RESEARCH ARTICLE

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Preparatory states in crossmodal spatial attention: spatial specificity and possible control mechanisms

Abstract We used event-related functional magnetic resonance imaging to study the neural correlates of endogenous spatial attention for vision and touch. We examined activity associated with attention-directing cues (central auditory pure tones), symbolically instructing subjects to attend to one hemifield or the other prior to upcoming stimuli, for a visual or tactile task. In different sessions, subjects discriminated either visual or tactile stimuli at the covertly attended side, during bilateral visuotactile stimulation. To distinguish cue-related *preparatory* activity from any modulation of stimulus processing, unpredictably on some trials only the auditory cue was presented. The use of attend-vision and attend-touch blocks revealed whether preparatory attentional effects were modality-specific or multimodal. Unimodal effects of spatial attention were found in somatosensory cortex for attention to touch, and in occipital areas for attention to vision, both contralateral to the attended side. Multimodal spatial effects (i.e. effects of attended side irrespective of task-relevant modality) were detected in contralateral intraparietal sulcus, traditionally considered a multimodal brain region; and also in the middle occipital gyrus, an area traditionally considered purely visual. Critically, all these activations were observed even on *cue-only* trials, when no visual or tactile stimuli were subsequently presented. Endogenous shifts of spatial attention result in changes of brain activity *prior* to the presentation of target stimulation (baseline shifts). Here, we show for the first time the separable multimodal and unimodal components of such preparatory activations. Additionally, irrespective of the attended side and modality, attention-directing auditory cues activated a network of superior frontal and parietal association areas that may play a role in voluntary control of spatial attention for both vision and touch.

Keywords Attention · Space · Multimodal · Vision · Touch

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Introduction

In recent years neuroimaging techniques have began to unveil regions of the human brain engaged during spatial attention tasks (see, for example, Corbetta et al. 1993; Heinze et al. 1994; Nobre et al. 1997). The results of such studies have highlighted two basic phenomena. First, a stimulus presented at an attended location can produce more activity than the same stimulus presented at an unattended location. Characteristically, these effects can be observed in relatively "early" modality-specific cortices. Thus, studies employing visual stimuli have revealed modulation of extrastriate (Heinze et al. 1994; Hopfinger et al. 2000) and striate visual cortex (see, for example, Brefczynski and DeYoe 1999; Somers et al. 1999), while studies that used auditory or tactile stimuli have typically found attentional modulations in superior temporal auditory regions (Tzourio et al. 1997) or postcentral somatosensory areas (Macaluso et al. 2000), respectively. Modulations by spatial attention thus appear to affect brain regions that represent the location of the attended stimulus in the relevant modality. For example, when attention is directed to a peripheral visual stimulus in one hemifield, enhancements are typically detected in visual areas in the contralateral hemisphere (see, for example, Heinze et al. 1994; Brefczynski and DeYoe 1999; Martinez et al. 1999).

A second consistent finding in imaging research on spatial attention is the involvement of higher-order frontoparietal association areas (Corbetta et al. 1993;

Gitelman et al. 1999; Corbetta and Shulman 2002). These regions have been activated using a variety of comparisons, often involving "low-level" baselines not requiring any deployment of spatial attention to peripheral locations (Corbetta et al. 1993; Gitelman et al. 1999), and in some cases not requiring any task at all (see, for example, Nobre et al. 1997). The observation that a frontoparietal network of brain areas tends to activate concurrently (Gitelman et al. 1999) and that lesions anywhere in this network can cause deficits in spatial attention (Mesulam 1981; Posner et al. 1984; Vallar and Perani 1986; Husain and Kennard 1996; Friedrich et al. 1998) has led to the hypothesis that these regions may constitute an "attention-control network" (Mesulam 1981, 1998; Gitelman et al. 1999). Although the exact functions of this network are still largely unspecified, recent purely visual studies have suggested that one possible role of such a control network is to generate spatial biases that influence activity in lower-level visual areas (see, for example, Kastner et al. 1999; Corbetta et al. 2000; Hopfinger et al. 2000; see also Chawla et al. 1999).

It has been proposed (see, for example, Desimone and Duncan 1995), that top-down biasing signals may affect activity in lower-level visual areas even *prior* to presentation of any target stimulus. Indeed, recent functional magnetic resonance imaging (fMRI) studies have reported modulation of visual occipital cortex while the subject merely *prepared* to perform visual discriminations at one or another location (see, for example, Kastner et al. 1999; Hopfinger et al. 2000). These studies demonstrate that activity in relatively early visual areas can be affected by the current direction of covert spatial attention even in the absence of visual stimuli; and that such effects can be spatially specific (i.e. the anatomical locus of the attentional effect depends on the attended location, for example depending on the attended quadrant in a manner consistent with the known retinotopy of areas in early visual cortex). In agreement with the control network proposal outlined above, these studies also showed activity increases in frontoparietal regions upon presentation of attention-directing cues (Kastner et al. 1999; Corbetta et al. 2000; Hopfinger et al. 2000). Unlike earlier visual areas, frontoparietal association regions typically did not show any spatial specificity depending on the attended location (Kastner et al. 1999; Corbetta et al. 2000; Hopfinger et al. 2000, but see also Sereno et al. 2001; Corbetta and Shulman 2002).

Recently, the issue of spatial attention has been addressed from a crossmodal perspective. Behavioural evidence has demonstrated for some time that directing attention towards one or another location is not a purely modality-specific process (Driver and Spence 1998; McDonald et al. 2000; Spence et al. 2000). For example, when attention in one modality is directed towards one location, stimuli in a different modality, but presented at the same location, also appear to receive enhanced processing. Neuroimaging and electroencephalographic techniques have recently begun to investigate possible neural substrates for such crossmodal effects. For exam-

ple, our group previously showed both unimodal and multimodal effects of spatial selective attention for vision and touch using PET (Macaluso et al. 2000, 2002a). The results highlighted several types of multimodal activations. First, in the intraparietal sulcus (a multimodal region) we found multimodal effects that depend on the attended location, with activity increases for attention to the contralateral hemifield, irrespective of stimulated or attended modality. Second, we found that activity in occipital cortex (traditionally considered "unimodal") was influenced not only by the direction of visual attention but also by the direction of tactile attention (see also Eimer and Driver 2000, for analogous ERP effects of crossmodal attention affecting "early", sensory-specific processing; see Eimer 2001, for review). Finally, our PET study on selective spatial attention (Macaluso et al. 2002a) and also several other studies that used more than one modality at a time (Downar et al. 2000; Bremmer et al. 2001) found multimodal brain responses for higher-order areas in frontal, parietal and posterior temporal cortices, which in the Macaluso et al. (2002a) study were activated by the spatial attention task but were not specifically affected by the direction of spatial attention.

Thus, results of studies examining several modalities appear to follow the general pattern previously highlighted in unimodal visual studies, with a segregation between effects specific to the direction of attention (for example, attend left versus right, or vice versa) and the activation of a frontoparietal network for deployment of spatial attention, irrespective of attended location. However, none of the crossmodal imaging studies on endogenous spatial attention to date could determine whether the observed multimodal attentional effects depend on enhanced activation in response to the presentation of attended targets in one or the other modality, or instead, as recently found for the visual modality (see, for example, Kastner et al. 1999; Hopfinger et al. 2000), might also reflect changes in *preparatory* activity (for example, baseline shifts), not just modulation of target processing.

