Intraparietal Sulcus Activity and Functional Connectivity Supporting Spatial Working Memory Manipulation

Signe Bray1,2,3, Ramsha Almas1,2, Aiden E. G. F. Arnold3,4, Giuseppe Iaria2,3,4,5 and Glenda MacQueen1,2

1Department of Psychiatry, 2Hotchkiss Institute, 3Alberta Children’s Hospital Research Institute, 4Department of Psychology and 5Department of Clinical Neurosciences, University of Calgary, 2500 University Dr NW, Calgary, AB T2N 1N4, Canada

Address correspondence to Dr Signe Bray, Alberta Children’s Hospital, University of Calgary, 2888 Shaganappi Trail NW, Calgary, AB, Canada T3B 6A8. Email: slbray@ucalgary.ca

The intraparietal sulcus (IPS) is recruited during tasks requiring attention, maintenance and manipulation of information in working memory (WM). While WM tasks often show broad bilateral engagement along the IPS, topographic maps of contralateral (CL) visual space have been identified along the IPS, similar to retinotopic maps in visual cortex. In the present study, we asked how these visuotopic IPS regions are differentially involved in the maintenance and manipulation of spatial information in WM. Visuotopic mapping was performed in 26 participants to define regions of interest along the IPS, corresponding to previously described IPS0-4. In a separate task, we showed that while maintaining the location of a briefly flashed target in WM preferentially engaged CL IPS, manipulation of spatial information by mentally rotating the target around a circle engaged bilateral IPS, peaking in IPS1 in most participants. Functional connectivity analyses showed increased interaction between the IPS and prefrontal regions during manipulation, as well as interhemispheric interactions. Two control tasks demonstrated that covert attention shifts, and nonspatial manipulation (arithmetic), engaged patterns of IPS activation and connectivity that were distinct from WM manipulation. These findings add to our understanding of the role of IPS in spatial WM maintenance and manipulation.

Keywords: intraparietal sulcus, spatial, visuotopic, working memory manipulation

Introduction

In both human and nonhuman primate studies, the intraparietal sulcus (IPS) has been associated with a range of cognitive functions, including attention in multiple sensory domains (Colby et al. 1996; Anderson et al. 2010), short-term and working memory (WM; Constantinidis and Steinmetz 1996; Pessoa et al. 2002), spatial imagery (Sack et al. 2002), and mathematical cognition (Rosenberg-Lee et al. 2011). While WM tasks engage relatively large bilateral IPS regions (Pessoa et al. 2002), topographic mapping studies (reviewed in (Silver and Kastner 2009)) have uncovered a set of regions along the IPS, similar to retinotopic areas in early visual cortex. While WM typically engages a distributed network of regions, manipulation of information in WM has shown a specific dependence on the IPS (Champod and Petrides 2007, 2010). Here, we investigated the functional overlap between topographically organized IPS regions and the maintenance and manipulation of spatial information in WM.

Topographically organized regions along the IPS have been mapped using several different tasks, including: covert attention to visual stimuli (Silver et al. 2005), central fixation while a flashing checkerboard wedge rotates around the screen, with covert attention to the wedge (Bressler and Silver 2010) or attention to the center (Swisher et al. 2007) and visual-/memory-guided saccades (Sereno et al. 2001; Koen and Kastner 2008a). These regions show a retinotopic organization similar to early visual areas (Sereno et al. 1995; Wandell et al. 2007). To date, 7 such regions have been identified, each containing a map of contralateral (CL) visual space and together forming a continuous band along the IPS. They have been labeled IPS0 (equivalent to V7), IPS1–5, and SPL1 which branches off into the superior parietal lobule. Similar mapping tasks have been used to delineate topographically organized regions in prefrontal cortex, in or near the human frontal eye fields (FEFs) and inferior branch of the precentral sulcus (Hagler and Sereno 2006; Kastner et al. 2007).

