

Multisensory stimulation with or without saccades: fMRI evidence for crossmodal effects on sensory-specific cortices that reflect multisensory location-congruence rather than task-relevance

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During covert attention to peripheral visual targets, presenting a concurrent tactile stimulus at the same location as a visual target can boost neural responses to it, even in sensory-specific occipital areas. Here, we examined any such crossmodal spatial-congruence effects in the context of overt spatial orienting, when saccadic eye-movements were directed to each peripheral target or central fixation maintained. In addition, we tested whether crossmodal spatial-congruence effects depend on the task-relevance of visual or tactile stimuli. On each trial, subjects received spatially congruent (same location) or incongruent (opposite hemifields) visuo-tactile stimulation. In different blocks, they made saccades either to the location of each visual stimulus, or to the location of each tactile stimulus; or else passively received the multisensory stimulation. Activity in visual extrastriate areas and in somatosensory parietal operculum was modulated by spatial congruence of the multisensory stimulation, with stronger activations when concurrent visual and tactile stimuli were both delivered at the same contralateral location. Critically, lateral occipital cortex and parietal operculum showed such crossmodal spatial effects irrespective of which modality was task relevant; and also of whether the stimuli were used to guide eye-movements or were just passively received. These results reveal crossmodal spatial-congruence effects upon visual and somatosensory sensory-specific areas that are relatively 'automatic', determined by the spatial relation of multisensory input rather than by its task-relevance.

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Introduction

Events and objects in the external world can produce multisensory signals that the brain registers via several distinct sensory

modalities. The signals for each sensory modality will initially be processed in anatomically distant cortical brain areas. But to achieve optimal behavior and produce appropriate responses, signals in different modalities that relate to a single event or object in the external world will often have to be integrated (Stein and Meredith, 1993). Many different factors are known to play a role in multisensory integration, such as the location of the sources (Meredith and Stein, 1996) and the relative timings of multisensory signals (Meredith et al., 1987). On the spatial aspects, many behavioral studies have now demonstrated that the relative location of two stimuli in different sensory modalities can affect performance. For example, in the case of crossmodal spatial effects between vision and touch, Spence et al. (1998) showed that tactile stimulation on one hand can improve judgement of visual targets presented near to the stimulated hand, compared to visual targets presented near to the opposite hand (see also Driver and Spence, 1998; McDonald et al., 2000). Electro-physiological studies in animals have demonstrated the existence of multisensory neurons that can respond to stimuli in more than one modality (Bruce et al., 1981; Duhamel et al., 1998; Graziano and Gross, 1995). Critically, the activity of some of these neurons appears to reflect temporal and spatial relations between multisensory stimuli in the external world, for example, showing modulation of responses according to relative position of the unimodal sources in space (e.g., under- or over-additive responses to multisensory versus unimodal inputs; Meredith and Stein, 1986a,b; Stein and Meredith, 1993).

Some human neuroimaging studies have sought to identify candidate multisensory regions in the human brain. One approach has been to stimulate one or other modality at a time, and analyse for areas that respond not just to one modality but to several or to all. This approach has revealed multimodal responses in several brain areas, including intraparietal sulcus, inferior parietal cortex, superior temporal sulcus and premotor regions (Bremmer et al., 2001; Macaluso and Driver, 2001), in agreement with the single cell literature reporting multimodal neurons in these regions (Bruce et al., 1981; Duhamel et al., 1998; Graziano and Gross, 1995). To

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date, relatively few human neuroimaging studies with combined multisensory stimulation have shown supra-additive responses (i.e., greater than the combination of the responses to each modality alone in such regions; though see Calvert et al., 2000, for one example).

Several studies have manipulated the spatial congruence of concurrent bimodal stimuli (i.e., unimodal sources at the same versus different locations), but instead of observing crossmodal effects primarily in heteromodal association cortices, have instead reported crossmodal modulations for spatially congruent multisensory stimulation arising within what would traditionally be regarded as unimodal, sensory-specific cortices (Macaluso et al., 2000b, 2002a; see also Misaki et al., 2002). This implies that spatial multisensory interactions may not only involve brain areas traditionally considered to be heteromodal, but may also affect sensory-specific cortex (see Spence and Driver, 2004, for reviews and discussion).

Macaluso et al. (2000b) presented subjects with left or right visual targets for covert attention and detection (i.e., without any overt orienting) during fMRI. Unpredictably, on some trials, a task-irrelevant tactile stimulation was delivered either at the position of the visual target or in the opposite hemifield. The results showed that combining visual and tactile stimuli at the same location (bimodal stimulation that was ‘congruent’ in this way) resulted in increased activity in occipital cortex contralateral to the stimulated side. When the visual target and the task-irrelevant tactile stimulation were delivered in opposite hemifields, this amplification did not occur, demonstrating the spatial nature of this crossmodal effect upon unimodal visual cortex (see also Macaluso et al., 2002a).

Crossmodal spatial congruence not only affects perceptual judgments in covert spatial attention tasks (e.g., McDonald et al., 2000; Spence et al., 1998), but can also influence overt spatial orienting, such as saccades. For example, Diederich et al. (2003) measured the effect of task-irrelevant tactile stimuli on saccadic reaction times (RT) to visual targets. Tactile stimulation to a hand placed in the same hemifield as the visual target resulted in faster saccadic RTs, compared to tactile stimuli to the hand placed in the opposite visual hemifield (see also Amlot et al., 2003). Rorden et al. (2002) provided further behavioral evidence suggesting possible links between crossmodal effects observed during covert orienting tasks and those reported during overt saccadic tasks. In their study, participants performed leftward or rightward saccades depending on the position of a peripheral visual cue. After the visual onset, but before initiation of the saccade, a task-relevant tactile target was presented either at the location of the visual target (congruent spatial configuration) or in the opposite hemifield (incongruent configuration). The task of the subject was to saccade toward the visual cue, and then perform a perceptual discrimination regarding the tactile target (up/down judgement, thus judging a property orthogonal to target or saccadic side; see Spence and Driver, 1997). Again, the results showed that the spatially congruent situation (touch at the same location of the impending saccade) yielded better performance for the tactile judgement. This indicates a possible relationship between perceptual crossmodal enhancements typically observed in covert attention tasks, and facilitatory effects observed during overt saccadic tasks.

The aim of the present fMRI study was to investigate neural crossmodal spatial effects between vision and touch, now during presence (or absence) of overt saccadic spatial orienting, and also to determine the extent to which these may depend on the task-

relevance of either modality. On each trial here, subjects received concurrent bimodal visuo-tactile stimulation that was either spatially congruent (i.e., vision and touch at the same location) or spatially incongruent (with concurrent visual and tactile stimuli presented in opposite hemifields). In different fMRI scanning sessions, subjects were instructed either to saccade to the position of the visual stimulus (vision relevant, ignoring any tactile stimulus); or to saccade to the position of the tactile stimulus instead (touch relevant, now ignoring any visual stimulus); or to maintain central fixation and receive the stimuli passively (peripheral stimuli now task-irrelevant in both modalities). Comparing brain activity for spatially congruent versus spatially incongruent stimulation should reveal brain regions affected by crossmodal processes that depends on the relative position of concurrent multisensory stimuli (as found by Macaluso et al., 2000b, 2002a, for regions of visual cortex in a covert-attention visual detection task). Critically, the inclusion here of tasks requiring overt saccadic orienting (to visual or tactile stimuli), plus a passive control task that did not require any spatial orienting, should allow us to separate crossmodal spatial effects that depend solely on the spatial stimulus configuration, versus those that depend on the task-relevance of sensory information for guiding overt spatial orienting. Note that in the current paradigm the relevant modality (i.e., saccade to vision or saccade to touch) was blocked, and served only as a context to study spatial interactions between vision and touch. Thus, the brain activations of main interest reported here will reflect sensory interactions between vision and touch, rather than sensory-motor congruency effects per se.

