Delay activity and sensory-motor translation during planned eye or hand movements to visual or tactile targets

E. Macaluso¹², C.D. Frith³, J. Driver²³

¹Neuroimaging Laboratory, Santa Lucia Foundation, Rome Italy
²UCL Institute of Cognitive Neuroscience and Department of Psychology, University College London, UK
³Wellcome Centre for Neuroimaging, Institute of Neurology, London UK

RUNNING HEAD: Eyes or hand movements to visual or tactile targets

Corresponding Author:
Dr Emiliano Macaluso
Neuroimaging Laboratory, Fondazione Santa Lucia.
Via Ardeatina, 306 – 00179 Roma (Italy)
Tel.: 0039 - 06 - 51501493 ; Fax: 0039 - 06 - 06 5150 1213
E-mail: e.macaluso@hsantalucia.it
Abstract

To perform eye or hand movements towards a relevant location, the brain must translate sensory input into motor output. Recent studies revealed segregation between circuits for translating visual information into saccadic or manual movements, but less is known about translation of tactile information into such movements. Using human fMRI in a delay paradigm, we factorially crossed sensory modality (vision or touch) and motor effector (eyes or hands) for lateralised movements (gaze shifts to left or right, or pressing a left or right button with the corresponding left or right hand located there). We investigated activity in the delay-period between stimulation and response, asking whether the currently relevant side (left or right) during the delay was encoded according to sensory modality, upcoming motor response, or some interactive combination of these. Delay activity mainly reflected the motor response subsequently required. Irrespective of visual or tactile input, we found sustained activity in posterior partial cortex, frontal-eye field and contralateral visual cortex, when subjects would later make an eye-movement. For delays prior to manual button-press response, activity increased in contralateral pre-central regions, again regardless of stimulated modality. Posterior superior temporal sulcus showed sustained delay activity, irrespective of sensory modality, side, and response type. We conclude that the delay activations reflect translation of sensory signals into effector-specific motor circuits in parietal and frontal cortex (plus an impact on contralateral visual cortex for planned saccades), regardless of cue modality; while posterior STS provides a representation that generalises across both sensory modality and motor effector.
Eyes or hand movements to visual or tactile targets

Introduction

Representation of external space and performance of spatially-selective actions require many combined neural computations. These will include encoding of the position of sensory stimuli, in relation to current posture, as well as translation of the locations indicated via senses into planning of a movement toward a specific location. While in everyday life we can effortlessly direct gaze or move our hands to objects, brain structures that encode locations according to sensory input or motor output may be segregated anatomically. Moreover, we can acquire information about the position of an event or an object through different sensory modalities (e.g. vision and touch), and can spatially direct different parts of our body on the basis of information from these different modalities (e.g. shifting gaze and moving our hands to explore a seen and felt object that we are holding). The existence of distinct sensory modalities and motor modalities that can all encode spatial positions raises questions of whether and how the brain combines these different types of spatial representation, in order to achieve coherent perception of space and to control different types of spatially-selective movement (Andersen et al., 1997; Colby and Duhamel, 1996).

One possible architecture for integrating or translating between such spatial representations would be first to combine sensory information from different modalities into a common and unique representation of sensory space, and then feed such a ‘supramodal’ representation into different effector motor systems. Other possible architectures might include multiple, segregated representations of multisensory space, separately connected to each specific effector system. Intensive electro-physiological work on neurons in parietal cortex of awake behaving monkeys (Wurtz et al., 1982; Gottlieb et al., 1998; Duhamel et al., 1992; Andersen et al., 1997; Snyder et al., 1998; Quian et al., 2006; Colby and Goldberg, 1999; Batista and Andersen, 2001) has revealed the existence of distinct regions in and around the intra-parietal sulcus that may serve as sensori-motor interfaces, each selectively or predominantly connected with a specific effector system. The lateral intraparietal region (LIP)
Eyes or hand movements to visual or tactile targets

has been associated with planning and execution of eye movements, and primarily with visual responses (e.g. Snyder et al., 1997; Ben Hamed et al., 2001; although also showing some auditory responses in trained animals, Mullette-Gillman et al., 2005; Grunewald et al., 1999). A more medial region of the intraparietal cortex (variously termed parietal reach region, PRR, and/or medial intraparietal area, MIP) is thought to play a role in pointing and reaching movements with the hands (Kalaska et al., 1997; Cohen et al., 2002; Johnson et al., 1996). This region, as for several other intraparietal regions involved in spatial representation and movements (e.g. area AIP in the anterior part of the intraparietal sulcus, Murata et al., 2000; and area 5 in the superior parietal lobule, Rushworth et al., 1997; Kalaska, 1996), has also been shown to receive afferent input from several distinct sensory modalities, including touch as well as vision (Colby and Duhamel, 1991). Moreover, the anatomical connectivity of these different intraparietal regions mirrors their apparent functional specificity: LIP connects primarily with dorsal regions of prefrontal cortex (PM) involved in eye-movement control; while PRR/MIP and AIP project to premotor regions involved in arm and hand movement control, in dorso-caudal PM and ventro-rostral PM respectively (Jones and Powell, 1970; Luppino et al., 1999; Wise et al., 1997; Tanne-Gariepy et al., 2002). According to this anatomo-functional organisation, spatial information concerning several sensory modalities may be brought together in distinct parietal-premotor circuits that ultimately specialize in different aspects of spatial movement.

Some recent human neuroimaging studies have adapted classical electrophysiological paradigms to test for possible analogies (or differences) between the organisation of parietal cortex and related structures in human and non-human primates (Culham and Valyear, 2006; Prado et al., 2005; Simon et al., 2002; Schluppeck et al., 2005; Desouza et al., 2000; Grefkes et al., 2004; Bremmer et al., 2001; Kawashima et al., 1994; Astafiev et al., 2003). Many of these human studies typically employ visual cues specifying a location for subsequent eye (saccadic) or finger (e.g. pointing) movement. Overall, neuroimaging results from such
Eyes or hand movements to visual or tactile targets

studies have highlighted some segregation of saccade-related versus manual-related activations, although some overlap (or some degree of activation during the other task) has also been found (Simon et al., 2002; Astafiev et al., 2003; Medendorp et al., 2005a; Connolly et al., 2003). Overlapping responses across different effector systems (see also Wurtz et al., 1982; for related data from monkeys), when found, may indicate that location-encoding in the affected area is primarily associated with sensory or attentional representations there, rather than strictly motor output (Colby and Goldberg, 1999; Macaluso et al., 2003a; Astafiev et al., 2003).

One well-established approach to such issues, for both electrophysiological work in non-human primates as well as for neuroimaging studies in humans, has utilized delayed-response paradigms (Snyder et al., 1997; Calton et al., 2002; Schluppeck et al., 2006; Duhamel et al., 1992; Desouza et al., 2000). In such delay paradigms, a variable period separates the sensory stimulus specifying the target location from the subsequent overt movement, triggered by a later go-signal. Much recent interest has focused on the processes occurring during the delay period itself, when there is no sensory stimulus present at the cued location and as yet no overt motor behavior, although the target location for the upcoming movement has already been identified.

