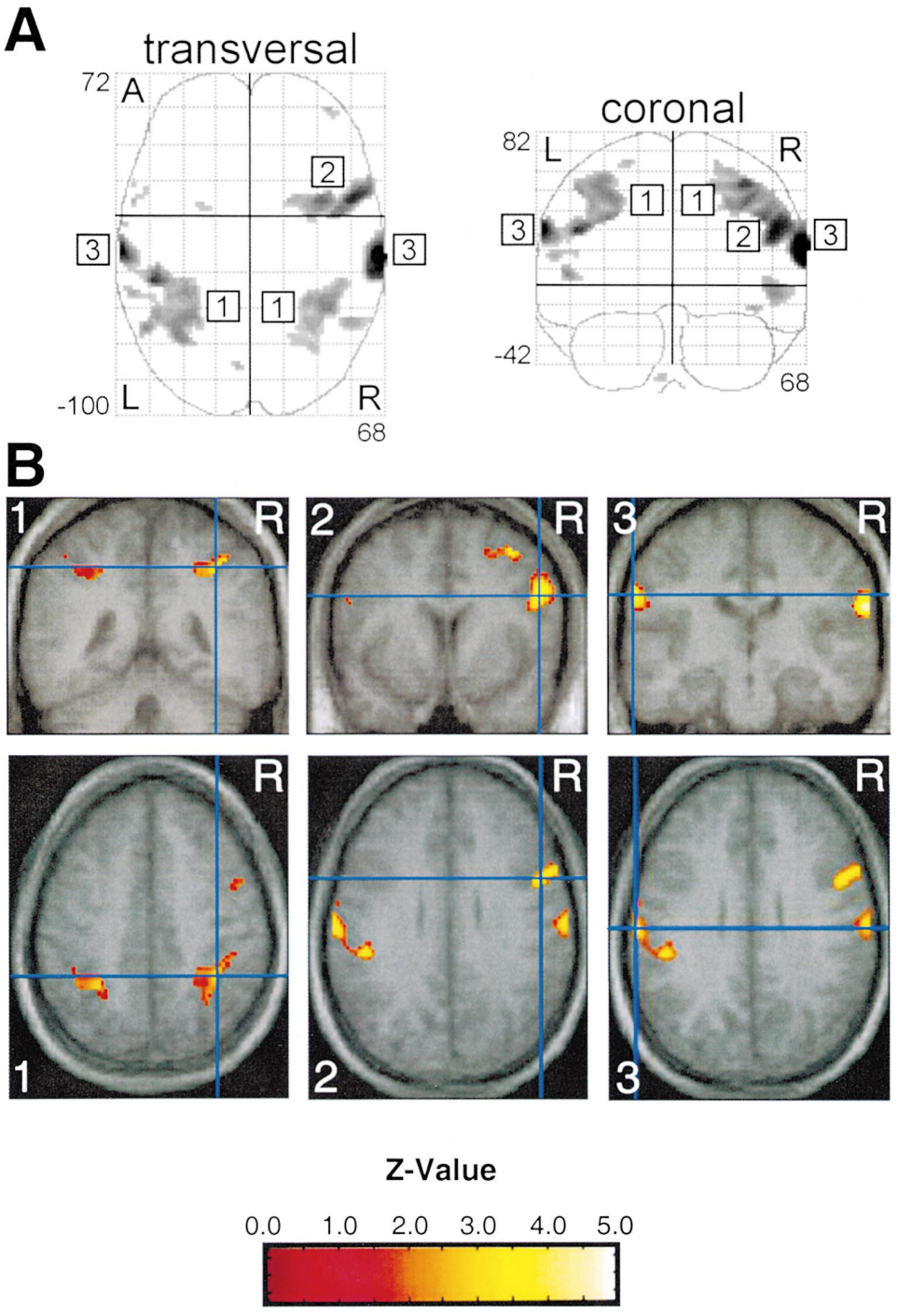

Figure 2. Polymodal Cortical Activation Patterns as Revealed by Conjunction Analysis