To address this issue, we performed an event-related fMRI study, which manipulated the direction of spatial attention (attend left or attend right, as instructed symbolically by an attention-directing cue), the relevant modality (judge vision or touch) and, critically, whether or not bimodal visuotactile stimulation followed the attention-directing central cues (auditory pure tones). While the relevant modality was blocked, the direction of attention (left or right), and the presence/absence of bimodal, bilateral visuotactile stimulation after the cue, were unpredictable and intermingled on a trial-by-trial basis. The critical comparisons concerned trials when no bimodal stimulation was delivered (cue-only trials), so that subjects directed attention to one or the other side, but did not perform any discrimination. These trials allowed us to investigate any *preparatory* effects of directing spatial attention, under condition of either visual or tactile task relevance, thus going beyond previous findings about unimodal versus multimodal mechanisms of spatial attention. Moreover, comparison of these cue-

only trials with a control condition, in which subjects received an auditory cue that instructed them *not* to covertly attend to either side, allowed us to highlight any brain areas involved in endogenous shifts of spatial attention, independently of attended side (i.e. common for attend left and attend right), again as a function of task-relevant modality.

Materials and methods

Subjects

Six right-handed volunteers (four males and two females) participated. After explanation of the experimental procedures, subjects gave informed written consent. The work was approved by the Joint Ethics Committee of the Institute of Neurology and the National Hospital for Neurology and Neurosurgery.

Paradigm

Subjects were tested in 2×2×2 factorial design, plus a control condition. One factor was the direction of covert spatial attention (equiprobably to the left or right hemifield, as specified by a central symbolic auditory cue). The second factor was whether attention-directing auditory cues were followed by visuotactile stimulation or not (stimulation present or absent, which had a 3:1 ratio). The choice of this particular ratio of target present/absent followed two considerations. First, the number of target-present trials should be sufficiently higher than the number of cue-only trials to ensure that subjects expected stimulation and so prepared accordingly. But second, given our primary interest in any preparatory activations on cue-only trials, a sufficiently high number of target-absent trials was also desirable. The 3:1 ratio appeared to be a reasonable compromise between these two requirements.

The direction of spatial attention and presence/absence of any bimodal stimulation changed unpredictably on a trial-by-trial basis. On trials with stimulation present subsequent to the cue, this consisted of bimodal (visuotactile) stimulation that was always bilateral for both modalities, with both sides and both modalities thus being stimulated at the same time. The third factor was the attended modality to be judged (vision or touch), which was blocked. Subjects attended one single modality throughout a scanning session (two sessions for each modality). The task was to discriminate stimuli in just the currently relevant modality, only on the side indicated by the symbolic auditory cue.

The randomly intermingled control condition consisted of the presentation of an auditory tone specifying with certainty that no visuotactile stimulation would follow. Accordingly, subjects should not direct attention to any peripheral location on such trials, as they would no longer anticipate stimulation or task-performance on either side. These control tones were presented during all sessions, randomly intermingled with the other trial types. This control condition served as a baseline aimed at highlighting any brain activity associated with attention-directing cues, but independent from the side that attention was directed to following those cues. Note that during both the cue-only trials and the control-tone trials, interpretation of a symbolic auditory cue was required, while no peripheral stimulation was delivered and no overt responses were made, making these conditions well-matched in all these respects.

Stimuli

Subjects lay in the scanner wearing headphones, with each hand resting on a plastic support on the corresponding side. On each side there was an LED pair to present visual stimuli, and a piezoelectric component (T220–H3BS–304, Piezo Systems, Cambridge, USA) to deliver unseen tactile stimulation to the thumb. The peripheral LEDs and the subject's thumbs were each 12 cm from a central LED that served as fixation point (approximately 10° of visual angle). The LEDs were placed directly in front of the thumbs, so that visual and tactile stimuli could be delivered in close spatial proximity on either side (see also Macaluso et al. 2002b, for a schematic illustration of the apparatus, but note that here tactile stimuli were delivered using piezoelectric components rather than air puffs). The scanner environment was dimly lit and subjects viewed all LEDs and both hands through a mirror system. This comprised two mirrors placed on top of the whole-head RF coil, such that LEDs and the subject's thumbs could be viewed without any mirror-image reversal. A third mirror was also placed on top of the RF coil, to allow monitoring of eye position throughout the experiment, with a remote optics eye-tracker (see below).

Each trial began with the illumination of the central fixation point. After 700 ms, one of three possible auditory tones was presented binaurally (see Fig. 1). The frequency of this central tone indicated whether the subject had to covertly attend to the left side, attend to the right side, or that no subsequent stimulation would be presented (control trials). The tones were square waves of three different frequencies (100, 400, 1,500 Hz), with 300 ms duration. Each subject was trained before fMRI scanning to associate one particular tone with one particular instruction (attend left, attend right or control). On cue-only trials and control trials (Fig. 1B, C), no subsequent visuotactile stimulation was presented: 3,600 ms after the onset of the auditory cue, the central fixation point was turned off to indicate the end of the trial. In trials where bilateral stimulation was presented, 1,500 ms after auditory cue onset the bilateral, bimodal visuotactile stimulation was delivered (see Fig. 1A).
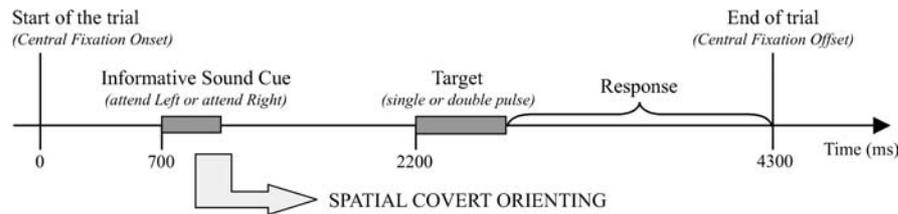
This visuotactile stimulation consisted of flashing red lights on both sides together with 130-Hz vibrations on both thumbs. Each of the four stimuli (vision on the left and on the right, and touch on the left and on the right) consisted of either a single pulse (150 ms on) or a double pulse (150 ms on, 150 ms off, 150 ms on). Single or double pulses, which were equiprobable, were presented in random order and independently in the two hemifields and two modalities. Subjects discriminated stimuli at the attended side and in the attended modality only, responding with a button-press to indicate a double or single target (see task, below). Again, 3,600 ms after the onset of the auditory cue the central fixation point was turned off, indicating the end of the trial. The intertrial interval was 6,230 ms.
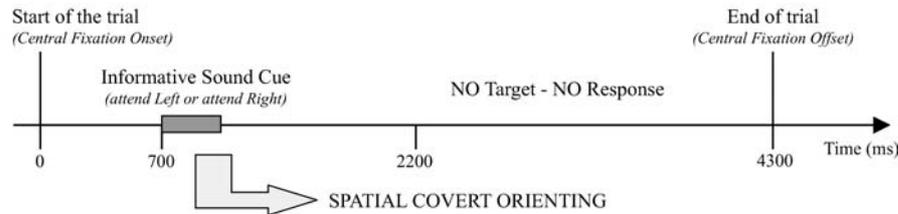
Task

Prior to the imaging experiment, subjects underwent approximately 45 min of training to learn their particular association between each of the three tones (100, 400 or 1,500 Hz) and the attentional task (attend left, attend right, control), and to learn that they should respond selectively to just the currently relevant modality on just the cued side. The association between particular tones and the tasks was arbitrary and counterbalanced across subjects.