Location-specific delay activity has been found both in apparently saccade-related (Duhamel et al., 1992) and apparently manual-related (Snyder et al., 1997) regions of parietal cortex. Nonetheless, it should be noted that such delay activity in specific regions linked to particular effector circuits is also typically coupled with strong responses to the initial sensory (visual) onset, leading increasingly to the perspective that such regions should be viewed as sensori-motor interfaces (Schluppeck et al., 2006; Snyder et al., 1998; Gottlieb et al., 2005). For example, in a recent human fMRI study on delay-activity during preparation for saccadic eye-movements, Schluppeck and colleagues (Schluppeck et al., 2006) showed that in medial and posterior intraparietal areas (IPS1, IPS2 and V7) activity increased during the delay
Eyes or hand movements to visual or tactile targets

period, but this sustained effect was relatively small compared to the initial response to the visual cue, and the subsequent response to the overt movement (saccade). Further, this study found spatially-specific activation (greater activity for contralateral than ipsilateral target/saccades) for the visual cue and during the delay period, but no side-specific effects were found for saccade execution. These findings suggest (in accord with much monkey electro-physiological data, e.g. Colby et al., 1996; Snyder et al., 1997) that location encoding in these apparently saccade-related parietal regions might not be fully segregated from sensory processing, with the same regions participating both in the “sensory” encoding of the relevant location, as well as the beginnings of motor preparation (see also Zhang and Barash, 2000; Connolly et al., 2000; Medendorp et al., 2005b; Beurze et al., 2007; Gottlieb et al., 2005; Gottlieb and Goldberg, 1999).

Such findings that, in humans as in monkeys, even those parietal regions that seems linked primarily to one or other type of upcoming movement can also show strong sensory-related responses, opens the issue of whether providing location cues in different sensory modalities (e.g. within touch, not only vision) will modulate activity in these regions. Although several studies have examined this issue for the monkey brain (Mullette-Gillman et al., 2005; Schlack et al., 2005; Cohen and Andersen, 2000), until recently there have been rather fewer human fMRI studies of the issue (though see Macaluso et al., 2003a), since most of the human neuroimaging studies examining different types of movements and/or delay periods have used only visual cues (e.g. Beurze et al., 2007; Connolly et al., 2003; Medendorp et al., 2005a; Schluppeck et al., 2005; Schluppeck et al., 2006). If different sensory modalities can trigger activation of regions related to particular types of motor circuit, the new question then arises of whether delay-activity in different regions may change as a function of the cue-modality, or if instead delay-activity will solely reflect the type of upcoming movement. We tested this here, in a human fMRI study of delay activity.
Eyes or hand movements to visual or tactile targets

We investigated possible effects and interactions concerning the modality of the cue (visual or tactile stimuli in the left or right hemifield, to specify the relevant spatial location for subsequent movement); and also concerning the motor effector used for the upcoming overt response at the end of the delay. Our design separated cue-related and response-related activity from the critical sustained activity occurring during the delay period between sensory cue and motor response movement (e.g. Schluppeck et al., 2006). For motor responses we used either saccades or lateralised manual responses, but included a variable delay period between stimulus cue and motor execution, with our focus being on the delay activity observed. The manual task involved button-presses with the left or right hand on the corresponding target side. Thus while left versus right eye-movements differed solely in term of end spatial position (i.e. with the same effector – the eyes - being used for both left and right movements), our manual task did not dissociate effector (left or right hand) from spatial position (target location in left or right hemifield; see also Beurze et al., 2007, who addressed the issue of position vs. effector specificity). Thus the present manual task of spatially-compatible button-pressing, following the delay after a visual or tactile stimulus cue, may require a step of effector selection (left or right hand; see also Thoenissen et al., 2002), as well as the location-selection involved in the oculomotor task also. Nonetheless, because the present paradigm factorially crossed cue-modality (visual or tactile) with movement-type (oculomotor or manual), this allowed us to determine whether during the delay-phase the relevant position would be encoded according to the modality of the cue (visual or tactile), the type of upcoming overt response (saccadic or manual) or some interactive combination of these two factors. Moreover, other potential designs (such as placing one hand in a central start-position, analogous to central fixation for the eyes) would have prevented us from placing tactile stimuli at identical locations to the visual stimuli on either side. We return to such issues in our Discussion. For now, the present design allowed us to assess whether brain
Eyes or hand movements to visual or tactile targets as measured with fMRI, for the delay period, would depend on the stimulus modality, the response type (oculomotor or manual) or some interaction between these.

Materials and Methods

Participants

Nine right-handed healthy volunteers (six males) participated (mean age 26 years). They gave written informed consent in accord with local ethics.

Paradigm

The experimental design was a 2x2x2 factorial; with cue-modality (vision/touch) and side (left/right) as orthogonal event-related factors, and movement-type (eyes/hand) as an orthogonal blocked factor. On each trial a visual cue or tactile cue on the left or right indicated the relevant position for the subsequent movement. After a variable delay (see below), an auditory “go-signal” instructed the subjects to execute the movement for the cued side. Eye-movements to left or right, or hand-movements (button-presses with left or right hand) were blocked within each fMRI-run, so subjects always knew whether the eyes or hands were currently relevant, but did not know which target side they should be directed to prior to the stimulus cue on each trial. The delay between the sensory-cue and the subsequent go-signal for movement initiation was varied (range 0.3-12.8 sec) to allow us to isolate preparatory activity in this delay (separated from the preceding stimulus and subsequent action; see also (Schluppeck et al., 2006), for the different combinations of cue-modality and movement-type (i.e. eye-to-vision, eye-to-touch, hand-to-vision and hand-to-touch). Our aim was to assess whether brain activity in this delay period would reflect the cue-modality (vision versus touch), the type of upcoming movement (hand versus eye), or some interactive combination thereof, and in which brain regions.
Eyes or hand movements to visual or tactile targets

Stimuli and Task

Subjects lay in the scanner with their hands on a plastic table positioned above the hips, where we placed LEDs for visual stimulation on either side; piezo-electric components (T220_H3BS_304, Piezo Systems, Cambridge, USA) to deliver unseen tactile stimulation to either hand; and electronic switches to record button-presses with either hand when these were made (see Fig 1a). Thus, on each side we could deliver visual or tactile cue-stimuli (either of these in correspondence with the index finger of one hand) and could also record motor responses (i.e. key-presses performed with either of the two thumbs, which were occluded to avoid any visual stimulation associated with manual responses; and any eye-movements towards either side). The visual scene was filmed with a shielded camera placed outside the head-only MR bore (SIEMENS, Allegra) and projected onto a screen at the back of the scanner (see Fig 1A, illustration on the left side). The subjects viewed the visual scene through a mirror system that also allowed monitoring of eye-position with a remote near infra-red scanner (see below). From inside the scanner, the scene appeared to the subjects as if they were looking down at their own hands resting on a table (see Fig 1A, on the right side of the panel), while they looked straight-ahead into the mirror system. The soft illumination of the MR room permitted continuous viewing of the scene throughout the experiment. On the table, the index fingers (and the LEDs) rested at 10 cm to the left or right of the central fixation point. The distance between the camera and the table was adjusted so that the index fingers were at 7.8 deg visual angle in the projected image, thus maintaining a realistic size scaling for the seen hands.

Before the beginning of each fMRI-run, the subjects were instructed verbally on whether they had to respond with eye-movements or with manual button-presses for the upcoming block of trials. Irrespective of effector type, each trial began with the illumination of a central fixation point. After 1500 ms this central fixation point was turned off, and either a visual or a tactile cue was presented on the left or on the right side for 200 ms. Cue modality
and position were randomised and unpredictable. The lateralised sensory-cue indicated the target position for subsequent movement, but subjects had to withhold their motor response until the auditory go-signal. After a variable delay (see below), an auditory tone (frequency of 500 Hz; duration of 200 ms) instructed the subject to execute the movement for the relevant location (go-signal). In two fMRI-runs subjects responded by manually pressing the button on the relevant side, and in the other two fMRI-runs they made a saccade toward the relevant position (i.e. towards the index finger of one or the other hand, at the same locations as the possible visual target) and back to the central fixation point, with the order of tasks counterbalanced.