Methods

Subjects

Eleven volunteers participated (7 males and 4 females). All but one were right-handed, with mean age of 23 years (range 18–32). After receiving an explanation of the procedures, subjects gave written informed consent, in a protocol approved by the Joint Ethics Committee of the Institute of Neurology and the National Hospital for Neurology and Neurosurgery.

Paradigm

Functional MRI data were acquired during presentation of four event types, under 3 types of instruction (i.e., 3 blocked task conditions). The four event-types were bimodal visuo-tactile stimulation organised according to a 2×2 factorial design, with the side of touch (left or right hand) and the side of vision (left or right visual hemifield) as crossed independent factors. Hence, for two event-types, the bimodal visuo-tactile stimulation was spatially *congruent* in location (touch and vision on the same side, either both left or both right), and for the other two types, the stimulation was spatially *incongruent* in location (with stimuli in the two modalities located in opposite hemifields; visual on left and tactile on right, or vice-versa). The order of these four event-types was randomised and unpredictable.

These four events were presented under 3 types of instructions (blocked tasks): saccade to the location of the tactile stimulus; saccade to the location of the visual stimulus; or maintain central fixation (i.e., do not respond to any of the stimuli). The three different tasks were presented in separate fMRI scanning sessions, with the instruction regarding the current task given verbally before

the start of each session, and eye-tracking implemented (see below) to confirm adherence to the task.

Stimuli and task

Subjects lay in the scanner with each hand resting on a plastic support placed on top of the RF-coil. Each hand rested on the corresponding side and on each side there was an LED to present visual stimuli, and a piezoelectric component (T220-H3BS-304, Piezo Systems Inc., Cambridge, USA) to deliver unseen and inaudible tactile stimulation to the index finger. To avoid the transmission of any vibration from the piezoelectric device to its support or the RF-coil, four MR-compatible springs were placed between each tactile device and the coil. This ensured that the activation of the vibrators did not result in any acoustical stimulation, which could otherwise have arisen because of vibrations being transmitted between various parts of the apparatus. Between this apparatus and the subject's eyes there was an opaque screen so that subjects could not see either their hands or the LEDs when unilluminated (the latter became visible only when illuminated). The LEDs were placed at approximately 24° visual angle to left or right of the central midline and were visible with both eyes. The tactile stimulators and index fingers were located immediately behind the LEDs. This allowed us to deliver visual and tactile stimuli in close spatial correspondence when both stimuli were on the same side ('congruent'). A cross drawn on the opaque screen served as a central fixation point. In addition, a 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).

On each trial, concurrent bimodal visuo-tactile stimulation was presented for 50 ms. This stimulation could be either spatially *congruent* (both stimuli at the same location) or *incongruent* (again concurrent stimulation of vision and touch, but now in the two opposite hemifields). According to the instruction (current task, blocked), the subject either performed a saccade to the position of the unseen tactile target (ignoring any visual stimulus), or performed a saccade to the position of the visual target (ignoring any tactile stimulus) or simply maintained central fixation (thus not responding to either type of stimulus). Because the stimulus sequence was randomised, on each trial, the saccade direction was unpredictable until presentation of the stimulation for that trial. Moreover, the short time of target presentation (50 ms) and the fact that the hands and unilluminated LEDs were not visible to the subject meant that by the time the saccade was initiated, the target position for the saccade was no longer marked in any way (hence, there was no trial-type-specific stimulation still visible to undergo a shift in retinal position due to the saccade). After the saccade to the target location, subjects made an eye-movement back to central fixation, so the current design cannot discriminate between brain activity for leftward versus rightward saccades. However, this would be beyond the aim of the present study, which sought instead to measure brain activity for sensory stimulation (vision and touch) at the same versus different locations, under different task conditions.

The mean inter-trial interval was 4 s (range 3–5 s, with a uniform distribution). During each session, there were 60 trials, with 15 repetitions for each of the four trial-types (i.e., spatially congruent visual–tactile stimulation on the left, spatially congruent on the right, touch on the left plus vision on the right, and touch on the right plus vision on the left). Each subject underwent six

separate scanning sessions (each lasting approximately 4.5 min), thus repeating each of the three tasks twice (saccade to touch, saccade to vision, or passive central fixation). All three tasks were presented once in the first 3 fMRI-sessions, and once in the second three fMRI-sessions, but in a different order. Across subjects, all six permutations of the three tasks were used, thus counterbalancing the order of task presentation within and across subjects.

Image acquisition

Functional images were acquired with a 1.5-T SONATA MRI scanner (Siemens, Erlangen, Germany). BOLD (blood oxygenation level dependent) contrast was obtained using echo-planar T2* weighted imaging (EPI). The acquisition of 32 transverse slices gave coverage of the whole cerebral cortex. Repetition time was 2.88 s. The in-plane resolution was 3 × 3 mm.

Data analysis

Data were analysed with SPM2 (<http://www.fil.ion.ucl.ac.uk>). For each subject, the 546 volumes were realigned with the first volume, and acquisition timing was corrected using the middle slice as reference (Henson et al., 1999). To allow inter-subject analysis, images were normalised to the Montreal Neurological Institute (MNI) standard space (Collins et al., 1994), using the mean of the 546 functional images. All images were smoothed using an 8 mm isotropic Gaussian kernel.

Statistical inference was based on a random effects approach (Holmes and Friston, 1998). This comprised two steps. First, for each subject, the data were best-fitted at every voxel using a linear combination of effects of interest, plus confounds. The effects of interest were the timing of the four event-types (given by crossing of the 2 stimulus factors: side of touch and side of vision), in each of the six sessions (two sessions for each of the three tasks). Trials containing any incorrect saccadic behaviour were modeled as confounds (see below). All event-types were convolved with the SPM2 standard haemodynamic response function. Linear compounds (contrasts) were then used to determine the main effect of position of the tactile stimulus and the main effect of position of the visual stimulus separately for each of the three tasks. This led to the creation of six contrast-images for each subject. Note that in the present design, these main effects of stimulus side for each modality are mathematically equivalent to the *interactions* between stimulus side of one modality and the spatial congruence of the multimodal stimulation (see below). Furthermore, these contrasts reflect *differential* effects (e.g., touch on the left versus touch on the right, during central fixation), and therefore any effect specific to just subject or session will automatically be removed from further analyses. These contrast-images then underwent the second step, which comprised an ANOVA that modeled the mean of each of the six differential effects (see below for further details). Finally, linear compounds were used to compare these effects, now using between-subjects variance (rather than between scans). Correction for non-sphericity (Friston et al., 2002) was used to account for possible differences in error variance across conditions and any non-independent error terms for the repeated measures.