The fMRI experiment was divided into four sessions of 7.9 min each. Before each scanning session subjects were instructed about which modality was relevant (two sessions of attend-vision and two sessions of attend-touch, in counterbalanced order). During scanning, on each trial subjects received an auditory tone and directed attention leftward or rightward in anticipation of discriminating visual or tactile targets (unless the tone specified that definitely no subsequent stimulation would be presented, i.e. control trials). Each session comprised 72 trials. On 44 trials (22 attend left and 22 attend right), bilateral-bimodal stimulation followed the attention-directing cues. Subjects responded with a button-press to indicate whether the stimulus at the attended side in the attended modality was either a single or a double pulse. All stimuli on the opposite side, and at the attended side but in the irrelevant modality, had to be ignored. Button-presses were made with the unseen index or middle finger. Three subjects used the index finger to report single pulses and the middle finger to report double pulses; the other three subjects used the reverse stimulus–response configuration. Irrespective of the attended side, unseen responses were always made

A. Cue plus Target Trials

Start of the trial
(Central Fixation Onset)

End of trial
(Central Fixation Offset)

Informative Sound Cue
(attend Left or attend Right)

Target
(single or double pulse)

Response

0   700   2200   4300   Time (ms)

SPATIAL COVERT ORIENTING

B. Cue-only Trials

Start of the trial
(Central Fixation Onset)

End of trial
(Central Fixation Offset)

Informative Sound Cue
(attend Left or attend Right)

NO Target - NO Response

0   700   2200   4300   Time (ms)

SPATIAL COVERT ORIENTING

C. Control Trials

Start of the trial
(Central Fixation Onset)

End of trial
(Central Fixation Offset)

Control Sound Cue
(NO target)

NO Target - NO Response

0   700   2200   4300   Time (ms)
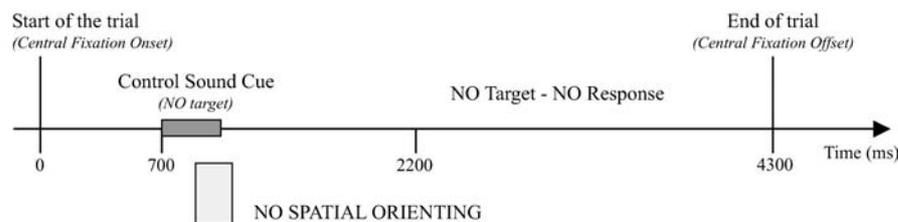
NO SPATIAL ORIENTING

Fig. 1A–C Schematic depiction of the three main trial types. **A** Cue-plus-stimulation trial. The attention-directing cue was followed by bimodal-bilateral stimulation, sensory discrimination and overt response. **B** Cue-only trial. Following the attention-directing cue, subjects shifted attention to one or the other side expecting to perform the sensory discrimination. However, the bimodal-bilateral stimulation was not presented and so no overt response was made. This trial type allowed us to investigate neural activity associated with the shift of spatial attention, irrespective of peripheral sensory stimulation and discrimination. **C** Control trial. The sensory and motor aspects of this trial type were equivalent to cue-only trials (i.e. no peripheral stimulation and no overt response). However, the auditory cue informed the subject that no subsequent stimulation would be presented, and thus spatial attention was not shifted to either side. Direct comparison of cue-only trials versus control trials should highlight brain activity associated with the spatial attention task, irrespective of attended location (common activity for attend left and attend right)

with the same hand during one session. The hand used to respond was counterbalanced across sessions. Hence, before the beginning of each session subjects were told which modality they should attend and also which hand they should use to respond.

Unpredictably on 14 attention-directing trials for each session (7 for left side attention-directing cues and 7 for right side), the bimodal-bilateral stimulation was not delivered. Thus subjects shifted attention towards one side in anticipation, but there was no subsequent stimulation and they did not perform any target discrimination. These trials (25% of the attention-directing trials) allowed us to investigate the effect of directing voluntary attention towards one side or the other, independently of any consequence of this for subsequent stimulus processing (i.e. excluding any modulation of target-related activity, measuring only "baseline shifts" instead; cf. Kastner et al. 1999). In addition, the use of control tones (14 trials per session) allowed us to highlight any brain region involved in preparing for the attentional task (following an attention-directing cue) independently of attended side.

Image acquisition

Functional images were acquired with a 2-Tesla Magnetom Vision MRI scanner (Siemens, Erlangen, Germany). Blood oxygenation level dependent contrast was obtained using echo-planar T2* weighted imaging. The acquisition of 32 transverse slices, with an effective repetition time of 2.93 s, gave coverage of the whole cerebral cortex. The in-plane resolution was 3×3 mm.

Data analysis

Event-related fMRI data were analysed with SPM99 (www.fil.ion.ucl.ac.uk). For each subject, acquisition timing was corrected using the middle slice as reference (Henson et al. 1999) and the 628 volumes (157 per session) were realigned with the first volume. To allow intersubject analysis, images were normalised to the Montreal Neurological Institute (MNI) standard space (Collins et al. 1994), using the mean of the functional images. All images were smoothed using a 10-mm isotropic Gaussian kernel.

The data were analysed using a fixed effects model. For each voxel, data were best-fitted (least square) using a linear combination of the effects of interest and confounds. The effects of interest were the timing of the five event types (i.e. attend left or right, with subsequent stimulation present or absent; plus control tones), convolved with the SPM99 standard haemodynamic response function (HRF), plus its first and second derivative. Trials in which subjects responded incorrectly during the stimulation discrimina-

tion were treated as confounds and modelled separately. Confounds also included the movement parameters of the realignment preprocessing. Linear compounds (contrasts) were used to compare the parameters of the multiple regression for the effects of interest.

We performed three types of comparison. First we tested for attentional effects specific for attention to one or the other hemifield, by directly comparing rightward versus leftward attention, and vice versa. The spatial effects were further divided into unimodal versus multimodal effects, depending on whether the activations were present only during attention to one particular modality, or were observed during both visual and tactile sessions. Moreover, given our central interest in any preparatory activity associated with attentional shifts prior to the presentation of the visuotactile stimulation, trials with only an attention-directing cue (no subsequent stimulation) were also considered. We used conjunction analyses (Price and Friston 1997; Friston et al. 1999) to detect multimodal effects of spatial attention. These conjunctions tested for common spatial effects during visual and tactile sessions, both for stimulation-present and for cue-only trials. Thus, these analyses tested for multimodal spatial effects that were also present when only the attention-directing cue was delivered. In addition, any unimodal effects were highlighted using the main effect of attention towards one side versus the other (with or without bimodal-bilateral stimulation), within either the visual or the tactile scanning sessions. To ensure that any such spatial effect was indeed unimodal, this comparison adopted the additional constraint that all activated voxels should also show an interaction between attended side and relevant modality.

The second type of comparison concerned the non-spatial effect of attending to one modality versus the other. Because the two different modalities (vision and touch) were attended in separate fMRI sessions, we could not directly compare brain responses to the bimodal stimulation during attention to vision versus the same stimulation for attention to touch. This would be confounded with any non-specific session effect. Accordingly, we tested instead for interactions between the effect of trials with bimodal stimulation minus control-tones trials, and the effect of the currently attended modality. This use of interactions between conditions and sessions ensured that any reported effects were not due to some spurious overall difference between scanning sessions. To investigate effects of attending to one modality versus another on preparatory activity, we ran analogous analyses on cue-only trials and control-tone trials.