Each fMRI-run consisted of 28 trials (inter-trial-interval = 16 sec). There were 14 visual-trials (7 on the left & 7 on the right side) and 14 tactile-trials (7 left & 7 right) in random order. We used cue-to-go-signal delay periods of between 0.3 and 12.8 seconds. In order to reduce the correlation between cue-related activity, movement-related activity, and preparatory/delay activity, we used long delays for 57% of the trials (864-12800 ms, uniform distribution); middle-range delays for 29% of the trials (447-863 ms); and short delays for 14% of the trials (300-446 ms). The high variability of possible delays also ensured that subjects could not anticipate the exact time of the go-signal, and therefore should prepare for whenever the go-signal might occur. The order of the 4 fMRI-runs (2 runs with eye-movements, and 2 runs with hand-movements) was counterbalanced across subjects. Each run lasted for 8 minutes. Prior to the fMRI session all subjects received approximately ten minutes of practice inside the scanner.

Magnetic resonance imaging

A Siemens Allegra (Siemens Medical Systems, Erlangen, Germany) operating at 3 T and equipped for echo-planar imaging acquired functional MR images. A quadrature volume head coil was used for radio frequency transmission and reception. Thirty-two slices of
Eyes or hand movements to visual or tactile targets

functional MR images were acquired using blood-oxygenation-level-dependent imaging (3x3mm, 2.5 mm thick, 50% distance factor, TR = 2.08 s, TE = 30 ms), covering the entirety of the cortex.

Data Analysis

We used SPM2 (http://www.fil.ion.ucl.ac.uk) for data pre-processing and statistical analyses. We acquired 920 fMRI volumes for each participant. After discarding the first four volumes of each run, all images were corrected for head movement. Slice-acquisition delays were corrected using the middle slice as reference. All images were normalized to the standard SPM2 EPI template, resampled to 2 mm isotropic voxel size, and spatially smoothed using an isotropic gaussian kernel of 10 mm FWHM (full-width half-maximum) in accord with the SPM approach. Time series at each voxel for each subject were high pass filtered at 220 seconds and pre-whitened by means of an autoregressive model AR(1).

Statistical inference was based on a random effects approach (Penny and Holmes, 2004), and assigned corrected p-values as described later. The SPM analysis comprised two steps. First, for each subject the data were best-fitted at every voxel using a combination of effects of interest. These represented the three phases of the trial: sensory-cue, variable-length delay and motor-response. Within each fMRI-run (either with eye- or hand-responses), these three phases (sensory, delay, motor) were modelled separately according to cue-modality (vision or touch) and relevant side (left or right hemifield). Thus, each fMRI-time series was fitted with 12 effects of interest (3 phases x 4 trial-types), plus some confounding effects of no interest that were modelled separately to remove their influence. These were rare trial-phases when subjects moved their eyes, when they should instead have maintained central fixation (see below). Linear contrasts were used to average responses for the 12 effects of interest, in the two fMRI-runs requiring the same motor response (i.e. eyes or hands). This procedure resulted in 24 contrast-images per subject, representing the four possible sensory-
Eyes or hand movements to visual or tactile targets

motor combinations (Eye-to-Vision, Eye-to-Touch, Hand-to-Vision, Hand-to-Touch), for either hemifield (Left or Right), and for the three trial-phases (sensory, delay and motor).

In the second stage (group analyses), we modelled 8 conditions (4 sensory-motor combinations, on each side) separately in three SPM group-analyses, one for each trial-phase. Finally, within each such SPM analysis, linear compounds were used to compare the 8 conditions, 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. In these group random-effects analyses we retained as statistically significant only activations surviving correction for multiple comparisons (p-corr. < 0.05; see section below for more details).

Preliminary analyses assessed activity in the sensory cue-phase and in the motor response-phase. In the sensory cue-phase we tested for any modality-dependent activation, plus any common activations that generalised over modalities (conjunction analysis, Price and Friston, 1997; Friston et al., 1999). To assess this, we compared activity during sensory-cueing versus rest (e.g. visual cue versus rest) with a whole-brain corrected threshold (p-corr. <.05). Furthermore, to ensure the specificity of any modality-dependent activation during sensory stimulation, we included the additional constraint that such activity during cueing for one modality also had to be greater than for the other modality (e.g. visual versus tactile cue; p-uncorr. <.001). Note that adding these additional constraints (i.e. requiring that a particular activation should pass a further uncorrected test also) can only make our analyses more conservative than the basic corrected contrast. Likewise, when testing for commonalities across vision/touch (whole-brain-corrected conjunction analyses), we also further required each of the individual modalities to activate at p-uncorr. <.001.

An analogous approach was used to assess brain activation in the motor response phase. Accordingly, we tested for any activation specific for a movement-type (saccade or
Eyes or hand movements to visual or tactile targets manual), plus any common activation that generalised over movement-types (using conjunction analyses). We compared activity during motor-response versus rest (whole-brain-corrected threshold: p-corr. <.05), plus added the further constraint that activity for one movement-type also had to be greater than for the other movement-type (e.g. saccade versus manual responses; p-uncorr. <.001). When testing for commonalities across eye/hand (whole-brain-corrected conjunction analyses), we additionally required each of the individual movement-types to activate at p-uncorr. <.001.

For the critical analyses of the preparatory delay-phase, again we tested for modality or effector-dependent delay-activity and for any common activations that generalised across modality (and/or effector) versus rest (whole-brain p-corr. <.05). To confirm modality- and/or effector-specific activation, we added the further constraint that activity for one modality (or effector) also had to be greater than for the other modality/effector (p-uncorr. <.001) to count as specific in this sense.

Further, we tested for any side-dependent activations (left minus right targets, or vice-versa), separately for the sensory-, delay- or motor-phases described above, within those regions already highlighted by the comparisons mentioned above (i.e. already characterised as modality-specific or generalising across modality; and as effector-specific or generalising across effectors). For these side-dependent contrasts, correction for multiple comparisons (p-corr. <.05) considered only the volumes already activated for the main comparisons (i.e. modality/effector-dependent or common activations).

Finally, for completeness only (and to allow some comparison with our prior work, Macaluso and others, 2003a), we also tested for side-dependent activations in the anterior intraparietal sulcus (aIPS). In a previous study that had used a similar design, but without the critical delay-period introduced here, we had found that this region was activated contralaterally, regardless of stimulus modality (vision or touch) or effector (hand versus eye) when immediate movements were made (Macaluso et al., 2003a). In the current experiment
we could assess whether any such side-dependent activations in the aIPS would be specific to the sensory cue-phase, delay-phase or motor response-phase. For this *a priori* defined aIPS region, we assigned corrected p-values using as the volume of interest a 10 mm sphere (small volume correction, Worsley et al., 1996) that was centred on the intraparietal peak found in Macaluso et al. (2003a).

**Eye Tracking**

In all subjects but one, eye-position was monitored using an ASL Eye-Tracking System with remote optics that was custom-adapted for use in the scanner (Applied Science Laboratories, Bedford, USA; Model 504, sampling rate = 60 Hz). Eye-position traces were examined in a 14.5 sec time-window, beginning with the cue-onset until the end of the trial. For each subject the eye-tracking system was calibrated before fMRI scanning. The subject performed a series of saccades from central fixation to the left and to the right LEDs, visiting each lateral position twice (duration of each fixation = 1500 ms). The calibration served to convert the (arbitrary) units of the eye-tracking system to degrees of visual angle. The eye-position data acquired during fMRI scanning were baseline-adjusted using the average horizontal position in a 500ms pre-cue window. We identified losses of fixation as changes in horizontal eye-position greater than 2 degrees with durations longer than 100 ms. To ensure that trials containing inappropriate losses of fixation would not affect our imaging results, these were modeled separately in the imaging data analysis (see section above on Data Analysis). After removal of those trials, no systematic gaze deviation could be found in any of the periods requiring maintenance of central fixation. For trials requiring saccadic responses, the first derivative of the eye-position (eye-velocity) was used to compute saccadic reaction time (i.e. here defined as the time between the auditory go-signal and eye-velocity exceeding 100 deg/s; see Fig 1B).
Results