Our main analyses then aimed to identify brain regions affected by the relative position of the tactile and visual stimuli (*congruent*: same location, versus *incongruent*: opposite side), and to assess whether any such crossmodal spatial effect was common to all

three types of task or was instead specific to just some or one of them. To reveal any modulation of brain responses when touch and vision were presented at the *same contralateral location* (as previously reported in Macaluso et al., 2000b, 2002a), we tested for a conjoint main effect of side of touch and main effect of side of vision (Friston et al., 1999; Price and Friston, 1997). Note that for this purpose, our basic 2×2 stimulus design (with side of touch and side of vision as independent factors) can be redefined as a 2×2 design with side of touch (or equivalently, side of vision) and *spatial congruence* of the bimodal visuo-tactile stimulation as independent factors. Accordingly, the test conducted for conjoint main effects of side for the two modalities is mathematically identical to testing for the effect of side for one modality (touch or vision) in presence of an interaction between side of that modality and spatial congruence of the bimodal stimulation. Therefore, this will specifically highlight brain areas where the effect of side for one modality was larger when the other modality was on the same side, compared with the other modality being on the opposite side, as can be predicted given the prior results of Macaluso et al. (2000b, 2002a).

To assess whether any such crossmodal–spatial modulation was *common* to all three tasks, we again used conjunction analyses (Friston et al., 1999; Price and Friston, 1997) that included the main effects of side of touch and main effect of side of vision for all three tasks. These conjunctions between all six effects modeled at the second-level (random effects) analysis will reveal brain regions that show specifically crossmodal spatial effects of the predicted type (larger effect of stimulus side for crossmodally congruent stimulation), irrespectively of the current task. Conversely, to test for crossmodal spatial modulations that were *specific* for one (or two) of the three tasks, we tested for the conjunction of the two main effects of side within one (or two) task(s) only, with the additional constraint that this conjoint effect had to be larger during the task(s) of interest compared with the other task(s). For this additional constraint (which can only make our analyses more conservative, since it is additional to the main contrast), a threshold of P -uncorr. = 0.01 was adopted.

For all comparisons corrected P values were assessed using a small volume correction procedure (Worsley et al., 1996). Given our specific interest in any crossmodal spatial-congruence effects upon sensory-specific cortex (in line with the previous results of Macaluso et al., 2000a, 2002b), the search volumes consisted of somatosensory and visual areas contralateral to the location of the critical spatially-congruent bimodal stimulation. These regions were highlighted using the main effects of side (left or right) for one or the other modality across all three tasks. As an initial definition of such regions, correction at the cluster-level was used (P -corr = 0.05, cluster size set by thresholding the SPM-maps at P -uncorrected = 0.001 for the voxel level). For the particular main effect of right visual stimulation, no cluster survived this cluster-level correction procedure (P -corr = 0.05), so for completeness, we dropped the constraint concerning correction for multiple comparisons, thus considering only the voxel-level threshold (P -uncorrected = 0.001 as before). Note that for this particular case of seeking left occipital regions responding to right visual stimulation, the issue of correction for multiple comparison is moot because of the innumerable prior studies showing contralateral occipital responses for lateralised visual stimulation. The location and the extent of the volumes of interest are reported in Table 1 and Fig. 2.

Table 1

Effect of the side of the sensory stimulation for touch and vision

Anatomical area	Co-ordinates	Z values	Cluster size	P values
<i>LEFT minus right SOMATOSENSORY stimulation</i>				
Right post-central gyrus	44 –30 62	5.4	246	0.002
Right parietal operculum	42 –24 4	4.4	179	0.009
<i>RIGHT minus left SOMATOSENSORY stimulation</i>				
Left post-central gyrus	–48 –22 56	4.9	177	0.010
Left parietal operculum	–64 –22 18	4.5	509	<0.001
<i>LEFT minus right VISUAL stimulation</i>				
Right middle occipital gyrus	46 –68 8	5.8	2649	<0.001
Right superior occipital gyrus	22 –86 36	6.2		
Right lingual/fusiform gyrus	22 –68 14	5.6		
Right striate cortex	12 –78 6	4.7	195	0.006
<i>RIGHT minus left VISUAL stimulation</i>				
Left middle occipital gyrus	–50 –74 0	3.7	82	0.184
Left superior occipital gyrus	–14 –84 24	4.0	73	0.248
Left lingual/fusiform gyrus	–34 –62 –10	4.0	43	0.625
Left intraparietal sulcus	–24 –36 50	4.5	102	0.096
Left inferior premotor cortex	–50 8 28	3.7	57	0.415

Anatomic areas, Talairach co-ordinates of the maxima within each cluster, Z values, cluster sizes and corrected P values of the regions that showed a main effect of the side of the sensory stimulation. For each modality, we directly compared stimulation of one versus the other hemifield, irrespectively of spatial congruence and current task. For the main effect of right minus left visual stimulation, none of the clusters survived correction for multiple comparisons, but the pattern of activation appeared convincingly lateralised to the contralateral occipital cortex. Coordinates in millimeters: x , distance to right (+) or left (–) of the mid-sagittal plane; y , distance anterior (+) or posterior (–) to vertical plane through anterior commissure; z , distance above (+) or below (–) intercommissural (AC–PC) line.

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. Eye-position data were analysed for 10 out of 11 subjects, for whom reliable eye-position was available throughout all imaging sessions. Eye-position traces were examined in a 2100-ms window, beginning 100 ms prior to stimulus onset. For trials requiring central fixation (central fixation task), losses of fixation were identified using the derivative of the horizontal eye-position trace (i.e., saccade velocity). When this exceeded $50^\circ/s$, the trial was considered a non-fixation trial and was modeled separately in the fMRI analysis as an erroneous saccade (exclusion rate: 20.8%). Note that the use of a velocity criterion, rather than eye-position, should make our exclusion

procedure sensitive also to small amplitude eye-movements (even micro-saccades), and was thus conservative. For trials that did require shifts of gaze direction (i.e., saccades to tactile or saccades to visual targets), we identified trials where either the subject made a saccade to the wrong side (e.g., saccade to the visual target during a spatially-incongruent trial under instructions to saccade to touch) or did not perform any saccade at all. Again, these trials were modeled separately in the fMRI analysis. Their rates were: 5.8% wrong saccade direction during tactile task, 1% wrong saccade direction during the visual task and overall 0.9% of no-response trials across the two saccadic tasks. For trials requiring saccadic responses, eye-velocity was used to compute saccadic reaction time, here defined as the time between target onset and eye-velocity first exceeding 50°/s. Note that saccade-error trials during spatially incongruent stimulation (5.8% during saccade to touch), might in principle be associated with interesting brain processes (e.g., failure to suppress some stimulus-driven saccadic mechanisms). However, we could not assess this in our imaging data because there were too few of these error-trials. Future studies may use weaker stimuli in the relevant modality and more salient distracters in order to produce more saccades to the wrong position, thus allowing for the analysis of brain activity associated with this potentially interesting type of error trial (Amador et al., 2004; Curtis and D'Esposito, 2003).