(A) Cortical regions significantly ($p < 0.05$, corrected for multiple comparisons) activated by visual, tactile, or auditory motion stimuli. The two images show, in a horizontal view (left) and coronal view (right), the result of the conjunction analysis; gray regions were activated significantly by each of the three different motion information–conveying stimuli. Images are projections along the viewing axis (i.e., visible activations are not all in the same horizontal or frontal plane). We have assigned numbers to the three clusters of activation, which are also referred to in Table 1. Region 1 indicates the posterior parietal area located in the depth of the intraparietal sulcus. Based on its anatomical location and its response features, we consider this bilaterally activated area the human equivalent of macaque area VIP. Region 2 refers to a frontal region lying in the dorsal aspect of PMv. Region 3 is found bilaterally in lateral inferior postcentral cortex and is likely to correspond to SII/PV or areas Ri/PA.

(B) Areas of activation are displayed superimposed on the group mean MR image derived from the individual MR images after stereotaxic normalization into standard space, as defined by Talairach and Tournoux (1988). Activated regions are shown in a coronal section in the upper row and in a horizontal section in the bottom row. R, right; numbers 1, 2, and 3 refer to the three different identified regions. The horizontal blue line in the coronal (horizontal) image indicates the z coordinate (y coordinate) of the horizontal (coronal) image. Significance of activation is color coded, with yellow and white corresponding to highest significance values.

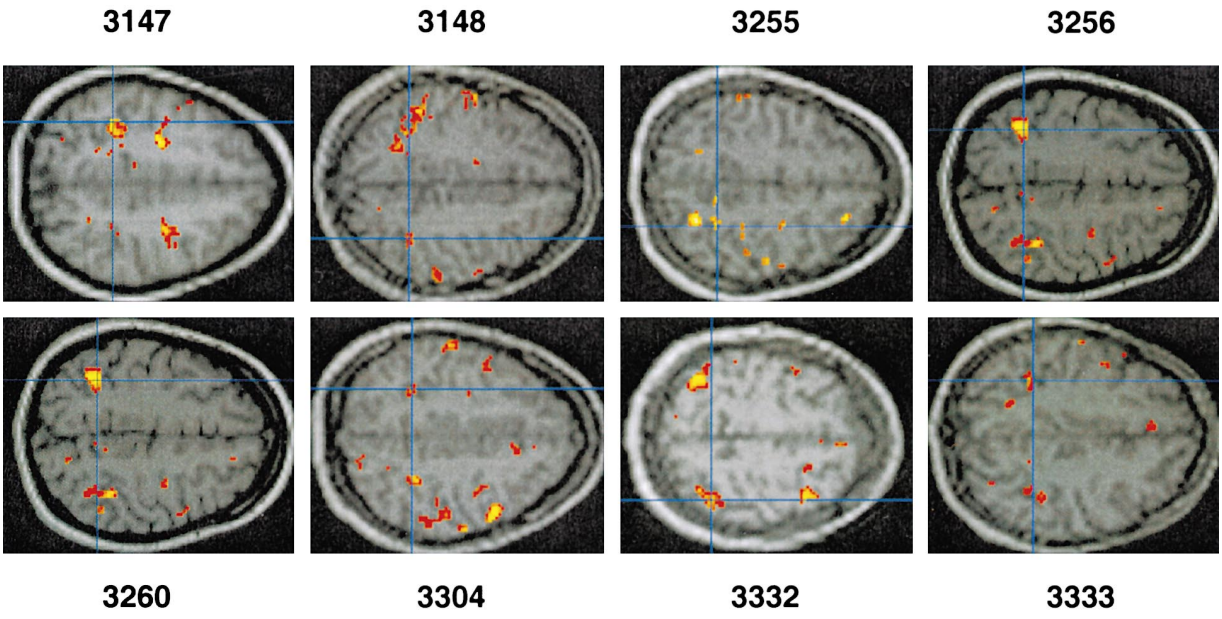

Figure 3. Single-Subject Data Showing Individual Activations in the Depth of the Intraparietal Sulcus