Behavioural data

Overt responses were measured throughout each scanning session using an eye-tracking system with remote optics (see above), plus electronic switches on each side to record manual button-presses. The percent of misses was 5% in the manual task, and 2% in the saccade task. Subjects never responded with a button-press on saccade trials, but in the manual task we detected losses of fixation after target onset on 18% of the trials. All error trials were excluded from the fMRI analyses. A within-subject ANOVA with cue-modality, movement-type and target-side as independent factors was used to compare the reaction times in the 8 conditions. This revealed a main effect of type of movement (F(1,7) = 49.1; p < 0.001), with saccades yielding faster reaction times (means [s.e.m]: 422 [36] ms for saccades and 567 [23] ms for button-presses). The main effect of side and the side-by-movement interaction almost reached significance (p = 0.058 and 0.051, respectively) due to faster responses with the right than the left hand (539 [29] ms versus 595 [22]; t(7) = 2.6; p = 0.036), especially on button-press trial, as might be expected in these right handed subjects. Overall the reaction times were quite slow (but similar to Macaluso et al., 2003a, who used a similar experimental set-up). A possible reason for this is because of the demanding fMRI environment in which subjects had to perform the tasks (i.e. a noisy surrounding where subjects have to lay still for approx. 1h, including set-up time). However, any such effect of the environment should presumably all conditions similarly, thus having no specific influence on our fMRI results.

fMRI results: sensory-cue-phase and movement-phase

SPM analyses of the sensory-cue-phase highlighted sensory circuits for touch or vision, plus any “common” multisensory activation (see Figure 2A, and Table 1); while fMRI
analyses of the movement-phase revealed motor circuits involved in eye- or hand-movement, and effector-independent responses (Fig. 2B and Tab. 2).

Analyses of brain activity associated with the sensory cues revealed “common” regions responding to both visual and tactile cues in and around the intraparietal sulcus and pre-motor regions, plus the occipito-temporal junction (see Fig 2A, magenta). Selective responses for the visual cues were found in ventral, lateral and dorsal occipital cortex, plus posterior parietal cortex (see Fig 2A, in cyan), as would be expected. For tactile cues, we found activation of the post-central gyrus plus parietal operculum (see Fig 2A, in yellow), again as expected.

Within both “bimodal” regions (activated in common by both vision and touch) and “unimodal” (visual- or tactile-specific) we then tested for any effect of stimulus position (left minus right, and vice-versa; see Table 1, rightmost columns). The bimodal regions in frontal, parietal and posterior temporal cortex did not show any significant effect of stimulus position at our whole-brain corrected threshold. But for completeness, we examined the anterior intraparietal sulcus (aIPS) region previously reported by Macaluso et al. (2003) as showing a contralateral response that generalised across vision and touch. We considered a spherical region of interest (10 mm radius) centred at the coordinates reported in that study (L hemisphere: x, y, z = -38 -36 54; Right hemisphere: x, y, z = -48 -32 46). This confirmed a significant (p-corrected <.05) main effect of contralateral minus ipsilateral cue side, regardless of cue modality (see also Table 1).

For areas responding selectively for visual cues, greater responses for contralateral minus ipsilateral stimulation were found within the occipital lobe (i.e. in ventral, lateral and dorsal occipital cortex; see Table 1). The visually-selective posterior parietal cortex did not show any lateralised effect in our study. A possible reason for this is that - unlike several studies that did find some spatiotopic responses in high-order visual areas - here we used small, low-contrast and brief visual stimuli to signal the relevant position, rather than the
Eyes or hand movements to visual or tactile targets

intensive periodic stimulation required for phase-mapping techniques (c.f. Hagler and Sereno, 2006; Schluppeck et al., 2005). For tactile cues, contralateral effects were found both in the post-central gyrus and in the parietal operculum, as expected.

We highlighted motor circuits by considering activity following the auditory “go-signal” that prompted movement execution (see Fig 2B, and Table 2). All movement conditions activated the medial frontal cortex and superior premotor areas (Fig 2B, in blue). In addition, regions along the superior temporal gyrus were activated but probably as an auditory response to the go-signal (common for all movement conditions). Saccadic eye-movements resulted in selective activation of posterior parietal cortex and superior pre-motor regions. The peaks of the dorsal premotor activation were located on the lateral side of the pre-central sulcus, thus in a somewhat more lateral location than the classical localisation of the frontal-eye-fields (e.g. see Petit et al., 1997; who reported peak activation in the depth of the sulcus, but with the activation cluster also extending to the lateral surface as here). Nonetheless, the current finding is consistent with our previous study that also directly compared eye- versus hand- movements revealing nearly identical co-ordinates (Macaluso et al., 2003a). The entirety of occipital cortex, including visual cortex in the calcarine fissure, also showed increased activity during eye-movements, presumably as a consequence of the changes of retinal input due to saccadic execution (see Fig 2B, in red). Hand-movements resulted in the activation of peri-central regions, extending posteriorly to the anterior part of the superior parietal lobule (see Fig 2B, in green). In addition we also found increased activity in the supplementary motor areas (partially overlapping with the region showing activation for both types of movements, cf. transverse section in Fig 2B), in the temporo-occipital junction and in the parietal operculum (see Table 2).

Analogously to the sensory-cue-phase, we then tested the motor-response-phase data for any effect of movement side, comparing leftward minus rightward trials and vice-versa (see Table 2, rightmost columns). For hand-responses, this showed activation in the pre-
central gyrus with greater activity for button-presses using the contralateral versus ipsilateral hand, as would be expected in primary motor regions. In addition, hand-responses activated also the anterior parietal cortex, parietal operculum, SMA and temporo-occipital junction. Fronto-parietal regions that activated selectively for eye-movements did not show any significant effect of the target side, possibly because each saccade to the target was followed by a saccade in the opposite direction, re-orienting gaze to the central fixation point (see also Macaluso et al., 2003a). Primary visual cortex in the calcarine fissure showed greater activity for ipsilateral than contralateral saccades, possibly due to changes of retinal input during the eye-movements. Auditory and medial frontal regions that activated in common for both hand- and eye-movements (see above) did not show any effect of movement side.

In summary, analyses of brain activity in the sensory-cue-phase and in the movement-phases revealed the expected effects according to the sensory stimulation (Fig 2A and Table 1) or the type of movement (Fig 2B and Table 2). We found unimodal visual, unimodal tactile, and bimodal visuo-tactile activations during the sensory-cue-phase; and effector-specific plus some effector-independent activations in the movement-phase. Several of the sensory and motor regions also showed some preference for stimulation or movement for the contralateral side (see Tables 1 & 2, rightmost columns).

fMRI results: during the critical delay-phase

The central aim of the current study was to investigate activity in the cue to movement time-interval (delay phase) and to assess the role of the cue-modality and/or movement-type for such delay activity. Importantly, we found no significant differences between delay activity following a visual or a tactile cue. By contrast, the type of movement that was prepared dramatically influenced brain activity in the delay phase. Thus, the type of upcoming movement but not a sensory-specific location appeared to be maintained during the delay.
Eyes or hand movements to visual or tactile targets

Preparing to perform an eye-movement toward the cued location resulted in selective activation of the posterior parietal cortex, superior premotor cortex and ventral occipital visual areas (see Fig 3 & 4A). The signal plots in Figure 3 & 4 shows the level of activation in posterior parietal cortex (Fig 3A) superior premotor cortex (Fig 3B) and ventral occipital cortex (Fig 4A) for the three trial-phases (cue [C], delay [D] and target [T]) as a function of the cue-modality (touch or vision), motor effector (hands or eyes) and side (left or right). Figure 3A shows that, in posterior intraparietal cortex, activity increased selectively during preparation for an eye-movement, irrespective of cue-modality (see red bars). There was a tendency for intraparietal activity to be higher for saccadic targets on the contralateral side compared to ipsilateral side. This reached statistical significance for a region in the right hemisphere, but the left hemisphere did not reach full corrected statistical significance and so is reported here for completeness only (see also Table 3A, rightmost columns) to avoid any misleading impression of strong hemispheric asymmetries in intraparietal cortex. In the superior premotor cortex we did not observe such a tendency for contralateral activity levels to be larger than ipsilateral (see signal plots in Fig 3B).