Results

Behavioral performance

Fig. 1 shows horizontal eye-position traces for the 10/11 subjects for whom reliable eye-tracking recording was available. The traces are divided according to the current task (saccade to touch, saccade to vision, or central fixation) and the spatial congruence of the bimodal stimulation (left congruent trials in red, right congruent trials in green and spatially incongruent trials in black). Generally subjects performed well, with only 5.8% wrong saccade direction during the tactile task, and 1% wrong saccade direction during the

visual task. Analysis of saccadic reaction times revealed: (a) a main effect of spatial congruency ($F(9,1) = 17.03$, $P = 0.003$), with faster saccades for spatially congruent trials compared to incongruent trials (mean RT: congruent = 325 ms, incongruent = 361 ms), consistent with the prior behavioral studies (Amlot et al., 2003; Diederich et al., 2003); (b) a main effect of task ($F(9,1) = 26.69$, $P = 0.001$), with saccades to visual targets faster than saccades to tactile targets (mean RT: vision = 311 ms, touch = 374 ms), again consistent with prior behavioral studies; (c) interaction between spatial congruency and task ($F(9,1) = 11.34$, $P = 0.008$), with larger congruency effects for the tactile task (congruent minus incongruent: touch = 63 ms, vision = 10 ms); and (d) an overall effect of the position of the tactile stimulus ($F(9,1) = 11.71$, $P = 0.008$), with overall saccadic RTs faster when touch was on the right hand. This marginally interacted with the current task also ($F(1,9) = 4.03$, $P = 0.076$), indicating that it may have been driven primarily by faster RTs for saccades to the right hand compared to the left hand, when touch was relevant. Overall, saccadic RT were slower than those reported in previous behavioral studies performed outside the scanner (e.g., Diederich et al., 2003). One possible explanation for this relates to the demanding environment in which subjects had to perform the task. Unlike behavioral studies, during fMRI, the subject had to lay still in a dark and noisy surrounding, often finding the MR-scanning session rather strenuous. However, we must note that there is no reason to believe that the fMRI-environment should have any differential effect for the different conditions. Moreover, the RTs reported here are consistent with the saccadic RTs we previously measured with a similar experimental set-up (Macaluso et al., 2003). In summary, the behavioral data showed the expected effect of spatial congruency, with faster saccades for spatially congruent bimodal stimulations, and also showed that saccades to visual targets were generally faster than saccades to tactile targets, as would be expected.

Imaging data

The analysis of the fMRI data aimed to highlight brain areas where activity was higher during *spatially congruent* bimodal stimulation (i.e., vision and touch at the same location) compared to

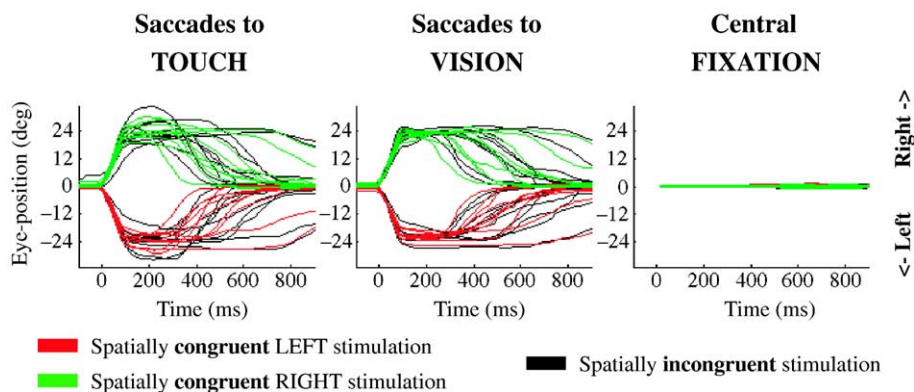


Fig. 1. Eye-position for 10 out of 11 participating subjects for whom this was available. Horizontal eye-position traces for each subject are plotted according to the task performed (left panel: saccade to touch; central panel: saccade to vision; right panel: central fixation). In each panel traces for spatially congruent trials are in red (both vision and touch on the left side) and in green (both vision and touch on the right side). Traces in black relate to spatially incongruent trials and these all show correct saccadic directions: for example, traces deflecting toward the right during the tactile task refer to trials when touch was on the right and vision was on the left. Eye-position traces are time-locked to the saccade-onset for the saccade to touch and saccade to vision tasks, and to the time of the stimulus-onset for the central fixation trials (rightmost plot). For each subject, as expected the plots show a sharp change in eye-position during the saccade tasks (left and central panels), but no systematic change for trials requiring central fixation (rightmost panel), once the few trials containing detected losses of fixation were removed (see Methods). All traces were adjusted using 100 ms pre-stimulus baseline and no further filtering was used. The position of the peripheral stimulation was approximately 24°.

spatially incongruent trials (vision and touch in opposite hemifields). Critically, we further assessed this in relation to whether the visual or the tactile stimuli served as task-relevant targets for saccades, or only passive central fixation was required. Given our previous results (Macaluso et al., 2000b, 2002a), we were particularly interested in spatially-specific effects whereby multimodal spatial congruence affects spatial representations in contralateral sensory-specific cortices, as we had previously shown for visual occipital cortex in a covert-attention visual detection task.

Therefore, our analyses first identified brain regions that show differential activity depending on stimulus position. Table 1 and Fig. 2 report these spatially-specific effects for tactile and visual stimulation. Lateralised tactile stimulation to the left or to the right hand (irrespective of location of the visual stimulus and the current task) revealed, as expected, activation in the contralateral post-central gyrus, plus a region comprising the parietal operculum and the posterior part of the insulae (see Table 1 and Fig. 2A). In the left hemisphere, the opercular cluster extended dorsally to include a region in the inferior part of the post-central gyrus (see Fig. 2A left panel). For visual stimulation, contralateral effects were observed in ventral, lateral and dorsal occipital cortex (see Table 1 and Fig. 2B). While in the right hemisphere, these effects were statistically robust for all three regions, in the left hemisphere, none

of the clusters survived full correction for multiple comparisons. However, dropping the constraint regarding cluster-level correction for multiple comparisons, while still maintaining the same voxel-level threshold (i.e., P -uncorr. = 0.001), revealed a specific pattern of primarily left occipital–parietal activation with all activations contralateral to the stimulated side (see Fig. 2B leftmost image). Thus, overall the lateralised tactile or visual stimulation showed the expected contralateral activations of sensory-specific cortices in postcentral and occipital regions, respectively (see Fig. 2). Subsequent analyses tested whether these spatially specific effects (i.e., higher activation for contralateral versus ipsilateral stimulation) were modulated by the spatial congruency of the bimodal stimulation (touch and vision stimulated in either the same or opposite hemifields).