For effects dependent on the spatial direction of attention, and effects of attending to one or the other modality (intermodal effects), thresholds for statistical significance were set at P uncorrected=0.001. For both these comparisons we had a priori anatomical hypotheses derived from our previous PET studies, which had used similar spatial attentional manipulations in vision and touch (Macaluso et al. 2000, 2002a), but could not separate preparatory activity versus modulation of stimulus processing (due to the blocked nature of PET). Those studies found spatial-attention effects in occipital visual areas, postcentral somatosensory regions and intraparietal areas, in the hemisphere contralateral to the attended side. Intermodal effects of attending to vision or touch were previously observed in occipital and posterior parietal areas for attending to vision and postcentral areas plus parietal operculum for attending to touch (Macaluso et al. 2002a).

Finally, the present design also allowed us to test for any preparatory effects induced by the attention-directing auditory cues, but independent of the spatial direction of attention. For this we compared all cue-only trials with all control-tone trials. During both these types of trial no peripheral stimulation was delivered and no overt responses were made. For this particular comparison the statistical threshold was set to P=0.05, corrected for multiple comparisons, as we had no specific a priori prediction from our previous studies.

Eye tracking

Eye position was monitored using an ASL Eye-Tracking System (Applied Science Laboratories, Bedford, USA), with remote optics (model 504, sampling rate=60 Hz) that was custom-adapted for use in the scanner. Due to technical difficulties with two subjects, reliable eye-tracking data were available throughout all scanning sessions for four subjects. For these subjects the horizontal eye position was examined according to the direction of attention. Blinks (which produce brief losses of the signal indicating pupil diameter) were removed from the raw data. Eye position was considered in a 3.6-s time window that began with the presentation of the auditory cue and ended with the end of the trial (central fixation off-set). The eye position data confirmed that these trained subjects satisfactorily followed the instruction of maintaining central fixation (mean deviation: attend left −0.02°; attend right 0.05°; control trials 0.03°; negative values indicate a leftward shift).

Results

Imaging data

The experimental design allowed us to address three central issues concerning mechanisms of spatial attention for vision and touch. First, we compared attention to one side or the other to reveal spatially specific effects of covert orienting. The inclusion of cue-only trials in our conjunction analyses specifically sought to highlight brain areas that were affected by the direction of spatial attention *irrespective* of the presence or absence of any peripheral visuotactile stimulation. Thus, the finding of any such areas would support the hypothesis that endogenous spatial attention can result in *preparatory* changes of brain activity (analogous to baseline shifts; cf. Kastner et al. 1999). Critically, the inclusion of visual and tactile sessions allowed us to determine for the first time whether any such effects were modality specific or multimodal.

Second, we compared brain responses to visuotactile bimodal stimulation (minus control trials) during either attend-vision blocks or attend-touch blocks. This should reveal the neural correlates of attending one modality versus another (i.e. intermodal selection). Finally, subtraction of baseline control tones from all attention-directing cue-only trials (i.e. attend left and attend right, for vision and touch) should highlight any brain regions involved in preparing for the covert spatial attention task, independently of attended modality and attended hemifield.

Spatial selective attention

Spatial attention effects were investigated by directly comparing trials of attention to one side versus attention to the opposite side. Critically, the inclusion of cue-only trials (without any bimodal visuotactile stimulation) enabled us to determine whether any effects of spatial attention related only to the modulation of responses to incoming sensory visuotactile input, or instead could also reflect changes in preparatory activity (for example, baseline shifts). In the latter case, spatial attentional effects should also be detected for cue-only trials. Moreover, the use of vision and touch within the same
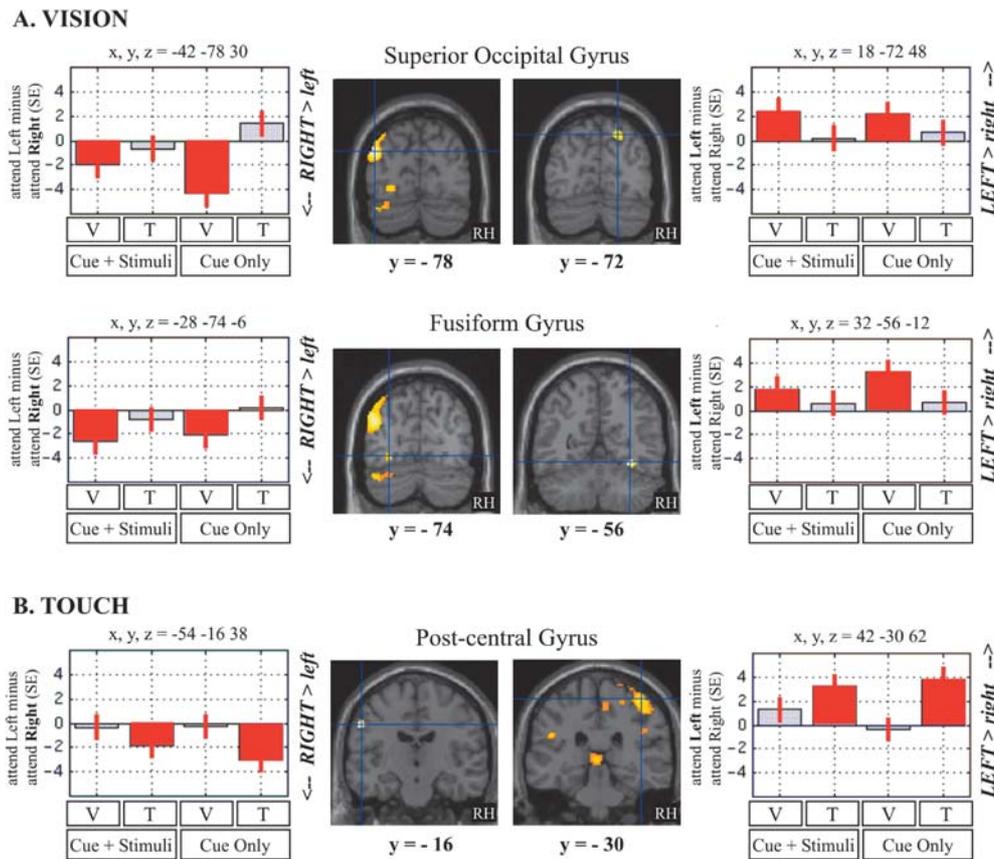
A. VISION

B. TOUCH

Fig. 2A, B Unimodal fMRI effects of spatial selective attention. **A** Superior occipital and fusiform gyri activations showing increased activity for attention to the contralateral side only during vision-relevant blocks. **B** Postcentral areas were affected by the direction of attention only when touch was relevant. Activities are expressed as differences between HRF amplitude of attend left minus attend right trials (i.e. positive values indicate greater activity during leftward attention, and negative values indicate greater activity during rightward attention), ± standard error (*SE*). For all regions, signal plots for the cross-haired region show that activity was higher for attention to the contralateral versus ipsilateral side, but only for attention to one of the two modalities (see *red bars*). Moreover, the plots also show that the differential effect of spatial attention was present for cue-only trials (*two rightmost bars* in each plot), not just for cue-plus-stimulus trials, thus revealing preparatory activity in all these areas. For display purposes, SPM thresholds were set to *P* uncorrected=0.01, thus also revealing non-significant clusters of increased activity. *V* Attend-vision, *T* attend-touch; *RH* right hemisphere, to indicate the use of neurological convention in all anatomical sections