Both functional (Lauritzen et al. 2009) and structural (Greenberg et al. 2012) connectivity studies suggest that interactions between IPS subregions, particularly the most posterior, and early visual areas relate to the control of visual attention. It remains unknown, however, why the IPS contains multiple regions with similar retinotopic or visuotopic maps. Several studies have used a within-subject region of interest (ROI) approach to elucidate the specific functional roles of IPS subregions, performing visuotopic mapping as well as a second functional task within each participant to investigate the role of these regions in classical posterior parietal cortex (PPC) functions. This work has found differences between IPS subregions in response to eye movements (Koen and Kastner 2008a), object recognition (Koen and Kastner 2008b), and spatial attention and memory (Lauritzen et al. 2009; Sheremata et al. 2010; Szczepanski et al. 2010; Jerde et al. 2012). It has been shown that similar to attention, short-term memory for simple targets in one hemifield preferentially engages visuotopic IPS regions in the hemisphere CL to the target (Sheremata et al. 2010; Jerde et al. 2012).

While the IPS has consistently been implicated in tasks involving mental manipulation of information in WM (Champod and Petrides 2007, 2010), no study to date has looked at functional overlap between visuotopic IPS and spatial WM manipulation. In the present study, we mapped visuotopic IPS regions and used a spatial WM task to engage lateralized activity along the IPS, with 50% of trials also requiring manipulation of the attended spatial location in WM. This design allowed us to 1) investigate lateralization of responses during manipulation, 2) identify differences between IPS regions in response to manipulation relative to maintenance and 3) test for manipulation-related changes in functional connectivity with visuotopic IPS. Finally, 2 similarly structured tasks were run in
a subset of participants to test the specificity of our findings, controlling for effects of covert attention shifts, and cognitive load/task difficulty.

Materials and Methods

Participants

Thirty-two participants (aged 18–29 years, mean age 22, 16 females) participated in this study. Participants were recruited primarily from the undergraduate student body at the University of Calgary. All participants were right-handed and self-reported having no history of neurological or psychiatric illness. All participants provided informed consent on a form approved by the Conjoint Health Research Ethics Board at the University of Calgary. Scans were terminated early in 2 participants due to technical difficulties, and 4 participants were excluded from the imaging analyses due to inadequate visuotopic mapping, possibly due to excessive head or eye movement. A total of 30 participants were included in the behavioral analyses and 26 participants were included in the neuroimaging analyses described here. Ten participants (aged 18–24 years, mean age 22, 5 females) returned for a second session within 1 year, during which they performed 2 additional functional tasks. Eye tracking was not available during MR scanning; however, an additional 13 participants (aged 19–31 years, mean age 24, 9 females) underwent eye-tracking on identical tasks outside the scanner, to confirm that with similar training people are generally able to comply with central fixation on the tasks used in this study.

MRI Scanning

MR scanning was conducted on a 3 T GE Signa scanner with an 8-channel head coil at the Seaman Family MR Research Center at the University of Calgary. All participants underwent a high resolution anatomical scan (3D SPGR, 180 slices, FoV = 25.6 cm, 1 × 1 × 1 mm, flip angle = 12°). Functional scans were T2*-weighted, gradient echo, echo-planar images. For visuotopic mapping scans, 25 axial slices were acquired covering occipital, parietal, and prefrontal regions (repetition time (TR) = 2.25 s, echo time = 30 ms, flip angle = 65°, voxel size 3 × 3 × 3 mm, FoV = 19.2 cm); all participants underwent six ~6-min mapping scans. To assist with spatial registration, a T2-weighted fast SPGR was acquired in the same orientation as the visuotopic mapping scans. For the spatial WM manipulation task, 30 axial slices were acquired parallel to AC-PC, for whole-brain coverage excluding the cerebellum (TR = 2.25 s, echo time = 30 ms, flip angle = 65°, voxel size 3.4 × 3.4 × 3.5 mm, FoV = 22 cm). Ten participants returned for 2 functional control tasks collected in the second session. Functional imaging parameters were identical to the WM task. In this follow-up session, a second high-resolution anatomical scan was collected, as well as a T2-weighted fast SPGR in the same orientation as the functional scans, to facilitate coregistration of functional data between imaging sessions.

Stimulus Presentation and Response Collection

Stimuli were presented to participants in the scanner using a projector located at the back of the room, which projected an image onto a screen at the rear of the bore. The image on the screen was visible to participants in the scanner using a mirror mounted to the MR head coil. The screen spanned ~20° of visual angle. Responses were collected using a 2-button Lumina response pad (Cedrus Corporation, San Pedro, CA, USA) held in the participants' right hand.