First, we tested for any such spatial congruency effects that were *common* to all three types of tasks (saccade to touch, saccade to vision, and central fixation). Importantly, this showed that activity in both extrastriate visual cortex (lateral occipital) and somatosensory cortex in the parietal operculum were affected by the spatial congruency of the bimodal stimulation, irrespective of current task (see Table 2). Fig. 3 shows the anatomical location and the pattern of activation for these regions (see also Fig. 5). The signal plots show that the effect of stimulus location (with higher

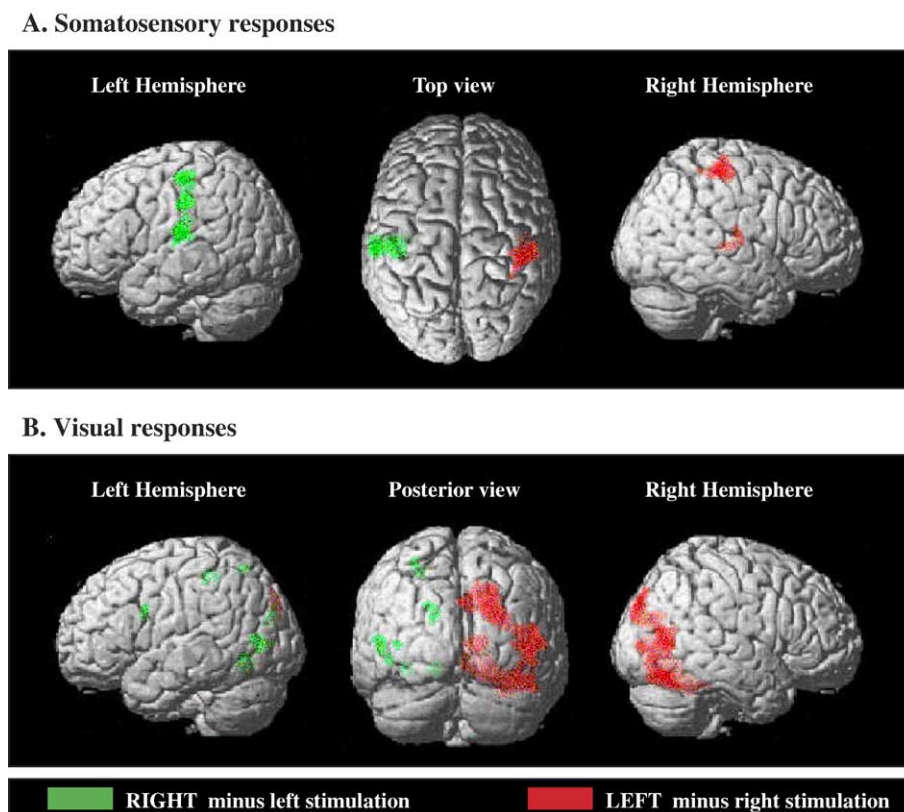


Fig. 2. Main effect of stimulus position for touch and vision. (A) Somatosensory responses for left minus right (red) and right minus left (green) tactile stimulation, irrespective of side of vision and current task. (B) Effect of side of the visual stimuli (red: left minus right; green: right minus left). All clusters are rendered on the surface of the MNI brain template. These comparisons revealed the expected activation of sensory-specific cortices contralateral to the stimulated side and they were successively used as volumes of interest to assess any effects of crossmodal spatial congruence in contralaterally-responsive visual or tactile cortex (see Figs. 3 and 4). SPM thresholds are set to P -corr. = 0.05 at cluster level, except for the main effect of right versus left visual stimulation for which a cluster-level correction procedure had to be dropped to reveal the expected activation in left occipital cortex (in green). At this uncorrected threshold, a left frontal region also appeared to be active (see leftmost panel). However, this is reported for completeness only because this activation was not predicted on the basis of previous experiments (unlike the contralateral responses in left occipital cortex).

Table 2
Crossmodal spatial effects

Anatomical area	Co-ordinates	Z values	P values
<i>A. Crossmodal effects INDEPENDENT of current task</i>			
Right parietal operculum	46 –18 10	3.6	0.036
Left parietal operculum	–40 –16 16	2.6	0.552
Right middle occipital gyrus	40 –60 16	3.9	0.088
Left middle occipital gyrus	–46 –62 –4	3.6	0.051
Right superior occipital gyrus	24 –82 38	4.3	0.025
<i>B. Crossmodal effects observed only during the FIXATION task</i>			
Right lingual/fusiform gyrus	22 –54 –10	3.1	0.385
Left lingual/fusiform gyrus	–32 –64 –12	4.7	<0.001

Anatomic areas, Talairach co-ordinates, Z values and corrected P values for the regions that showed crossmodal spatial effects. (A) Areas showing crossmodal effects during all three types of task (saccade to touch, saccade to vision and central fixation). (B) Areas showing crossmodal spatial effects only during the fixation task. All effects were contralateral to the location of the spatially congruent bimodal stimulation (touch and vision on the same side). Coordinates in millimeters: x, distance to right (+) or left (–) of the mid-sagittal plane; y, distance anterior (+) or posterior (–) to vertical plane through anterior commissure; z, distance above (+) or below (–) intercommissural (AC–PC) line.

activity for stimulation of the contralateral side) was significantly larger when the concurrent multisensory stimuli were at the same-contralateral-location compared to when one stimulus was contralateral and the other ipsilateral. In all plots, the effect of stimulus side specific to congruent multimodal stimulation is represented by the difference between the first two bars (shown in red and green), which is significantly reduced for the other two bars (gray). For clusters in the right hemisphere, activity was higher during left-hemifield congruent stimulation (red bars) compared to right-hemifield (green bars). The reverse applied for clusters in the left hemisphere, now with bar 2 (both stimuli on the right, in green) larger than bar 1 (both stimuli on the left, in red).

The critical multimodal spatial effect is represented by the fact that these differences (bars 1 and 2, red and green) cannot be explained by any difference observed during the spatially incongruent stimulation (bars 3 and 4, gray). For example, the signal plot for right occipital cortex during the saccade task (central plot in the first row of Fig. 3A) shows as expected that this region responded more to left than right visual stimuli. While this can be observed to some extent when touch was in a spatially incongruent configuration (compare bar 4 versus bar 3, for this plot), this difference was larger when touch was also on the left side (bar 1 minus bar 2; congruent trials). Thus, the lateralised visual responses in this region were modulated by the position of the tactile stimulation. Importantly, this effect was observed *irrespective of task*, that is both when vision was relevant (saccade to vision, central plot in top row of Fig. 3A), but also when vision was irrelevant (saccade to touch, plot on the left of Fig. 3A top row); and also when subjects simply maintained central fixation (plot on the right). This indicates that crossmodal-congruency effects in this region of occipital visual cortex are not dependent on the behavioral relevance of the contralateral visual location, nor on that location being a target for a saccadic eye-movement.

Analogous patterns of activation were found in a medial region of the parietal operculum (see Fig. 3B). This region showed a larger effect related to the position of the tactile stimulus (higher activity for touch at the contralateral versus ipsilateral side) when the visual stimulus was also at the contralateral side. For the right

hemisphere, the critical crossmodal spatial modulation can be seen by comparing the difference between bar 1 (in red) minus bar 2 (in green) to that for bar 3 minus bar 4. Again, the larger difference is found for the first two trial-types, indicating that effect of contralateral left somatosensory stimulation was larger when the concurrent visual stimulus was also on the left (spatially congruent condition), than when the visual stimulus was on the right. An analogous pattern of activation was observed in the left parietal operculum, but now with higher activity for spatially congruent bimodal stimulation on the right side, that is, activation again contralateral to the position of the spatially-congruent bimodal stimulation (green bars for the signal plots in the second row of Fig. 3B). These somatosensory regions were likewise modulated according to the relative position of tactile and visual stimuli *irrespective* of whether the visual or the tactile position was task relevant; and even when the stimuli were presented passively (central fixation condition, rightmost plots).