Table 1 Co-ordinates and Z values for the areas showing either unimodal or multimodal spatial effects of attended side. All activations were contralateral to the attended side and common for both stimulation-present trials and cue-only trials

	Attend right		Attend left	
	Co-ordinates	Z values	Co-ordinates	Z values
Unimodal, vision				
Superior occipital gyrus	−42 −78 30	4.8	18 −72 48	3.1
Fusiform gyrus	−28 −74 −6	3.2	32 −56 −12	3.7
Unimodal, touch				
Superior postcentral gyrus	−54 −16 38	3.6	42 −30 62	4.1
Multimodal				
Intraparietal sulcus	−32 −44 66	4.1	26 −46 52	3.3
Middle occipital gyrus	−44 −70 10	3.6	40 −76 6	4.5

experiment allowed us to assess whether any spatial attentional effects were unimodal (i.e. found for attention to one side for only one particular modality) or multimodal (spatial effects independent of attended modality).

Unimodal spatial effects for vision only. Unimodal effects of visual attention to one side or the other were found in the superior occipital gyrus and fusiform gyrus, in areas traditionally considered to be unimodal visual cortex (Fig. 2A; Table 1). Activity increased when visual

attention was directed to the contralateral hemifield, compared with attention to the ipsilateral hemifield. The patterns of activity for the superior occipital gyrus and the fusiform gyrus are shown in Fig. 2A. For both areas, the figure shows spatial-attention effects during attend-vision and attend-touch sessions, according to whether the bimodal stimulation was present or absent ("cue+stimulus" and "cue-only" trials, respectively). Spatial effects are plotted as the difference between attention to the left minus attention to the right. Thus, greater activity for leftward attention results in positive values in these plots, while greater activity for attention to the right side results in negative values. The critical spatial effects are highlighted in red in the plots, showing that activity increased during attention to the contralateral hemifield, but only when vision was relevant. Additionally, this analysis indicates that these spatial effects were present for both stimulus-present and cue-only trials, highlighting preparatory activity in these areas.

Indeed, some of the signal plots in Fig. 2 indicate that the spatial attentional effects were if anything larger during the cue-only trials than for "cue+stimulus" trials (for example, see plot for the left occipital gyrus). This might appear counterintuitive if one assumes that the size of the spatial effect for "cue+stimulus" trials should correspond to the sum of the preparatory effect plus any modulation of target-related activity. However, it should be noted that the size of the preparatory effect may differ between the two trial types. In particular, during "cue+stimulus" trials the presentation of the target stimuli should terminate any preparatory activity, while during cue-only trials such activity might be sustained for a longer period, until termination of the trial (see Fig. 1A, B). Such protracted preparatory activity during cue-only trials might therefore be associated with a relatively high level of spatial attentional modulation for this trial type. This could also explain why no brain region showed higher spatial attentional modulation for "cue+stimulus" trials compared with cue-only trials (i.e. interactions between attended side and presence/absence of bimodal-bilateral stimulation). But note that this possibility of the level of preparatory activity differing between "cue+stimulus) trials and cue-only trials does not alter our main finding that endogenous modulations by spatial attention can precede any sensory stimulation, with both modality-specific and multimodal (see below) forms of such preparatory modulation arising in different brain areas.

Unimodal effects for touch only. One region showed unimodal spatial attentional effects that were specific to attend-touch sessions. This was the superior part of the postcentral gyrus contralateral to the attended side (see Fig. 2B; Table 1), a unimodal somatosensory region. In the right hemisphere, the activation cluster extended anteriorly (with a maximum at x, y, z=34 −16 58, Z score=5.0) including the central sulcus, and possibly precentral areas. The signal plots in Fig. 2B show the spatial effects for the left hemisphere activation and for the more posterior maxima in the right hemisphere (see

also Table 1), which was definitely located in somato-sensory cortex. As highlighted by the red bars in the plots, in these areas of both hemispheres the spatial effects were present only when touch was relevant. Again, it is clear that these spatial attentional effects (now for touch) did not require the presence of any sensory stimulation, as the critical effect was observed also for the cue-only trials. This suggests that in this somatosensory region also, brain activation can reflect preparatory aspects of covert spatial orienting.

Multimodal spatial effects for both vision and touch. Two regions showed an effect of attending to one hemifield versus the other, *independently of the attended modality* (see Table 1). These were the anterior part of the intraparietal sulcus (Fig. 3A) and the middle occipital gyrus (Fig. 3B). While multimodal effects in the intraparietal sulcus can be naturally understood in relation to the known existence of multimodal spatial representations in this region (see, for example, Andersen et al. 1997; Bremmer et al. 2001, Macaluso and Driver 2001), it is of interest to observe multimodal spatial effects in the lateral occipital gyrus also, an area traditionally considered purely visual (see Discussion). The signal plots show that irrespective of attended modality, activity in both these areas was greater for attention to the contralateral versus ipsilateral hemifield. Moreover, the plots also show that all these multimodal effects were again independent of the presence or absence of visuotactile stimulation, with spatial effects also observed for cue-only trials (see two rightmost bars in all signal plots of Fig. 3).

Intermodal attention to one sensory modality versus another

Although attention was sustained to one modality throughout each scanning session (precluding the detection of any *sustained* effect of attention to one or other modality), we investigated any intermodal effects by looking at *transient* responses to the bimodal visuotactile stimulation during visual and tactile sessions. Note that the separation of "attend-to-vision" and "attend-to-touch" trials into different scanning sessions implied that intermodal effects could not be studied by direct comparison of trials under the two attentional conditions. Any differential brain activity resulting from such direct comparison could in principle be related to the main effect of scanning session (i.e. between-session differences), rather than the specific attentional task. This problem was addressed by testing for interactions between different conditions within the same session (for example, stimulation trials versus control tones) and session, thus removing the confounding main effect of scanning session. Hence, intermodal effects were highlighted using the interaction between the presence versus absence of attended bimodal-bilateral stimulation (stimulation trials versus control tones) and the attended
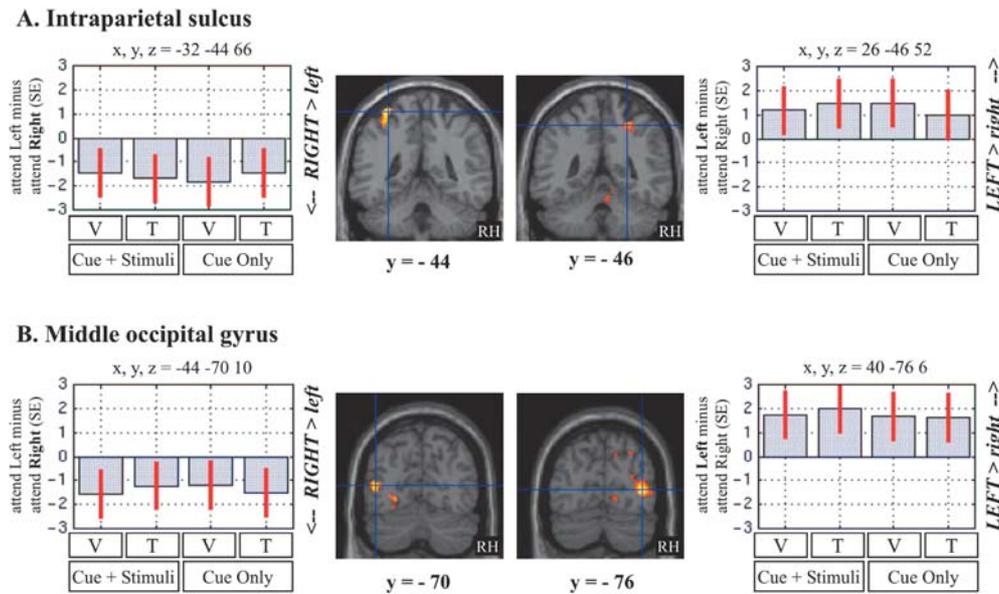
Fig. 3A, B Multimodal effects of spatial selective attention that were independent of the attended modality. **A** Intraparietal sulcus. **B** Middle occipital gyrus. Activities are expressed as differences between attend left minus attend right (i.e. positive values indicate greater activity during leftward attention, while negative values indicate greater activity during rightward attention). All multimodal effects of spatial attention were contralateral to the attended side. Again, the difference between contralateral and ipsilateral attention was present also in the cue-only trials (*two rightmost bars* in all signal plots), indicating preparatory activity in these regions regardless of which modality was task-relevant. For display purposes SPM thresholds were set to *P* uncorrected=0.01, exposing several other non-significant activation clusters. *V* Attend-vision, *T* attend-touch