Figure 4A shows activity in ventral occipital regions where the effect of saccade target position was stronger and delay activity was observed only when subjects prepared for an eye-movement to a contralateral location (see red bars, in Fig 4A and Table 3A). Note that unlike the ipsilateral activity observed during saccade execution (see Table 2), here visual areas activated contralaterally during saccade preparation (i.e. specifically during the delay, prior to an actual saccade). Hence this preparatory activity is unlikely to represent changes of retinal input due to small eye-movements that survived our exclusion criteria (see Methods), but may instead reflect visual enhancement of the target location for an upcoming saccade. Critically, we thus show a modulation of activity in visual cortex that was selective for the type of upcoming movement (oculomotor versus manual), but that generalised across both visual and tactile cues.
Analyses of delay activity preceding button-press responses (hand-movement trials) revealed selective activation of motor regions in the pre-central gyrus, plus supplementary motor areas (see Fig 4B and Table 3B). The medial activation did not show any selectivity according to relevant side, while the pre-central regions showed greater activity for preparation of movement with the contralateral hand (see signal plots in Fig 4B, green bars), as would be expected for a manual motor-plan.

Finally, we tested for any brain regions showing increased preparatory activity irrespective of both the modality of the cue and the type of upcoming motor response. This revealed robust bilateral activation in the posterior part of the superior temporal sulcus (see Fig 5 and Table 3C). Here activity increased during the delay phase of all trial types, responding also here irrespective of target side (see cyan bars in Fig 5).

Discussion

Spatial orienting to external events or objects often requires combination of signals from different modalities (as when we can both see and feel an object) and also co-ordination of different effector-systems. Here we asked whether encoding of a relevant position during a delay period follows primarily the sensory modality signaling the location, or the motor system used for the upcoming lateralized motor response (or some interaction of these). We examined brain activity in the interval between sensory cue and delayed motor response (delay activity), in the absence of any current sensory stimulation or motor response. We found that delay activity clearly reflected the type of upcoming movement rather than the sensory modality of the cue-stimulus. Activity increased in contralateral pre-central cortex when subjects prepared for a button-press with either the left or the right hand, irrespective of whether the left/right position had been cued with a visual or a tactile stimulus. When subjects prepared for an eye-movement instead, activity increased in the posterior parietal cortex, dorsal premotor cortex and ventral occipital cortex, again irrespective of the modality of the
Eyes or hand movements to visual or tactile targets

sensory-cue. In occipital cortex the delay-activity was strongly lateralised to the hemisphere contralateral to the relevant location, while posterior parietal cortex activated for both contralateral and for ipsilateral locations, but with larger effects during the preparation of saccades to the contralateral hemifield. In addition, a region in the superior temporal sulcus activated during the delay, irrespective of cue-modality, relevant-side, and type of movement. Our findings suggest that during a delay period intervening between a stimulus cue to target location and a later motor response to that location, the relevant location is coded according to the movement-type rather than the cue-modality, and - critically - that these effector-specific areas can be cued by spatially-specific signals from different sensory modalities.

Our finding of effector-dependent responses during the cue-to-movement delay is in general agreement with previous electrophysiological studies in non-human primates (Barash et al., 1991; Andersen et al., 1997; Snyder et al., 2000; Cohen et al., 2002; Kalaska et al., 1997) and with more recent fMRI experiments in humans (Culham and Valyear, 2006; Prado et al., 2005; Simon et al., 2002; Schluppeck et al., 2005; Desouza et al., 2000; Grefkes et al., 2004; Bremmer et al., 2001; Kawashima et al., 1994; Astafiev et al., 2003). We found preparatory activity in the posterior parietal cortex that was selective for eye-movements. This activation was located in the posterior part of the superior parietal gyrus, in an area that may correspond to the IPS2 region reported by Schluppeck and colleagues (Schluppeck et al., 2005), who showed some retinotopic organization there, in a detailed study using an overt saccade task. In a later study (Schluppeck et al., 2006), the same group reported that this area is active during saccade preparation, with greater activity during preparation of contralateral versus ipsilateral saccades. In the present study we demonstrate that preparatory activity in this posterior parietal region is selective for eye-movement, when comparing eye- versus hand-movement preparation directly for the first time in a delay-paradigm using both visual and tactile cues. As in previous studies (Schluppeck et al., 2006; Sereno et al., 2001), we also found larger activity during preparation of contralateral than ipsilateral saccades, albeit only
Eyes or hand movements to visual or tactile targets

the right hemisphere reached full statistical significance. A possible reason for the relatively weak lateralisation within posterior parietal cortex in the current study might be that here we did not use a phase and/or polar-angle mapping approach which requires predictable and extended sequences of saccades (Sereno et al., 2001; Schluppeck et al., 2005). But instead, we did introduce here for the first time both visual and tactile lateralised cue-stimuli to show that either of these can trigger effector-specific preparatory activity in posterior IPS. Thus, spatial information from different sensory modalities seems to converge on posterior parietal cortex that exhibit sustained activation selectively while subjects prepare for a saccadic eye-movement.

Together with the activation of the posterior parietal cortex, we also found saccade-specific preparatory activity in dorsal pre-motor cortex and in ventral occipital cortex. In pre-motor cortex the activity increased irrespective of planned saccade direction, while the occipital activation was contralateral to the side of the up-coming saccade. The finding of effector-specific modulation within visual occipital cortex suggests a link between motor preparation and visual processing as predicted by premotor theories of spatial selection (Rizzolatti et al., 1987). Recent micro-stimulation experiments in monkeys found that stimulation of oculomotor control structures can change the response proprieties of single neurons in occipital visual cortex (Tolias et al., 2001; Armstrong et al., 2006). Such interactions between anatomically distant neural populations emphasizes the potential for interplay between higher associative regions and lower sensory areas during eye-movement guidance and attention selection (Moore, 2006; see also Astafiev et al., 2003). Here, we show effector-specific and side-specific sustained activity in human occipital cortex that also generalised across the sensory modality of the cue for the prepared saccade. The finding of these spatially-specific crossmodal effects is consistent with proposals that spatial information from the somatosensory system can reach and modulate spatial representations within visual occipital cortex, possibly via higher-order control structures in frontal and parietal cortex.
Eyes or hand movements to visual or tactile targets (Macaluso et al., 2002; Macaluso and Driver, 2005), such as those involved in saccade preparation.