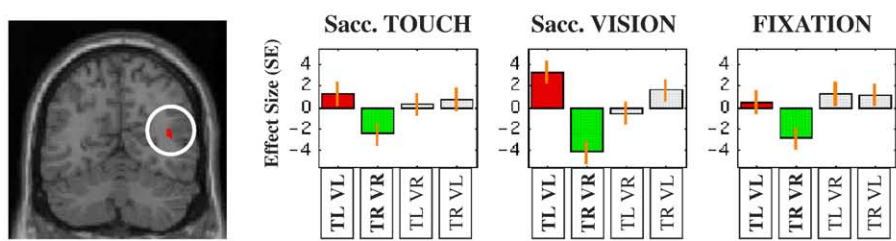
These results are summarised in Fig. 5, where the sizes of the modulatory effect of spatial congruence (vision and touch at the same location versus opposite sides) on contralateral responses are shown for all four regions (lateral occipital cortex and parietal operculum, in the two hemispheres). The modulatory effects are plotted separately for the three tasks (saccade to touch, saccade to vision and fixation) showing that for these four regions, the effect of spatial congruence was observed irrespective of task (the twelve leftmost bar-plots all have positive values). Thus, these data demonstrate that some visual regions (lateral occipital cortex) and also some somatosensory regions (parietal operculum) are modulated by the relative position of bimodal visuo-tactile stimuli (larger responses when both stimuli were at the contralateral location together, in a spatially-congruent arrangement); and that these crossmodal spatial effects do not simply reflect the behavioral relevance of one or the other modality, nor the stimulated location being the target for a saccade.

Further analyses assessed whether any region showed crossmodal spatial effects selectively during some tasks, but not during the others. The only area that showed a consistent pattern of activation in both hemispheres was the ventral occipital cortex, which showed crossmodal spatial effects only during central fixation (see Table 2). Anatomical location and signal plots for this region are shown in Fig. 4 (see also Fig. 5). The ventral occipital cortex showed higher activity for visual stimulation of the contralateral hemifield compared with ipsilateral visual stimulation, and this effect was selectively modulated by the position of the tactile stimulation only during central fixation. This can be seen in the rightmost plots of Fig. 4, where the difference between bar 1 and 2 (congruent conditions) cannot be explained by any difference between bar 3 and 4 (incongruent conditions). This was not the case during the saccade to touch tasks (leftmost plots in Fig. 4) nor during the saccade to vision task (central plots in Fig. 4), when the difference between left and right visual stimulation was similar in the crossmodally congruent and incongruent conditions. These effects are also summarised in Fig. 5 (last six bar-plots), showing that the spatial congruence of vision and touch resulted in higher contralateral responses (displayed as positive values in Fig. 5) only during fixation (white bar-plots). Thus, unlike the lateral occipital cortex (and parietal operculum), crossmodal effects in ventral occipital cortex were observed only when no overt spatial orienting took place, with the eyes maintained at fixation (see Fig. 5).

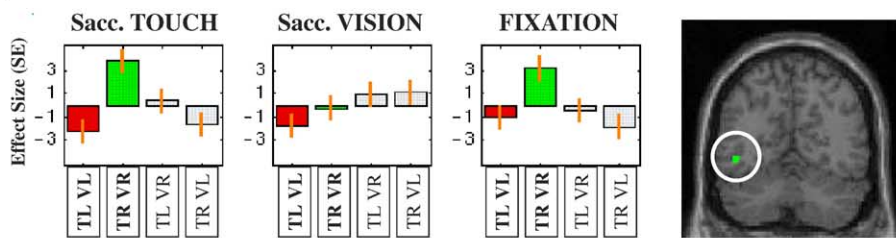
For completeness, we also tested for brain activation associated with spatially incongruent minus congruent trials. In particular, it

A. Visual regions: Lateral Occipital Cortex

RIGHT hemisphere: $x,y,z = 40 -60 16$

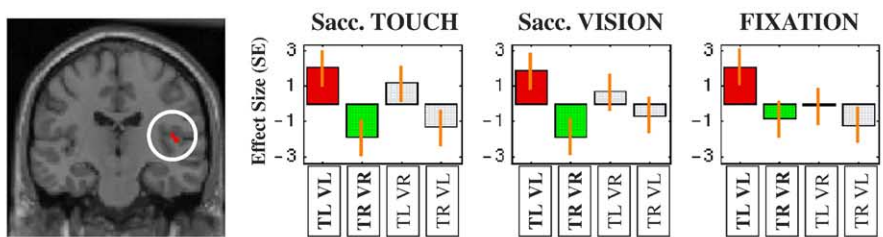


LEFT hemisphere: $x,y,z = -46 -62 -4$



B. Somatosensory regions: Parietal Operculum

RIGHT hemisphere: $x,y,z = 46 -18 10$



LEFT hemisphere: $x,y,z = -40 -16 16$

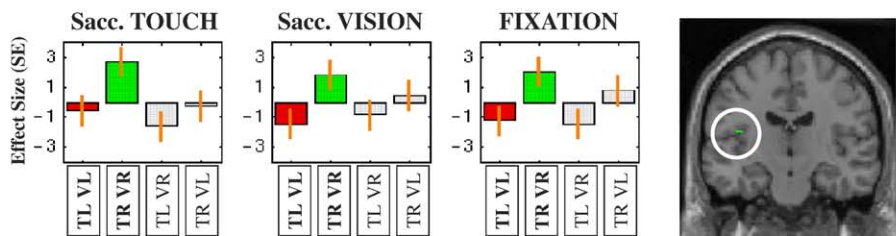
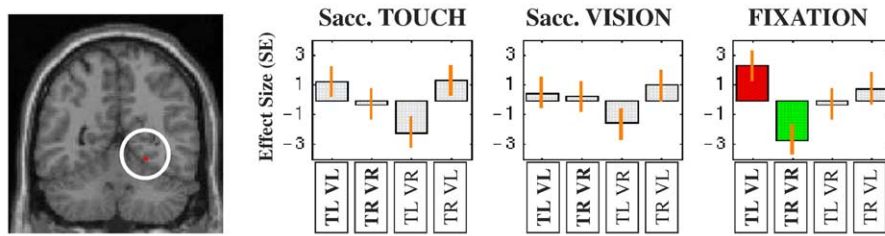