Table 2 Non-spatial effects of attending one modality versus another, as revealed by the interaction between responses to target trials versus control tones during either visual or tactile sessions

Attend	Anatomical area	Co-ordinates	Z values
Vision	Fusiform gyrus	42 56 −18	3.5
		−22 −66 −10	4.2
	Middle occipital gyrus	40 76 14	3.8
		−42 −78 −4	3.1
Touch	Parietal operculum	44 14 12	3.2
		−46 −14 6	2.9

modality (visual versus tactile sessions, and vice versa). These analyses will show how the transient response to incoming bimodal-bilateral stimulation is affected by the instructions to attend vision or touch, over and above any unspecific difference in evoked brain activity that might occur across scanning sessions.

For attention to vision this revealed activation of the fusiform gyrus and the middle occipital gyrus (see Table 2). Both regions are within unimodal visual cortex and they were also affected by the direction of spatial attention (except for the left middle occipital gyrus, where the two effects did not overlap). Interestingly, this intermodal effect was observed only for trials with stimulation-present, with no preparatory transient effect for the cue-only trials (but note that the task-relevant modality was blocked, and that sustained intermodal preparatory activity cannot be excluded). Thus, activity in these regions combines spatial selectivity for one or the other hemifield with modality selection, yielding maximal response for stimuli at the attended side when vision was relevant (see also Macaluso et al. 2002a; for similar findings using blocked PET scanning).

For attention to touch, higher responses to bimodal visuotactile stimulation for blocks of tactile attention were found in the parietal operculum (Table 2), in correspondence with secondary somatosensory cortex (SII). Again the intermodal effect was observed only when the bimodal stimulation was present indicating that, unlike the spatial effects, this was not a transient change in purely preparatory activity (although any sustained intermodal preparatory effects could not be assessed). More dorsal areas, where unimodal tactile spatial attentional effects had been detected, did not show any intermodal modulation. Examination of activity in the postcentral gyrus revealed that attention to the ipsilateral hand during tactile blocks resulted in deactivation (see also Drevets et al. 1995; Macaluso et al. 2002a), thus preventing the detection of any overall increase in activity for tactile attention versus visual attention here.

Non-spatial activations associated with attention-directing cues

Our design also allowed us to test for brain responses associated with attention-directing cues, but independent of attended side. This was investigated by comparing the four cue-only trial types (attend left or right, in visual or

Fig. 4A–E Areas activated by attention-directing cues (cue-only trials) versus control tones. **A** Overall effect of the attention-directing cues rendered on a 3-D view of the canonical MNI brain (also marking the activations illustrated in the panels below). **B–D** Anatomical location and signal plots for three areas that were activated by all types of attention-directing cue. Activity during each attention-directing cue is plotted minus activity during the control tones. Note that the responses were not only independent of attended side, but were also seen for both visual and tactile blocks, suggesting a multimodal role of these areas in spatial covert orienting. **E** For completeness, panel **E** also shows activity in a region of the right inferior parietal lobule that was symmetric to the activated cluster in the left hemisphere. This shows that not all four types of attention-directing cues activated above the control-tone baseline, and thus this region was not considered to be significant for this analysis (hence the different colour schema for this plot). For display purposes SPM thresholds were set to *P* uncorrected=0.001. *L* Attend left, *R* attend right
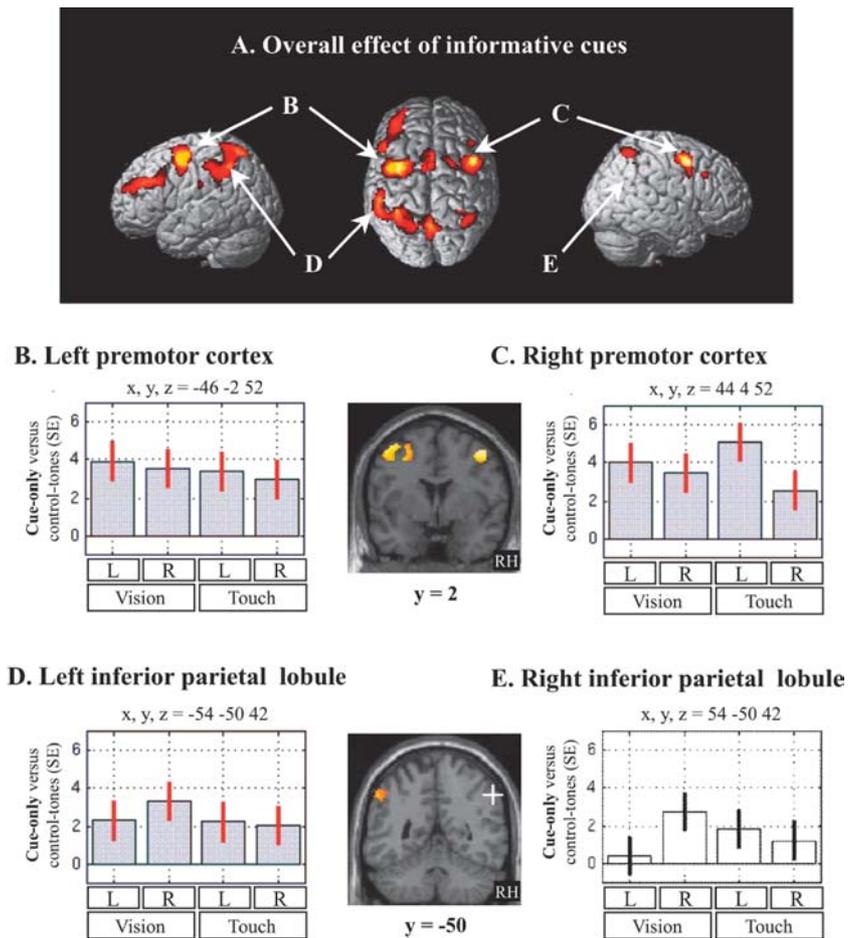

Table 3 Non-spatial effects of informative auditory cues compared with control tones. All areas were activated for the informative cues irrespective of the direction of spatial attention (left or right) or relevant modality (vision or touch)

Anatomical area	Co-ordinates	Z values
Right premotor cortex	44 4 52	6.5
Left premotor cortex	−46 −2 52	5.9
Left inferior parietal lobule	−54 −50 42	4.3
Superior frontal gyrus	−4 10 50	6.0
Precuneus	−2 −62 48	5.9

tactile blocks) with the control tones, which did not require any shift of spatial attention.