As revealed by conjunction analysis, significant activations ($p < 0.05$, corrected for multiple comparisons) by visual, tactile, or auditory motion stimuli were observed bilaterally in the depth of the IPS. For each subject, this area of activation is displayed superimposed on the individual MR images after stereotaxic normalization into standard space, as defined by Talairach and Tournoux (1988). The activated region is shown in a horizontal section. The horizontal blue line indicates the y coordinate of the local maximum within the area of activation; the vertical blue line indicates the corresponding x coordinate. The actual coordinates, the respective number of voxels of the area activated, and the associated Z score of the activation are given in Table 2 for each individual.

tion (Figures 2A and 2B, area 3) was located bilaterally in the lateral inferior postcentral cortex (upper bank of sylvian fissure) and might represent either the very lateral aspect of area SII (Fink et al., 1997b) and area PV (parietal ventral area; Disbrow et al., 2000) or areas being functionally equivalent to areas Ri (retroinsular cortex) and/or PA (postauditory fields) described in the macaque (Robinson and Burton, 1980b).

Single-Subject Analysis

All eight subjects showed a pattern of neural activations consistent with the group results for both the simple main effects of unimodal motion stimulation versus its respective no motion control condition and the conjunction analysis of all three modalities (i.e., vision, somatosensation, and audition) when conveying motion information (relative to the respective no motion control conditions). Accordingly, all subjects showed activations in the relevant primary, secondary, and higher order cortices ($p < 0.01$, uncorrected or better) as a simple main effect. Individual conjunction analyses revealed that all eight subjects showed areas of activation resulting from polymodal motion stimulation in the ventral intraparietal cortex, the ventral premotor cortex, and the lateral inferior postcentral cortex ($p < 0.01$; uncorrected or better).

Figure 3 illustrates the activations in the posterior parietal cortex in the depth of the intraparietal sulcus of each individual subject in order to exemplify the consistency of the pattern and extent of activations observed across subjects. In addition, Table 2 provides the local maxima within these areas of activation in the intraparietal sulcus (in Talairach and Tournoux atlas space) and the respective number of voxels for each subject. Note, the size of an area of activation crucially depends on the statistical threshold applied.

Discussion

Our functional imaging data clearly show that the human brain contains a set of areas in the parietal and frontal lobes in which the senses converge. The network of areas activated by polymodal motion information closely matches the pattern of activation observed in electrophysiological (single-cell recording) studies of the monkey brain. The data thus confirm our a priori hypothesis (based on our own data and the literature) of the existence of an area in human posterior parietal cortex that responds to polymodal motion stimuli. In the macaque, the intraparietal sulcus is composed of several functionally distinct areas (AIP, LIP, VIP, MIP, and PIP or CIP [Jeannerod et al., 1995; Colby and Duhamel, 1996; Taira et al., 2000]). The only area within macaque IPS for which motion sensitivity for stimuli of different sensory modalities has been demonstrated is area VIP (Colby et al., 1993; Bremmer et al., 1997a, 2000). Our functional imaging data reveal an area in the depth of human IPS that responds to polymodal stimuli conveying motion information. We accordingly suggest that this area constitutes the human equivalent of monkey area VIP. As in the original studies that described macaque area VIP

Table 2. Spatial Coordinates of the Local Maxima within the Posterior Parietal Cortex of the Individual Subjects

Subject Number	Side	X	Y	Z	Volume	Z Score
3147	L	−40	−40	44	626	4.66
	R	38	−40	48	11	3.47
3148	L	−46	−40	44	485	4.04
	R	36	−48	44	181	3.68
3255	L	−40	−36	44	11	2.20*
	R	28	−48	52	53	3.48
3256	L	−36	−46	40	420	4.47
	R	32	−50	42	1574	5.82
3260	L	−36	−50	50	283	4.78
	R	34	−42	44	618	5.82
3304	L	−30	−46	46	361	3.75
	R	38	−46	48	364	2.48
3332	L	−30	−52	50	293	2.52
	R	42	−52	58	202	4.14
3333	L	−36	−46	44	300	4.09
	R	36	−44	44	15	2.99