Unlike most previous studies on preparatory activity for saccadic eye-movements (Desouza et al., 2000; Sereno et al., 2001; Schluppeck et al., 2006), our paradigm included not only left/right saccades, but also left/right manual button-presses (see also Simon et al., 2002; Connolly et al., 2000; Connolly et al., 2006, for studies that also used more than one effector-system in a within-subject fMRI design). Due to this, we could show here that our occipital, premotor and posterior parietal findings for saccade preparation are truly effector-specific (specific to oculomotor preparation), and cannot be accounted for by any more general process common to the two spatial-motor tasks (such as general shifts of spatial attention). Nonetheless, we should note that our manual button-press task differed from the pointing/reaching tasks used in most electrophysiological studies to date (Calton et al., 2002; Snyder et al., 1997; Batista and Andersen, 2001; Johnson et al., 1996) and in some neuroimaging studies (Desouza et al., 2000; Prado et al., 2005; Connolly et al., 2003). We used a simple button-press task with the left or the right hand (see also Macaluso et al., 2003a). One potentially important difference between traditional pointing tasks and the current button-press task is that here we did not dissociate the left/right location of the manual response from the selection of one or other hand (i.e. here the left hand always pressed the left button, and the right hand pressed the right button, within their respective hemispaces). On hand-trials the sensory cue thus signaled both relevant location and relevant hand. Several previous studies addressed the issue of location versus hand/limb selection in manual responses (Beurze et al., 2007; Medendorp et al., 2005a). Double cueing studies can separate in time signals relating to the selection of the desired end position and of the responding effector. For example, Beurze and colleagues used a pointing task with the left or the right hand, and found that the posterior parietal cortex and dorsal premotor cortex participate in selection of both the desired end location and effector (Beurze et al., 2007). Maximal activity
was observed when both components were specified, i.e. in correspondence with the final, second cue. Furthermore, the IPS showed laterized responses (contralateral greater than ipsilateral) in respect of both the responding hand and the target location, whereas in pre-central cortex (M1) activity reflected effector selection only. Medendorp and colleagues obtained similar results in a fMRI experiment, where subjects either pointed with the left or the right hand, or they saccaded toward laterized visual targets (Medendorp et al., 2005a). A retinotopic region of IPS combined responding-hand and target-side during the pointing task, while M1 activated for movements of the contralateral hand, irrespective of target side. Given these findings, it may be that effector (left or right hand) may have contributed more than external position for the preparatory activity in pre-central gyrus during the manual task (see Fig 4B). Future work might further address spatial issues (concerning the respective roles of target external position, effector side, movement direction etc) by involving crossed-reaching responses to visual or tactile targets, thus dissociating not only sensory versus motor preparation, as here, but also investigating the relative contribution of each potential spatial framework to each stage of the sensory-motor spatial translation.

Within our current paradigm, it might be even argued that the sensory cues acted as “symbolic” signals instructing subjects to move one or the other hand (somewhat similar to presenting verbal cues: “move left” or “move right”), or to saccade left or right. But while it is indeed possible that subjects converted the exogenous laterized sensory-cue signals into some other form of representation, and then issued an endogenous motor command upon presentation of the auditory go-signal, we note that in fact we found strong motor-specific activations during the delay period. Moreover, prior to obtaining our actual results, it was entirely possible that subjects might maintain an internal representation of the relevant location in sensory rather than motor terms. Thus, in principle subjects could process the cue and then select a sensory representation endogenously to represent the critical location during the delay (e.g. simply ‘attending’ to the relevant visual or tactile location during the delay).
Eyes or hand movements to visual or tactile targets

Our results show decisively that this does not happen; instead, the activity during delay reflects only the motor requirements.

Concerning the IPS, Medendorp et al also (2005) reported greater activity during saccades than pointing, but note that their study did not explicitly separate cue, delay and movement phases unlike here. Delay-activity during pointing or saccades was recently investigated in a fMRI study that dissociated position versus effector cuing (Connolly et al., 2006). This revealed increased activity in IPS, even when the instruction cue concerned only the relevant effector system (i.e. not specifying relevant location). IPS activation was observed both for saccadic and pointing preparation, but with greater effects for saccade than pointing. Our IPS findings during the delay-phase (larger activation for saccade-task versus manual-task, see Fig 3A) appear consistent with Medendorp’s and Connolly’s findings (Medendorp et al., 2005a; Connolly et al., 2006), although our button-press task differs from previous pointing tasks as noted earlier. For present purposes, an advantage of the button-press task was that it allowed us to present tactile cue-stimuli on each side (to the index-finger) at exactly the same location as the possible visual stimuli, and which always required spatially-compatible motor responses to the corresponding location. Pointing or reaching tasks would have precluded the possibility of using tactile cues in the same way, which was critical for the current aim of assessing the possible role of cue-modality (as well as movement type) during the cue-to-movement delay phase. But these differences in the type of hand-motor responses between the current study and previous pointing/reaching tasks may explain also why here we found preparatory activity in precentral cortex, but not within the parietal cortex itself for hand movements. A possible alternative design could have used tactile cues on the left/right hand to instruct leftward/rightward pointing movement. While this design might reveal tactually-triggered pointing activity in parietal cortex, it would have required placing visual and tactile cue stimuli at different positions, or using different target locations for saccade and pointing tasks.
Together with our effector-specific findings (i.e. posterior parietal, dorsal pre-motor plus ventral occipital cortex for saccade preparation; versus pre-central cortex for button-press preparation) we also found sustained delay activity in the superior temporal sulcus, but now irrespective of movement-type. Also in this region, the delay response was observed irrespective of the modality that had cued the relevant location. Several previous studies implicated the STS in spatial covert orienting (Macaluso et al., 2001; Yamaguchi et al., 1994); see also Luh et al., 1986, for related studies in non-human primates). Using PET, we previously reported STS activation when subjects sustained attention either to the left or to the right hemifield (Macaluso et al., 2001), and – as in the current study – irrespective of whether vision or touch was used to define the currently relevant position. Our present results of sustained activity in the delay phase thus appear consistent with the interpretation that STS may be involved in committing spatial attention to a given spatial location prior to the go-signal for executing a movement, and that this process can happen supramodally.

While the primary aim of the current study was to investigate preparatory activity in the absence of any sensory stimulation or motor response, we also examined brain activity in the cue-phase and the movement-phase to highlight patterns of sensory (cue-phase) and motor (movement-phase) activity. For the movement-phase, we observed the expected activation of the contralateral pre-central gyrus for button-press responses, and posterior parietal plus dorsal pre-motor regions (FEF) for saccade execution. In the cue-phase, we could discriminate between “unimodal” (i.e. specific just for vision or touch) versus bimodal sensory activations. This revealed the expected unimodal effects in occipital cortex for vision, versus post-central gyrus plus parietal operculum for touch. Bimodal responses were observed at the occipito-temporal junction, posterior parietal cortex and pre-motor regions. Several of these regions are likely to contain neurons responding to more than one modality (Colby and Duhamel, 1991; Graziano et al., 1994; Bruce et al., 1981), although more general attentional or task-related processes might also explain some “common, bimodal” responses in fronto-
Eyes or hand movements to visual or tactile targets

parietal regions (Corbetta and Shulman, 2002; Yantis et al., 2002; Mesulam, 1998; Gitelman et al., 1999). Further, we also replicated (albeit only at a small volume corrected level) our previous observation of bimodal, but spatially-specific (contralateral) responses in the anterior parietal sulcus. We had previously reported bimodal effects in this region for both covert (Macaluso et al., 2003b; Macaluso et al., 2002) and overt (Macaluso et al., 2003a) spatial orienting, but here we could show that multisensory effects in anterior IPS relate to the sensory stimulation or transient covert orienting, rather than to more sustained attentional or motor preparation (since the present aIPS result was specific to the sensory-cue phase, not the delay or motor phase).

In summary, sustained delay activity while subjects prepared for an overt response toward a cued location was found to reflect primarily motor preparation, rather than sensory or attentional encoding of the relevant location. We found separate, effector-specific responses in posterior parietal cortex, frontal-eye-field and ventral occipital cortex for saccade preparation; versus contralateral pre-central cortex for hand responses. Our findings are in general agreement with single-cell work in monkeys, by indicating that sensory input is transformed into nascent motor plans during the delay. Critically, here we show that this generalizes across sensory modalities, with spatial signals from vision and touch feeding into effector-specific motor representations in the human brain.

Reference List


56. **Quian QR, Snyder LH, Batista AP, Cui H and Andersen RA.** Movement intention is better predicted than attention in the posterior parietal cortex. *J Neurosci* 26: 3615-3620, 2006.