This showed activation of a network of areas comprising premotor cortex, superior parietal cortex, prefrontal cortex, left inferior parietal lobule and both anterior and posterior medial brain regions (see Fig. 4A). To further ensure the presence of activation on all types of cue-only trials relative to control trials, the overall comparison was masked with the simple effect of each cue type versus control (threshold for each of the four additional comparisons in this mask each set at *P* uncorrected=0.05). Prefrontal and superior parietal areas did not survive these additional constraints, with attention-directing cues in the tactile blocks not activating above

baseline. Table 3 reports activations that did survive the additional constraints. Figure 4B–D shows the anatomical location and pattern of activity in left and right premotor areas and left inferior parietal lobule. The premotor activations were found in the fundus of the precentral sulci, at the intersection with the superior frontal sulci, possibly in correspondence with the human frontal eye field (Petit et al. 1997). The activation of the left inferior parietal lobule was centred on the supramarginal gyrus. The signal plots in Fig. 4 show activity for the four types of attention-directing cues compared with the control tones; activity increased upon presentation of all attention-directing cues, independently of which side and modality was attended. Figure 4D also shows activity in a corresponding region in the right inferior parietal lobule (see *right panel*), revealing that in this hemisphere the four types of attention-directing cues did not all induce increased activity. Overall, the comparison between spatially directing cues versus control tones highlighted a network of higher associative areas in parietal and frontal cortex that may have a multimodal role in the present spatial attentional task.

Behavioural performance

There were four trial types with bimodal stimulation following the attention-directing cues, with attention directed to the left or right, in sessions where vision or touch was task relevant. Subjects discriminated single pulses versus double pulses at the attended side in the relevant modality. Note that this task can only be performed correctly (i.e. at >50% correct) if the attentional cue is utilised. Percentage accuracy was 95% for vision left, 94% for vision right, 77% for touch left and 81% for touch right. Means (SEM) of the reaction times were 982 (36) ms for vision left, 975 (33) ms for vision right, 1,195 (45) ms for touch left and 1,173 (48) ms for touch right. Reaction times were calculated from the initial stimulus onset, but note that at least 300 ms must pass before the subject could decide whether the attended stimulus was either a single or a double pulse. A two-way ANOVA on the reaction times found no significant effect of attended side ($P>0.40$; but note that stimuli on the currently unattended side never received any behavioural response) and no interaction between side and attended modality ($P>0.46$). Nevertheless an effect of attended modality was present ($P<0.002$), with vision yielding faster performance than touch overall, consistent with the accuracy pattern. The behavioural data indicate that subjects were able to attend one or the other hemifield with comparable accuracy, and thus that the brain imaging results showing higher activity for spatial attention to the contralateral hemifield are unlikely to be affected by unspecific task components (for example, differences in task difficulty when attending left versus right).

Discussion

The present study investigated the neural basis of crossmodal links in spatial selective attention, with a particular interest in the possible role of *preparatory* changes of brain activity induced by attention-directing central symbolic cues. On a trial-by-trial basis, auditory pure tones instructed subjects to direct attention either to the left or the right hemifield. Following these cues, bilateral-bimodal visuotactile stimulation could be presented. Subjects discriminated single versus double pulses at just the attended location and only in the relevant modality (which was blocked and determined by prescanning instructions). We found increased brain activity in areas contralateral to the attended side. More specifically we found both unimodal effects and multimodal effects of this type. Unimodal effects of spatial attention (i.e. observed for attention to a particular side only when one specific modality was relevant) were found in superior occipital and fusiform gyrus for vision, and in postcentral gyrus for touch (see Fig. 2). Multimodal spatial effects (i.e. found irrespective of attended modality) were detected in the intraparietal sulcus, but also in the lateral occipital gyrus (see Fig. 3), an area traditionally considered purely visual.

Critically, our paradigm included "cue-only" trials, when no visuotactile stimulation was delivered after the attention-directing cue. These allowed us to investigate the effect of attention-directing cues, independently of any subsequent stimulation and discrimination in vision or touch. Conjunction analyses with these "cue-only" trials revealed that both unimodal and multimodal spatial effects could be observed regardless of the presence or absence of any peripheral stimulation, thus suggesting that *preparatory* activity plays a role in spatial covert orienting at the level of both unimodal and multimodal neural mechanisms. The present study is the first to demonstrate multimodal examples of such spatially specific "baseline shifts" (cf. Kastner et al. 1999, for a purely visual study). Finally the inclusion of a control condition, in which subjects did not direct attention to either the left or right hemifield, highlighted activation of a network of frontoparietal areas on cued trials that might be involved in the control of voluntary covert spatial orienting, irrespective of attended location and relevant modality.

We directly compared attention to one side versus the other for bilateral (and bimodal) stimulation to investigate the neural consequences of endogenous spatial selection. In addition, the use of blocks of attending to vision or attending to touch allowed us to separate between multimodal spatial attentional effects (i.e. independent of attended modality) versus unimodal effects, specific to one or the other modality. Multimodal, but spatially specific, responses were detected in the intraparietal sulcus and superior occipital gyrus, contralateral to the attended side. The intraparietal responses may represent attentional modulation of multimodal spatial representations. Both single-cell recordings in monkeys (Andersen et al. 1997; Duhamel et al. 1998) and brain imaging studies using stimulation of one or another modality in humans (Bremmer et al. 2001; Macaluso and Driver 2001) have found multimodal responses in several intraparietal regions. Critically, here we show for the first time that these representations can be modulated endogenously, even when no peripheral stimulus is presented. These findings resemble the observation of changes of baseline activity in visual cortex following informative central cues in purely visual studies (Kastner et al. 1999; Hopfinger et al. 2000), but here we show *preparatory* and *spatially specific* changes that are *independent* of the attended modality.

A second region showing multimodal effects here that depended on the attended location was the lateral occipital gyrus (see Fig. 3B). The finding of multimodal spatial effects in occipital cortex might at first seem surprising, given that these brain regions are traditionally considered to be specific for just visual processing, often showing spatial attentional effects in visual tasks (see, for example, Mangun et al. 1997). However, it should be noted that using comparable paradigms we have previously showed similar multimodal effects in visual cortex

during PET scanning (Macaluso et al. 2000, 2002a). In these previous studies, the blocked nature of PET scanning did not allow us to assess whether the multimodal effects in visual areas (and in the intraparietal sulcus) were associated with preparatory attention towards one side, or instead reflected modulation of transient responses to incoming stimuli (although note that in Macaluso et al. 2000, no visual target was presented at the attended location during the tactile task). The present fMRI results demonstrate that crossmodal spatial influences on regions of visual cortex (and on intraparietal regions) can occur also in the absence of any peripheral stimulation (i.e. on cue-only trials), suggesting that our previous PET findings might indeed be partially related to the *preparation* to attend to stimuli at a given location, even when the task requires discrimination of tactile stimuli only. Using ERPs in a similar spatial attention paradigm, Eimer et al. (2002) observed a component (late directing attention positivity; LDAP) over lateral posterior sites specific to the direction of a covert attention shift in the cue-to-target interval. Again these brain responses were independent of the attended modality, but specific to the attended side (as in the present study). Because of the poor spatial resolution of the ERP method, Eimer et al. (2002) could not infer the source of their preparatory effects. The present fMRI results identify possible sources in the lateral occipital gyrus and in the intraparietal sulcus, which may be jointly responsible for the LDAP (although see also Harter et al. 1989, for a different view on this).