All subjects showed activations in the relevant primary, secondary, and higher order cortices ($p < 0.01$, uncorrected or better, except for subject 3255, for whom activation in the left hemisphere was significant at $p < 0.05$, as indicated) as a simple main effect. R, right; L, left. Volume, cluster size of voxels significantly activated. Note, the size of an area of activation crucially depends on the statistical threshold applied.

* $p < 0.05$, uncorrected.

on an anatomical (Maunsell and Van Essen, 1983) and functional basis (Colby et al., 1993), the identification of the human equivalent of area VIP in our study is based on its anatomical location in the depth of the IPS and the responsiveness of neurons in this area to polymodal stimulation conveying motion information.

Previous fMRI and PET studies on visuospatial attention and eye movements have implicated the superior posterior parietal cortex as well as areas along the IPS (e.g., Fink et al., 1997a; Corbetta et al., 1998; Nobre et al., 2000); however, the locations of activations reported in these studies for pursuit, saccades, suppression of eye movements, or attention have been more posterior and more superior to the areas of activation that we identified in the depth of the IPS. We accordingly suggest that the previous studies have not shown area VIP but rather neural activations not concerned with polymodal motion processing.

Based on macaque electrophysiological and anatomical data, we also expected parts of human premotor cortex to be activated by our polymodal motion stimuli. Anatomical studies have been able to demonstrate distinct projections of macaque area VIP into a region within PMv cortex that subserves head movements (Luppino et al., 1999). Electrophysiological data obtained from neurons located within this region of PMv demonstrate polymodal response properties to visual, tactile, and auditory stimulation (Graziano and Gross, 1998) with a somatotopic organization (Graziano et al., 1999; Graziano and Gandhi, 2000). Our human functional imaging data show an activation of the dorsal part of the human ventral premotor cortex and thus parallel the anatomical organization of macaque PMv and its functional characteristics.

It could be the case that the third area of activation, which we observed in the very lateral aspect of inferior postcentral cortex, corresponds to areas SII/PV (Fink et al., 1997b; Servos et al., 1999; Disbrow et al., 2000). However, at present no data exist, be it anatomical, electrophysiological, or functional, that allow us to further characterize the area activated here. Earlier experiments in macaques have shown polymodal responses in cortical regions surrounding SII cortex (i.e., Ri and PA) (Robinson and Burton, 1980a). It therefore seems likely that either (1) human SII cortex contains neurons responding to polymodal stimulation in a way similar to the macaque or that (2) in humans equivalent areas to macaque areas Ri and PA exist. Both conjectures would then help to explain the polymodal activation observed in our functional imaging study; however, further work is necessary to shed light on polymodal motion information processing in this area.

In the monkey, area STP has also been demonstrated to contain neurons responsive to polymodal stimulation. This area is located around the superior temporal sulcus and responds to visual, tactile, and/or auditory stimuli irrespective of whether they convey motion information or not (Desimone and Gross, 1979; Bruce et al., 1981). As our modality-specific visual control involved a stationary visual stimulus, the design and type of analysis used in the present study are likely to account for the "missing" activation of area STP (or its human equivalent); the modality-specific simple main effect shows no additional activation in superior temporal cortex during visual motion stimulation (relative to the stationary visual control). Furthermore, the simple main effect of tactile stimulation also failed to detect any significant activation around the superior temporal sulcus. It is noteworthy,

however, that our results concerning the missing polymodal activation of an area around the STS when using motion information–conveying stimuli are in perfect agreement with a recent study on visual and auditory motion processing in humans (Lewis et al., 2000).