Fig. 3. Crossmodal spatial effects independent of current task. (A) Modulation of visual responses for bimodal visuo-tactile stimulation with both modalities at the *same* location on the contralateral side. In lateral occipital cortex, the effect of side in vision was larger when touch was at the same location as the visual stimulus (bar 1 and bar 2) than when touch was on the opposite side (bar 3 and bar 4). (B) Analogously, in the parietal operculum (a somatosensory region), the responses to contralateral tactile stimulation was larger when vision was also at the same-contralateral-location (compare bar 1 versus 2, and bar 3 versus bar 4, for all signal plots). All these effects were *contralateral* to the position of the spatially congruent multimodal stimulation and they were all observed irrespective of current task. The bars in color indicate the critical crossmodal spatial effect for *spatially congruent* trials. Note that for illustrative purposes here each plot shows the level of activity for each of the four trial-types, while statistical inference was based on a model focusing on the appropriate *differences* between conditions (see Methods). Note also that because all analyses considered “differences of differences” (i.e., interactions, or modulations), the activity plotted in this figure and Fig. 4 are mean-adjusted to have a sum of zero, and thus, the absolute level of activity for each condition is arbitrary. The critical multimodal spatial effect is represented by the fact that the activation related to the stimulus position during congruent stimulation (e.g., vision left minus vision right, bar 1 minus bar 2) is consistently larger than the same subtraction for spatially incongruent stimulation (e.g., bar 4 minus bar 3). All coronal sections are taken through the maxima and the effect sizes are expressed in standard error units (SE). For display purpose, SPM thresholds are set to P -uncorr = 0.01. (TL: touch left; TR: touch right; VL: vision left; VR: vision right).

Ventral occipital cortex

RIGHT hemisphere: $x,y,z = 22 -54 -10$



LEFT hemisphere: $x,y,z = -32 -64 -12$

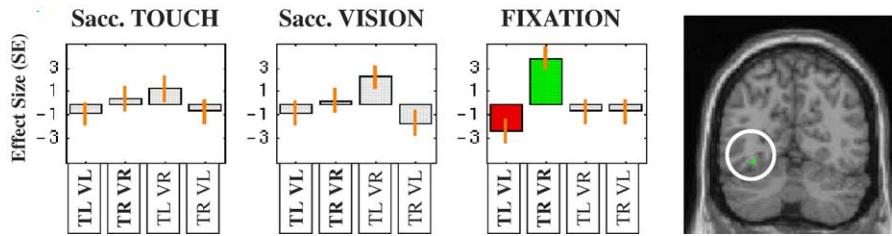


Fig. 4. Task-specific crossmodal spatial effects. This figure shows anatomical location and signal plots for the ventral occipital cortex, the only region where spatial crossmodal effects were observed only during the central fixation task. This can be observed in the rightmost plots of the two rows, where the difference between left and right visual stimulation was larger when touch and vision were at the same contralateral side (see red bar 1 and green bar 2), compared with trials when the two modalities were presented in opposite hemifields (bars 3 and 4). This modulatory effect of multimodal spatial congruence was not observed when subjects used the stimuli to direct saccadic eye-movements (see leftmost and central plots on both rows). All coronal sections are taken through the maxima and the effect sizes are expressed in standard error units (SE). For display purpose, SPM thresholds are set to $P\text{-uncorr} = 0.01$. (TL: touch left; TR: touch right; VL: vision left; VR: vision right).

might be suggested that potential conflict-monitoring areas (e.g., the anterior cingulate cortex; e.g., Van Veen et al., 2001) or areas involved in anti-saccades (e.g., supplementary frontal eye-field; Everling et al., 1998) might activate when subjects performed

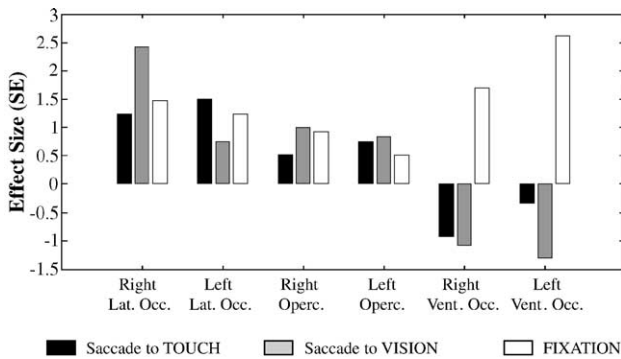


Fig. 5. Summary of all crossmodal enhancements for spatially congruent trials. This figure shows the size of the interaction between stimulus position (left versus right hemifield) and spatial congruence of the bimodal stimulation (same versus opposite side) for the areas also displayed in Figs. 3 and 4. Data are divided according to the task (saccade to touch, saccade to vision or fixation). Positive values indicate that the difference of brain activity for contralateral minus ipsilateral stimulation was larger when the two modalities were spatially congruent (both at same location) than when they were spatially incongruent (opposite sides), see also Figs. 3 and 4. Lateral occipital cortex and parietal operculum showed crossmodal spatial enhancements irrespective of task (all bar-plots show positive values), while ventral occipital cortex showed this modulation only during the fixation task (see white bar-plots for this region). (Occ.: Occipital cortex; Lat.: Lateral; Vent.: Ventral; Operc.: Parietal Operculum).

either of our saccade-tasks with spatially incongruent stimuli. Thus, we examined the pattern of activation for incongruent minus congruent trials in the two saccade tasks. This did not reveal any significant activation, when cluster-level correction for multiple comparison was used. When this constraint was dropped (while maintaining the voxel-level threshold at $P\text{-uncorr} = 0.001$), several voxels in frontal areas showed some activation, but none of these passed even this less conservative threshold for both tasks. The lack of activation specific to incongruent trials might be due to relatively little conflict being produced by them, and/or the fact that the task (saccade to vision or saccade to touch) was blocked in different sessions here. Accordingly, the selection of one or the other modality as the target for motor responses, possibly in frontal cortex, might have entail sustained activity during the whole fMRI session, which would not be detected with the current design.

Discussion

The present study investigated crossmodal spatial-congruence effects (with visual and tactile stimuli at the same location or opposite sides concurrently). It did so in the presence or absence of overt spatial saccadic orienting, and assessed the role of modality task-relevance (for saccadic targeting) on any such crossmodal effects. The fMRI results showed that activity in visual extrastriate areas and the parietal operculum was modulated by the spatial congruence of the bimodal stimulation, with larger responses when both the visual and tactile stimuli were delivered together at the same contralateral location (spatially congruent conditions). These crossmodal spatial effects were found in lateral occipital and parietal operculum regions irrespective of which modality was

currently task-relevant, and of whether the stimuli were used to guide eye-movements or were received passively. This suggests that crossmodal spatial effects in these sensory-specific (i.e., visual or tactile) areas relate to an automatic mechanism that depends predominantly on the spatial configuration of the multisensory stimuli, rather than on endogenous task-relevant factors (such as which modality had to be saccaded to; or indeed whether any saccade had to be initiated at all).

The present study used variations on a prototypical paradigm for studying crossmodal spatial interactions, where bimodal stimulation (here in vision and touch) is presented either in spatially congruent configurations (both stimuli at the same location) or in spatially incongruent configurations (here with vision and touch delivered in opposite hemifields). In agreement with our previous fMRI work (e.g., Macaluso et al., 2000b, 2002a), boosting of sensory responses was observed in occipital cortex contralateral to the hemifield where spatially congruent bimodal stimulation was presented (see Fig. 3A). This activation was located in the lateral occipital cortex here (see Fig. 3A). Previous imaging studies of visual-tactile interactions in a visual detection task without saccades (Macaluso et al., 2000b, 2002a) did not detect crossmodal effects at fully corrected significance in this specific occipital area, but in fact corresponding trends were observed just below statistical threshold in those studies for this region. Moreover, the same region did previously show spatially-specific crossmodal visual-tactile effects in tasks concerning endogenous covert spatial attention (Macaluso et al., 2000a, 2002b).