In addition to these multimodal preparatory spatial effects, the present study also detected modality-specific changes in activity as a function of attended side, regardless of stimulus presence or absence. In agreement with previous visual studies (Heinze et al. 1994; Hopfinger et al. 2000), unimodal visual effects were detected in superior and inferior occipital cortex, contralateral to the attended side. For the tactile modality, modulations specific to the attended hand were found in the postcentral gyrus. This confirms our previous PET results, showing that tactile selective attention can modulate activity in somatosensory cortex (Macaluso et al. 2000, 2002a) and extending these previous findings to highlight the role of preparatory activity in unimodal somatosensory cortex also.

Although for both modalities we were able to detect spatial attentional effects in both hemispheres, a certain degree of variability of the exact location of the peaks in the two hemispheres (i.e. apparent asymmetries) was also observed (see Fig. 2). One possible reason for this might lie in variability of the relation between functional organisation and structural landmarks in sensory specific cortices (Amunts et al. 2000), and/or in the consistency with which a given region will show spatial attentional modulation across subjects (Mangun et al. 1997).

In combination with these spatial attentional effects, we also found modulatory influences of intermodal attention (i.e. attention to one modality versus the other), when comparing brain responses to the bimodal-bilateral stimulation under conditions of visual attention versus tactile attention, and vice versa. These consisted in increased activity in occipital visual areas when vision was relevant, and in the parietal operculum (possibly in correspondence with the secondary somatosensory cortex: SII) when touch was relevant. For the activation in visual cortex there was an overlap between spatial attentional effects and intermodal effects. As a result of this, activity in visual cortex was maximal for attention to the contralateral hemifield in attend-vision blocks, despite the presence of multimodal spatial effects in some occipital areas (see also Macaluso et al. 2002a, for further discussion of this). Unlike the spatial attentional effects, intermodal effects appeared to be dependent upon the presence of the bimodal-bilateral stimulation, hence their nature did not appear to be preparatory. However, it must be noted that while spatial cues were delivered on a trial-by-trial basis, the relevant modality remained unchanged throughout each scanning block. It is therefore possible that preparatory effects of intermodal attention were sustained rather than transient, thus eluding detection in our analyses.

Another important comparison in the present design concerned activations associated with the attention-directing cues, but that were not specific for attention to one or the other side. These were revealed by comparing activity during the attention-directing cues (cue-only trials) versus baseline control tones that informed the subjects that no peripheral stimulation would be presented. Note that the identity of the three cues (attend left, attend right and control) was counterbalanced across subjects, and there were no visual or tactile stimuli or responses for all these conditions, so that no trivial sensory or motor confounds should affect this comparison. It revealed activation of a network of frontoparietal areas including posterior parietal cortex, premotor and prefrontal cortices and inferior parietal lobule. However, when additional criteria were included to ensure that activation was present for each of the four attention-directing cues (i.e. attend left or right in vision or touch; see Results section) only superior premotor areas and the left inferior parietal lobule remained significant on our conservative criteria of corrected P values. Thus, these areas were activated independently of attended side, and also showed a multimodal role in the present spatial attention task. The finding of "cue-related" activation in frontoparietal areas fits with recent results from purely visual tasks (Kastner et al. 1999; Hopfinger et al. 2000), but here we demonstrate the multimodal nature of these preparatory processes for the first time.

The activation of frontoparietal structure in tasks of visuospatial attention has often been associated with the notion of an attention-control network (Mesulam 1981, 1998; Gitelman et al. 1999, as described in our Introduction). Recently, the observation that these areas can be activated during presentation of attention-directing cues has been linked to the concomitant finding of spatially specific preparatory activity in visual areas. In particular, it has been suggested that one possible role of an

attention-control network is to bias activity in early visual regions (Kastner et al. 1999; Hopfinger et al. 2000; see also Corbetta and Shulman 2002).

Our present findings appear consistent with such proposals while extending them to a multimodal context. In accord with previous visual studies we show both spatially specific attentional modulations that precede presentation of peripheral targets (baseline shifts), and we also observe activation of frontoparietal structures by the attention-directing cues. Unlike previous studies, we additionally demonstrate the multimodal nature of these processes. In particular, the inferior parietal lobule and superior premotor areas activated independently of attended side and of relevant modality, while a region in the intraparietal sulcus, plus the lateral occipital gyrus, were modulated according to the attended location but irrespective of modality. Several other sources of evidence (see, for example, Farah et al. 1989; Mesulam 1998; Downar et al. 2000; Macaluso and Driver 2001; Eimer et al. 2002) likewise support the suggestion that frontoparietal areas might be involved in controlling the direction of attention across sensory modalities.

The present finding of preparatory activity in occipital visual cortex during tactile discrimination (see Fig. 3B), in conjunction with the activation of a common, multimodal network of frontoparietal areas, provides new information for understanding the possible significance of crossmodal effects in unimodal visual areas (Macaluso et al. 2000, 2002a). As already discussed above, purely visual studies have suggested that high-level structures in parietal (and frontal) cortex might bias activity in lower-level sensory-specific areas (Kastner et al. 1999; Hopfinger et al. 2000). This increased baseline activity might then facilitate processing of incoming sensory input (Chawla et al. 1999). The present finding that frontoparietal regions appear to be involved in directing attention following spatially informative cues, irrespective of sensory modality (see Fig. 4), suggests that anticipatory spatial biases may stem from multimodal brain areas, and thus come to influence sensory areas for multiple modalities even when only one is currently task-relevant. Thus, biasing influences originating from multimodal attentional control structures might produce spatially specific modulatory signals to influence lower-level sensory-specific areas, effectively relaying multimodal signals between unimodal areas. This could lead to the observed crossmodal effects in unimodal areas, providing an integrated system for the representation of space across sensory modalities. Such a system would boost processing of information arising from the attended location, irrespective of the currently attended modality (see also Driver and Spence 2000; Eimer and Driver 2000; Macaluso and Driver 2001).

In conclusion, the present study found both unimodal and multimodal effects of spatial selective attention to one versus the other side of space. Critically, the inclusion of cue-only trials enabled us to demonstrate that both the unimodal and the multimodal spatial effects could occur even in the absence of any visuotactile peripheral stimulation for discrimination. This implicates preparatory changes of baseline activity in spatial covert attention, at the level of both unimodal and multimodal processes. Moreover, the finding of multimodal preparatory activity in a frontoparietal network previously associated with control of visuospatial attention, suggests that this network may mediate the allocation of spatial attentional resources across sensory modalities.

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