To detect a network of areas with polymodal characteristics in the human brain, we chose to present moving rather than stationary stimuli of different sensory modalities for a variety of reasons. First, in the macaque, many neurons in posterior parietal cortex respond not only to visual but also to other types of sensory stimulation. Yet, the only area that contains neurons responsive to visual, auditory, and tactile stimulation is macaque area VIP. Neurons in the latter area, however, are best activated when stimuli convey motion information (Colby et al., 1993). Moreover, visual motion stimuli, if contrasted with stationary visual stimuli, allow a clear cut separation of area VIP from its neighboring areas LIP, MIP, AIP, and PIP (Bremmer et al., 2000). And finally, single-cell recordings from macaque ventral premotor cortex are also most often performed with visual stimuli that move relative to the animal (Graziano et al., 1997). Taken together, these electrophysiological studies suggested that motion is the most relevant stimulus feature for activation of polymodal cells in monkey areas VIP and PMv, and we therefore decided to use equivalent stimuli in our current study.

Considering the type of stimuli used (and the respective controls), however, one needs to acknowledge that perceptual salience rather than motion may have caused the increased neural responses observed in posterior parietal cortex, ventral premotor cortex, and the postcentral area SII/Ri and PA. The design of our study does not allow us to distinguish explicitly between these two different stimulus features (i.e., "moving versus stationary" and "salient versus nonsalient"). However, there are a number of reasons why we suggest that it is indeed the motion information rather than differences in salience that caused the observed activation. Although the argument mainly refers to the activation in the depth of the intraparietal sulcus (as the relevant electrophysiological studies have concentrated on this area), the logic also applies to the premotor and perisylvian activations. It is well accepted that neurons in area VIP respond to moving rather than stationary visual pattern (Colby et al., 1993; Bremmer et al., 1997a). In these experiments, the monkey's task was to fixate a central target and to indicate a luminance change of the target. While the monkey performed the task successfully, another visual stimulus (irrelevant to the task and the monkey's reward) was moved across the receptive field of the neuron from which the recording was obtained. Accordingly, the visual stimulus was not salient in the sense of e.g., Gottlieb et al. (1998), as the stimulus was of no primary behavioral interest to the macaque and did hence not demand the animal's attention. Nevertheless, presentation of the unattended visual stimulus pattern within the receptive field per se led to increased neural discharges in area VIP. By contrast, Gottlieb and Goldberg demonstrated in a second experiment that the onset of visual stimulus motion led to enhanced activity in posterior parietal cortex (Gottlieb and Goldberg, 1998). In our study, however, such a "motion onset" (i.e., the change from the modality-specific control to the respective motion condition) only occurred once at the beginning of each stimulus period (30 s), and it is therefore unlikely that these onsets of motion may have accounted for the observed increases in neural activity. Furthermore, in a recent PET study, we have been able to demonstrate that changes in (visual) salience modulate neural activity in early (visual) processing areas (Fink et al., 1999)—areas much further down the processing stream then posterior parietal cortex or ventral premotor cortex. We accordingly suggest that the increases in neural activity observed with polymodal motion processing in our study are thus related to the processing of motion per se. Further support for this notion stems from a recent functional imaging study in which the neural mechanisms of detecting changes in the sensory environment were investigated. Transitions of visual, auditory, and tactile stimuli led to increased neural activity in an area centered on the temporoparietal junction but did not activate the regions implicated in our study in polymodal motion information processing (Downar et al., 2000).