Eyes or hand movements to visual or tactile targets


Eyes or hand movements to visual or tactile targets

Figure and Table Legends

**Figure 1:** A. Schematic illustration of the experimental set-up. A camera attached in front of the MR-bore filmed the visual scene around the subject’s hands that was then simultaneously projected onto a screen at the back of the scanner (see illustration on the left). The subjects viewed the visual scene as if in front of them (as the filmed image indeed was), via a mirror system. The scene comprised a central fixation point, LEDs for presentation of the visual cues, plus the top part of the hands (see schematic illustration on the right). The unseen tactile cues were delivered to the finger-pad of index fingers, and the occluded thumbs were used for button-press responses. B. Mean (and therefore smooth) horizontal eye-position traces against time in the response phase are plotted for each subject, according to the modality of the cue (tactile or visual), the target side (left or right) and the type of motor response (manual or saccades; see legend). For clarity, all eye-position traces are aligned at saccade onset.

**Figure 2:** Cue-related and Target-related responses. A. Brain areas activating in the cue-phase are rendered on 3D views and a transverse section of the SPM template. Activations are divided according to whether the response was modality-specific (Visual in cyan; Tactile in yellow) or was ‘bimodal’ (i.e. common for vision and touch; in magenta) B. Regions responding in the target-phase. Activations are displayed in different colors according to the specificity of the responses: effector-specific (saccade in red; manual in green), versus common responses in blue. It should be noted that an auditory signal was used as a go-signal for the motor response, thereby yielding also bilateral activation of the auditory cortex in common for eye and hand movements. All statistical maps are thresholded at p-corr = 0.05 (cluster level), plus additional constraints to ensuring “specificity” or “commonality” for the relevant effect (see Method Section), with the exception of the map relating to the
Eyes or hand movements to visual or tactile targets

saccade-specific response (panel B, in red; thresholded at p-uncorr = 0.001 for display purposes, to fully show the bilateral activation of dorsal premotor cortex).

**Figure 3:** Activations in the delay-phase specific for the preparation of eye-movement responses, irrespective of target side. While subjects prepared to perform an eye-movement, activity increased in the posterior parietal cortex (A) and in the superior premotor cortex (B). Critically, these preparatory effects occurred irrespective of the modality of the cue (visual or tactile), indicating that sensory signals from both modalities can trigger sustained preparatory-activity within these areas. Premotor cortex activated during preparation of both contralateral and ipsilateral saccades. Parietal cortex also activated irrespective of target side, albeit with stronger responses during preparation of contralateral saccades. The signal plots show activity for all sensory-motor combinations (crossing sensory-modality of the cue with effector-type), for the three trial-phases (C: cue; D: delay; T: Target/response), and separately for Left–hemifield and Right–hemifield trials. Bars in red highlight the critical bimodal (common to visual and tactile) but effector-specific activation in the delay-phase. Activations are rendered on anatomical sections at a threshold of p-uncorr = 0.001.

**Figure 4:** Activations in the delay-phase, specific for the preparation of eye- or hand-movements, and contralateral to the target side. A. Eye-movement preparatory activity in occipital visual cortex was strongly lateralised to the hemisphere contralateral to the location of the impending eye-movement. This side specific effect was observed irrespective of the sensory modality of the cue (touch or vision). B. Hand-movement preparation was associated with increased activation in the contralateral pre-central cortex, again irrespective of the cue modality (touch or vision).

The signal plots show activity for all sensory-motor combinations (crossing sensory-modality of the cue with effector-type), for the three trial-phases (C: cue; D: delay; T:
Eyes or hand movements to visual or tactile targets Target/response), and separately for Left–hemifield and Right–hemifield trials. Bars in red highlight the activation that was selective for preparation of a contralateral eye-response, while bars in green highlight contralateral hand-responses. Activations are rendered on anatomical sections at a threshold of p-uncorr = 0.001 for display purposes.

**Figure 5:** Activations in the delay-phase common to the preparation of eye- and hand-movements. In the posterior part of the superior temporal sulcus, activity increased during the delay-phase, irrespective of both cue-modality (touch or vision) and movement-effector (eyes or hands). The signal plots show activity for all sensory-motor combinations (crossing sensory-modality of the cue with effector-type), for the three trial-phases (C: cue; D: delay; T: Target/response), and separately for Left–hemifield and Right–hemifield trials. The bars in cyan highlight the bimodal, effector-independent and side-independent activation in the delay-phase. Activations are rendered on anatomical sections at a threshold of p-corr = 0.05 (cluster level).
Table 1: Cue related activity (sensory responses). Main Effects: Anatomical location, peak co-ordinates, Z-values and corrected p-values for regions activated in the cue-phase. Areas are divided according to whether the activation was modality-specific (A: Visual; B: Tactile) or bimodal (i.e. common for vision and touch, in C). P-values are corrected for multiple comparisons considering the whole brain as the volume of interest. Spatial Effects: Within areas responding in the cue-phase, we assessed any effect of stimulus-side comparing left-cues versus right-cues and vice-versa. All areas with a significant effect of side showed greater activity for stimulation of the contralateral versus ipsilateral hemifield. For these side-specific effects, p-values are corrected for multiple comparisons considering all voxels showing a main effect of the stimulation (modality-specific or bimodal), as the volumes of interest.

(*) We also tested for side-specific responses in the anterior intraparietal sulcus, now using a priori regions-of-interest, taken from prior work, to assign corrected p-values (see method section). This highlighted contralateral responses, irrespective of cue-modality.

Table 2: Target related activity (motor responses). Main Effects: Anatomical location, peak co-ordinates, Z-values and corrected p-values for regions activated in the movement-phase. Areas are divided according to whether the activation was effector-specific (A: Eye-movement; B: Hand-movement) or it generalized across effectors (i.e. common activation for eye- and hand-movements, in C). P-values are corrected for multiple comparisons considering the whole brain as the volume of interest. Spatial Effects: Within areas responding in the movement-phase, we tested for any effect of movement-direction (left versus right, and vice-versa). P-values are corrected for multiple comparisons considering all voxels showing a main effect of the movement (effector-specific or effector-independent), as the volumes of interest. While for hand-movements all side-specific effects were contralateral to the responding hand,
Eyes or hand movements to visual or tactile targets during saccade execution the side-effects in visual cortex (*) were ipsilateral to the movement/target direction.

Table 3: Delay related activity (preparatory activity). Main Effects: Anatomical location, peak co-ordinates, Z-values and corrected p-values for regions activating during the delay-phase. We could distinguish between areas showing selective preparatory activity depending on the type of upcoming movement (A: preparation for an eye-movement; B: preparation for a hand-movement); plus areas showing sustained activity irrespective of effector (C). Critically, all areas activated irrespective of the modality (vision or touch) that was used to cue the relevant position. P-values are corrected for multiple comparisons considering the whole brain as the volume of interest. Spatial Effects: Within areas responding during the delay-phase, we tested for any effect of relevant location (left versus right, and vice-versa). P-values are corrected for multiple comparisons considering all voxels showing effector-specific or effector-independent preparatory activity, as the volumes of interest. For the right ventral occipital cortex and the left pre-central gyrus, the side-specific effects did not overlap with the main effects (n.v.: not in volume of interest), hence we do not report corrected p-values. (ns: not significant)
A. Schematics of the experimental set-up

Subject’s view of the set-up

B. Horizontal eye-position in the target-phase

<table>
<thead>
<tr>
<th>Tactile Targets</th>
<th>Visual Targets</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time (ms)</td>
<td>Time (ms)</td>
</tr>
<tr>
<td>Eye-position (deg)</td>
<td>Eye-position (deg)</td>
</tr>
<tr>
<td>Left</td>
<td>Right</td>
</tr>
<tr>
<td>-10</td>
<td>10</td>
</tr>
<tr>
<td>-5</td>
<td>5</td>
</tr>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>-5</td>
</tr>
<tr>
<td>10</td>
<td>-10</td>
</tr>
</tbody>
</table>