Here, we show for the first time that spatially specific crossmodal spatial-congruence effects (of multisensory stimulation at the same rather than opposite locations) can be observed also in the context of saccade tasks, when stimuli are used to guide spatially directed overt responses. These findings may accord with the notion that overt and covert spatial orienting might overlap to some extent, both at the level of brain activations (e.g., see Corbetta et al., 1998) and at the level of behavioral effects related to spatial orienting to multimodal stimuli (c.f. Diederich et al., 2003; Spence et al., 1998). The present paradigm further allowed us to investigate crossmodal spatial interactions when either touch was task-relevant (i.e., tactile position used to direct saccades, while ignoring any visual stimulus), or vision was relevant (i.e., saccade to vision, ignoring any tactile stimulus). The results showed that spatially-specific crossmodal modulation of responses in visual cortex did not depend on vision being behaviorally relevant, thus highlighting the automatic, stimulus-driven nature of these crossmodal effects. Such findings are in agreement with suggestions that crossmodal influences upon unimodal visual cortex elicited with this prototypical paradigm might be related to mechanisms of integration of spatial representations (see Macaluso and Driver, 2001; and also Technical Comments by McDonald et al., 2001; and Technical Response by Macaluso et al., 2001; on this issue). Macaluso et al. (2002b) also found that lateral visual cortex can be influenced by the currently attended location in a tactile task (when vision was task-irrelevant), while several ERP studies have demonstrated modulation of early, sensory-specific visual components according to the direction of tactile spatial attention (Eimer and Driver, 2000; Kennett et al., 2001). Thus, it appears that, regardless of the current task (e.g., endogenous or exogenous covert spatial attention, or with vision task-relevant or not in overt saccadic spatial orienting as here), the level of activity in occipital visual cortex can reflect not only task-

relevant visual processing but also spatial aspects involving other modalities, here touch.

Unlike previous studies that used similar paradigms (Macaluso et al., 2000b, 2002a), the present study was able to demonstrate crossmodal spatial effects also in *somatosensory* cortex for the first time. Analogously to the effects in the lateral occipital cortex, crossmodal amplification was again observed in the hemisphere contralateral to the hemifield where spatially congruent visual and tactile stimuli were presented together, in the parietal operculum. This may correspond to secondary somatosensory cortex (Burton et al., 1993). Note that while some studies have demonstrated somatotopic organisation of the secondary somatosensory cortex within the parietal operculum (e.g., Ruben et al., 2001), here we did not compare stimulation of two different body-parts (e.g., hallux versus index-finger) in single-subject analyses, and thus our vibro-tactile stimulation produced activation of the contralateral operculum extending from the lip of the lateral sulcus to the insulae. A possible role of secondary somatosensory cortex in spatial processing of multi-sensory stimuli is further supported by some electro-physiological reports of crossmodal effects in single neurons of awake monkeys (Burton et al., 1997).

One possible reason why previous imaging studies that used similar paradigms (e.g., Macaluso et al., 2000b, 2002a) did not find crossmodal spatial effects in these somatosensory regions might be that here, for the first time, tactile stimulations were delivered directly in front of the subject, albeit unseen, without any reflection of seen hands due to the use of mirrors (cf. Macaluso et al., 2000b, see also Misaki et al., 2002). Thus, the felt position of the hands corresponded directly with the location (in external space) where visual stimuli were also presented, resulting in a correct alignment of visual, proprioceptive and tactile signals. As with the cross-modal modulation in lateral occipital cortex, the effects in the parietal operculum were obtained here regardless of the currently relevant modality for the saccade task, and indeed regardless of whether the stimulated locations were saccade targets or not. Accordingly, both visual and somatosensory cortices appear to be influenced by spatial congruence of a bimodal visual-tactile event in the contralateral hemifield, regardless of the task. These patterns of activation are consistent with the proposal that integration of spatial representations between senses involves coordination of activity in anatomically distant areas, responsible for the processing of stimuli in different modalities but originating from the same position in external space (Macaluso and Driver, 2001).

The only area that showed crossmodal spatial-congruence effects specific to one of the three tasks was ventral occipital cortex. In this region crossmodal effects, characterised by larger brain activity for spatially congruent bimodal stimulation in the contralateral hemifield, were observed exclusively when subjects maintained central fixation and did not use the stimuli to guide any eye-movements (see Fig. 4). This confirms that our analysis approach is appropriate for revealing any crossmodal effects that are specific for only one task (hence the task-independent effects reported above are not merely due to some bias in our statistical approach). The activation of this ventral area specifically in task conditions requiring central fixation accords with some of our previous results (Macaluso et al., 2000b, 2002a) that showed crossmodal spatial visual-tactile effects in ventral occipital cortex during *covert* orienting (i.e., again with central fixation and no saccades). Here, we observe that such effects in this ventral region were abolished when the sensory signals (vision or touch) were

used to guide overt responses. This might reflect the well-known specialisation of ventral regions for stimulus identification and analysis, with a lesser involvement when the sensory input is used to guide direct overt spatial responses (Goodale and Milner, 1992).

All effects of spatial congruency between vision and touch were observed in regions of the brain primarily concerned with sensory processing (i.e., visual areas in occipital cortex, and somatosensory regions in the parietal operculum), that here also showed a main effect of stimulated hemifield for one or the other modality (see Fig. 2). A different outcome might be expected in designs manipulating the spatial relation between the position of the target stimuli and the direction of motor responses (e.g., employing anti-versus pro-saccade tasks), rather than the spatial congruence of stimuli in different sensory modalities, as done here. For example, frontal areas involved in saccadic control (e.g., supplementary frontal eye-fields) might show interesting effects related to voluntary overt orienting versus more reflexive behaviour using stimuli in a different modality than vision (e.g., Curtis and D'Esposito, 2003).

In conclusion, the present study demonstrated that particular visual (lateral occipital) and somatosensory (parietal operculum) areas can both be affected by the spatial congruence of multi-sensory visual–tactile stimulation. These effects were spatially-specific, with boosting of sensory responses observed in brain regions contralateral to the position of spatially congruent bimodal stimulation. The effects in visual cortex accord with some of our prior work (e.g., Macaluso et al., 2000b; 2002a), while we show such an influence on somatosensory cortex (parietal operculum) also, for the first time. Critically, here we also show for the first time that these effects do not depend on the behavioral relevance of one or the other sensory modality, nor on their serving as saccade targets. Instead, they appear to reflect an automatic, stimulus-driven mechanism. These observations support a recent proposal (see Driver and Spence, 1998; Macaluso and Driver, 2001) that integration of spatial representations between sensory modalities does not rely solely on sensory convergence to multimodal areas, but can also involve crossmodal influences upon sensory-specific cortices, providing a distributed – but integrated – system for representing space across sensory modalities.

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