Taken together, monkey physiology and human functional imaging data strongly suggest that polymodal motion processing in humans and monkeys is supported by an equivalent network of areas in posterior parietal and premotor cortex. Complementary studies of macaque single-cell recordings and functional imaging in humans thus help to elucidate the functional role of posterior parietal and premotor cortex in polymodal spatial perception, as they allow further characterization of the modular organization of human cortex. Furthermore, our findings shed light on neuropsychological deficits observed in patients with posterior parietal lobe injury; the most prominent functional characteristics of macaque areas VIP and PMv are (1) polymodal sensory responses and (2) the encoding of sensory information from different modalities in a body-centered frame of reference (Colby et al., 1993; Duhamel et al., 1997; Bremmer et al., 2000). We note that it is exactly this type of attentive behavioral sensorimotor deficit (defined as crossmodal neglect or extinction organized in a head- or body-centered spatial frame of reference) that in patients most often and most reliably results from lesions centered on the posterior parietal cortex but that can also arise from lesions to premotor and prefrontal areas (Vallar, 1998).

Experimental Procedures

Subjects

Eight (three female, five male) healthy, right-handed volunteers (aged 21–36 years; mean age 27) were studied. Informed consent was obtained prior to participation. The study was approved by the local ethics committee. Subjects had normal or corrected-to-normal visual acuity.

Experimental Design and Stimuli

As this experiment was designed specifically to reveal neural activity common to all three stimulus modalities (see Introduction), the control tasks were not primarily designed to control for all but the component of interest (as in cognitive subtraction experiments) but rather to allow the depiction of the putative polymodal areas in the intraparietal sulcus and the ventral premotor cortex. Thus, modality-specific considerations were taken into account (see Introduction) to maximize the chances of depicting motion-sensitive areas in the intraparietal sulcus and the ventral premotor cortex.

Three different stimulus modalities were employed: vision, audi-

tion, and somatosensation. For visual stimulation we used a random dot pattern moving coherently in the frontoparallel plane, as described recently (Bremmer et al., 1997b). Stimuli were generated on a Silicon Graphics workstation (O2) and back projected using an LCD projector onto a translucent screen. This image was reflected by a mirror above the subject's eyes. Viewing distance was 25 cm. The visible stimulus subtended the central 60° (horizontal) by 31° (vertical) of the visual field. During presentation of visual stimuli, subjects fixated upon a central target. As a control, subjects fixated upon the central target, while the random dot pattern remained stationary (see Introduction).

For tactile stimulation, we used room air flowing continuously across the subject's forehead. During the control condition, there was no airflow (see Introduction). Subjects were instructed to keep their eyes closed both during stimulation and the control.

For auditory stimulation we employed so called binaural beats stimuli (Griffiths et al., 1994). To this end, pure sinusoidal tones with slightly different frequencies were presented via headphones to each ear individually—500 Hz to the one ear, 501 Hz to the other. This configuration leads to a strong illusory perception of a sound source moving in the azimuth, with a frequency of 1 Hz. Again, in the control condition, no additional auditory stimulus was presented (see Introduction). As in the tactile conditions, subjects were instructed to keep their eyes closed both during stimulation and the control.

The critical conditions of this cognitive conjunction design (see Introduction) are the conditions with visual, auditory, and tactile motion (experimental factor: motion information) relative to the modality-specific controls, which should allow delineation of the neural mechanisms common to all three motion information–conveying stimulus types.