Figure 1.
A. Cue related activity *(sensory responses)*

B. Target related activity *(motor responses)*

Figure 2.
A. Parietal delay activity specific for EYE responses (irrespective of target side)

Left posterior parietal cortex \((x,y,z = -22 -64 56)\)
- Touch: \(z = 56\)
- Vision: \(z = 56\)

Right posterior parietal cortex \((x,y,z = 24 -62 58)\)
- Touch: \(z = 56\)
- Vision: \(z = 56\)

B. Frontal delay activity specific for EYE responses (irrespective of target side)

Left superior premotor cortex \((x,y,z = -48 -10 42)\)
- Touch: \(z = 44\)
- Vision: \(z = 44\)

Right superior premotor cortex \((x,y,z = 58 0 44)\)
- Touch: \(z = 44\)
- Vision: \(z = 44\)

Figure 3.
A. Delay activity specific for EYE responses (contralateral to the target side)

*Left ventral occipital cortex (x,y,z = -18 -80 -10)*

<table>
<thead>
<tr>
<th>TOUCH</th>
<th>VISION</th>
</tr>
</thead>
<tbody>
<tr>
<td>LEFT</td>
<td>RIGHT</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>EFFECT SIZE (SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LEFT 0</td>
</tr>
<tr>
<td>LEFT 11</td>
</tr>
</tbody>
</table>

*Right ventral occipital cortex (x,y,z = 20 -72 -16)*

<table>
<thead>
<tr>
<th>TOUCH</th>
<th>VISION</th>
</tr>
</thead>
<tbody>
<tr>
<td>LEFT</td>
<td>RIGHT</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>EFFECT SIZE (SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LEFT 0</td>
</tr>
<tr>
<td>LEFT 11</td>
</tr>
</tbody>
</table>


B. Delay activity specific for HAND responses (contralateral to the target side)

*Left pre-central gyrus (x,y,z = -36 -28 60)*

<table>
<thead>
<tr>
<th>TOUCH</th>
<th>VISION</th>
</tr>
</thead>
<tbody>
<tr>
<td>LEFT</td>
<td>RIGHT</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>EFFECT SIZE (SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LEFT 0</td>
</tr>
<tr>
<td>LEFT 12</td>
</tr>
</tbody>
</table>

*Right pre-central gyrus (x,y,z = 34 -20 58)*

<table>
<thead>
<tr>
<th>TOUCH</th>
<th>VISION</th>
</tr>
</thead>
<tbody>
<tr>
<td>LEFT</td>
<td>RIGHT</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>EFFECT SIZE (SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LEFT 0</td>
</tr>
<tr>
<td>LEFT 12</td>
</tr>
</tbody>
</table>

Figure 4.
Delay activity INDEPENDENT of cue-modality, motor-effector and target side

**Left Superior Temporal Sulcus** \((x,y,z = -58 \ -28 \ 2)\)

**Right Superior Temporal Sulcus** \((x,y,z = 68 \ -22 \ -2)\)

Figure 5.
<table>
<thead>
<tr>
<th>Table 1. Cue related activity (sensory responses)</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image" alt="Table 1. Cue related activity (sensory responses)" /></td>
</tr>
</tbody>
</table>
### Table 2. Target related activity (motor responses)

<table>
<thead>
<tr>
<th></th>
<th>Main Effects</th>
<th>Spatial effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A. EYE movements</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L posterior parietal cortex</td>
<td>-26 –62 52</td>
<td>6.1</td>
</tr>
<tr>
<td>R posterior parietal cortex</td>
<td>28 –62 56</td>
<td>5.1</td>
</tr>
<tr>
<td>L superior premotor cortex</td>
<td>-52 –4 46</td>
<td>4.4</td>
</tr>
<tr>
<td>R superior premotor cortex</td>
<td>52 0 46</td>
<td>6.4</td>
</tr>
<tr>
<td>L Occipital cortex (*)</td>
<td>-10 –78 4</td>
<td>&gt; 8</td>
</tr>
<tr>
<td>R Occipital cortex (*)</td>
<td>14 –72 6</td>
<td>&gt; 8</td>
</tr>
<tr>
<td><strong>B. HAND movements</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>R pre-central gyrus</td>
<td>34 –24 72</td>
<td>7.1</td>
</tr>
<tr>
<td>L pre-central gyrus</td>
<td>-28 –14 66</td>
<td>&gt; 8</td>
</tr>
<tr>
<td>L anterior parietal cortex</td>
<td>-32 –44 66</td>
<td>6.3</td>
</tr>
<tr>
<td>R anterior parietal cortex</td>
<td>36 –42 64</td>
<td>5.3</td>
</tr>
<tr>
<td>L parietal operculum</td>
<td>-52 –24 12</td>
<td>&gt; 8</td>
</tr>
<tr>
<td>R parietal operculum</td>
<td>62 –24 12</td>
<td>&gt; 8</td>
</tr>
<tr>
<td>L occipito-temporal junct.</td>
<td>-52 –76 2</td>
<td>6.9</td>
</tr>
<tr>
<td>R occipito-temporal junct.</td>
<td>56 –72 –4</td>
<td>6.3</td>
</tr>
<tr>
<td>SMA</td>
<td>-2 –4 46</td>
<td>&gt; 8</td>
</tr>
<tr>
<td><strong>C. COMMON responses for eye and hand movements</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L superior temporal cortex</td>
<td>-54 –22 4</td>
<td>5.3</td>
</tr>
<tr>
<td>R superior temporal cortex</td>
<td>64 –26 10</td>
<td>7.2</td>
</tr>
<tr>
<td>SMA</td>
<td>2 –4 56</td>
<td>6.3</td>
</tr>
<tr>
<td>L superior premotor cortex</td>
<td>-40 –10 60</td>
<td>5.8</td>
</tr>
<tr>
<td>R superior premotor cortex</td>
<td>46 –10 60</td>
<td>6.0</td>
</tr>
<tr>
<td>L lateral occipital cortex</td>
<td>-50 –82 2</td>
<td>7.1</td>
</tr>
</tbody>
</table>
### Table 3. Delay activity (preparatory activity)

<table>
<thead>
<tr>
<th>A. Delay activity specific for EYE responses</th>
<th>Main Effects</th>
<th>Spatial effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>L superior premotor cortex</td>
<td>-48 –10 42</td>
<td>4.9</td>
</tr>
<tr>
<td>R superior premotor cortex</td>
<td>58 0 44</td>
<td>4.0</td>
</tr>
<tr>
<td>L posterior parietal cortex</td>
<td>-22 –64 56</td>
<td>4.6</td>
</tr>
<tr>
<td>R posterior parietal cortex</td>
<td>24 –62 58</td>
<td>4.4</td>
</tr>
<tr>
<td>L ventral occipital cortex</td>
<td>-14 –72 0</td>
<td>4.9</td>
</tr>
<tr>
<td>R ventral occipital cortex</td>
<td>12 –62 -8</td>
<td>4.1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>B. Delay activity specific for HAND responses</th>
<th>Main Effects</th>
<th>Spatial effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>L pre-central gyrus</td>
<td>-26 –28 64</td>
<td>5.7</td>
</tr>
<tr>
<td>R pre-central gyrus</td>
<td>30 –26 58</td>
<td>4.6</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>C. Delay activity INDEPENDENT of cue-modality and motor-effector</th>
<th>Main Effects</th>
<th>Spatial effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>L superior temporal sulcus</td>
<td>-58 –28 2</td>
<td>7.6</td>
</tr>
<tr>
<td>R superior temporal sulcus</td>
<td>68 –22 -2</td>
<td>&gt; 8</td>
</tr>
</tbody>
</table>