Data Acquisition: fMRI

Functional MR images were acquired on a Siemens Vision 1.5T whole-body scanner with echo-planar imaging (EPI) capability and using the standard radiofrequency (RF) head coil for transmit and receive. To achieve whole-brain coverage, we used a modified version of our EPI sequence, which enables an arbitrary number of slices to be acquired. Sequence parameters were Gradient-echo EPI, TE = 66 ms, TR = 5 s, flip angle = 90°, slice thickness = 4.00 mm, interslice gap = 0.4 mm, FOV = 200 mm, in-plane resolution = 3.125 mm × 3.125 mm. We chose 32 slices for whole-brain coverage. Using a midsagittal scout image, the slices were oriented in the plane of the anterior-posterior commissure (AC-PC). In addition, high-resolution anatomical images were acquired for all subjects using the 3D MP-RAGE (magnetization-prepared, rapid acquisition gradient echo) sequence with the following parameters: TE = 4.4 ms, TR = 11.4 ms, flip angle = 15°, inversion time (TI) = 300 ms, matrix = 200 × 256, FOV = 200 mm, 128 sagittal slices, slice thickness = 1.33 mm. The fMRI paradigm was designed as follows: stimuli of different modalities were presented in blocks of unimodal scans (henceforth referred to as a trial). Each trial consisted of ninety-nine whole-brain scans (99 × TR). The first three scans allowed the establishment of steady-state magnetization and were excluded from offline analysis. These initial scans were followed by eight periods each of 12 scans: six scans without stimulation (baseline) and six scans with stimulation (either visual [v], auditory [a], or tactile [t]). This paradigm resulted in a total number of 8 × 12 + 3 = 99 scans. Two such trials (99 scans) were presented to each individual subject for each stimulus modality, resulting in a total number of six trials per subject. The serial order of modalities was changed in a pseudorandomized way between subjects, but trials of the same modality were always followed and/or preceded by trials of the two other modalities. This experimental design led to modality sequences like v-a-t-v-a-t, a-v-t-a-v-t, t-v-a-t-v-a, etc, and was aimed at avoiding temporal effects of specific stimulus modalities. Rather than using blocks of trials with stimuli of only one sensory modality each, we could have used trials with alternating sensory stimulation. Both experimental designs would have supported a subsequent conjunction analysis, because each stimulus would have had its own baseline. Yet, compared to the second approach, the first one (which we used for our experiment) avoids the potential effects of task switching (i.e., the cognitive set of our subjects was not influenced by switching between sensory modalities across scans).

Image Processing and Statistical Analysis

All calculations and image manipulations were performed on Ultra 10 workstations (SUN Microsystems computers) using MATLAB (The Mathworks Inc.) and SPM99 (statistical parametric mapping software; Wellcome Department of Cognitive Neurology, London, UK). SPM was used for image realignment, image normalization, smoothing (10 mm for group analysis), and to create statistical maps of significant relative regional BOLD response changes (Friston et al., 1995a, 1995b).

In a first step, activations for each individual sensory modality (relative to the respective baseline) were computed (i.e., visual motion–visual control; tactile motion–tactile control; auditory motion–auditory control). In a second step, a conjunction analysis was performed to reveal the cortical regions activated by all three sensory modalities (Price and Friston, 1997). All activations reported are significant at $p < 0.05$, corrected for multiple comparisons. Note, however, that only activations in area VIP and premotor cortex were hypothesized a priori on the basis of electrophysiological data from the macaque. Although, there was no a priori hypothesis for the activation in the lateral inferior postcentral cortex, the latter activation is reported for data completeness, as it met the criteria for significance.

Finally, transformed functional data sets from each subject were smoothed with a Gaussian kernel of 6 mm for single-subject analysis. For single-subject analysis, fMRI data were analyzed in an identical way to the group data. The SPM was now thresholded at $p < 0.01$, uncorrected, as this analysis was restricted to areas showing significant activations in the group analysis.

These statistical analyses constitute fixed-effects analyses. As such, our inferences pertain only to the subjects reported in this study.

Localization of Activations

The stereotactic coordinates of the pixels of the local maximum significant activation were determined within areas of significant relative activity change associated with the tasks. The anatomical localization of these local maxima was assessed with reference to the standard stereotactic atlas (Talairach and Tournoux, 1988), and validation of this method of localization was obtained by superimposition of the SPM maps on the group mean MR image calculated after each individual's MR image had been stereotactically transformed into the same standard stereotactic space (Friston et al., 1995b).

The spatial normalization removes positional and shape differences down to about 2–6 mm (Friston et al., 1995b; Meyer et al., 1999). Localization errors are irrelevant at this level, as smoothing of 6 mm for single-subject analysis and of 10 mm in the group analysis was applied. The resulting spatial resolution of about 8 mm is sufficient, as at present the true variability of functional anatomy even with exact anatomical registration is not known. Furthermore, no anatomical data is available that would allow us further characterization of the areas activated here.

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