Anatomical Image Processing

Cortical reconstruction was performed with the FreeSurfer 5.1 image analysis suite (Dale et al. 1999; Fischl et al. 1999) (http://surfer.nmr.mgh.harvard.edu/). Segmented volumes were visually inspected, and where needed, appropriate manual corrections were performed.

Visuotopic Mapping Task and Analysis

A visuotopic mapping task similar to Bressler and Silver (2010) was performed, in which participants fixated a small cross at the center of the screen, while a flashing checkerboard wedge rotated around the screen once per 36 s (Fig. 1a). Participants were asked to fixate the center of the screen, while attending to the rotating wedge, and press a button whenever a target (small gray circle; Fig. 1a, right panel) appeared in the wedge. The dot appeared at different eccentricities and the size of the circle was scaled to be larger at greater eccentricities. The checkerboard wedge subtended 40° in width and extended from the center of the screen to ~10° of visual angle. Contrast was reversed (black/white) at a rate of 5 Hz. During each scan, the wedge rotated continuously around the screen 8 times, for a total of ~6 min per run; all participants performed 6 runs of this task. These data were preprocessed using SPM8 (http://www.fil.ion.ucl.ac.uk/spm/software/ spm8/) software in MATLAB (MathWorks, Natick, MA, USA), by coregistering the in-plane T2 images to the high-resolution anatomical image and applying this transformation to the functional images. Functional images were then slice-time corrected and realigned to the first scan from the first session. ArtRepair software (http://www.nitrc.org/projects/art_repair/) was used to mitigate the effects of large head movements (>0.5 mm/TR) by interpolating between non-contaminated images. Finally, images were smoothed with a 2-mm FWHM Gaussian kernel.

At each voxel, a linear trend was subtracted from the timecourse and the %signal change from the mean was calculated. A Fourier transform was then calculated on the time series from each session, yielding an amplitude and phase component at each frequency; these were averaged across sessions in the frequency domain (Sasgin and Sereno 2008). At each voxel, a coherence value between the harmonic at the stimulus frequency and the time series was calculated as the amplitude of the harmonic component divided by the time series power (Bandettini et al. 1993; Engel et al. 1997). This coherence was thresholded at r > 0.3, and the resulting phase-encoded maps were overlaid onto FreeSurfer generated cortical surfaces. The borders between adjacent early visual and IPS regions were manually drawn at regions of phase-reversal (see Fig. 2; Bray et al. 2013a). These regions included: V1, V2v, V2d, V3v(VP), V3d, V3A/B, IPS0, IPS1, IPS2, IPS3, and IPS4 in the left and right hemisphere (IPS4 could not be reliably delineated in one participant). ROIs included voxels that were suprathreshold on the mapping task (r > 0.3); these labels were used to generate binary masks for each ROI.

Spatial Working Memory Manipulation Task

In the same scan session, after the visuotopic mapping task, participants performed 2 runs of the spatial WM manipulation task. Participants were asked to fixate the center of the screen throughout this task. The background on the screen was light gray with a slightly darker gray ring indicating the circle around which targets flashed. The darker circle spanned from ~5°–5.5° in eccentricity (Fig. 1b). All trials started with the appearance of ‘++’ at the center of the screen. Next, a white target flashed on the background circle for 250 ms at 1 of 8 peripheral locations equally distributed around the circle. All targets and subsequent probes spanned the width of the background circle (0.5°), and subtended 5° of visual angle. On consecutive trials, targets appeared at consecutive locations around the circle in a clockwise fashion (45°, 0°, −45°, −90°, −135°, −180°, 135°, 90°—relative to right horizontal), with a random jitter of ±5°. Because participants fixated the center of the screen throughout the task, predictable target location was chosen over a randomized presentation around the circle, in order to ensure that targets were easily noticed. Participants were asked to fixate the center of the screen while covertly attending to the target location, during a delay period of 1.75 s. More specifically, instructions were to remember the location of this target by continuing to pay attention to the location where the target flashed. Following the delay, for 250 ms, a white ‘+’ changed to ‘+’ on 50% of trials for one trial of trials (+30, +45, +60, +75°) on the remaining 50% of trials. This number cued the participant to mentally rotate the remembered position by the given angle,
in the clockwise direction. After 1.5 s, a blue probe flashed for 250 ms and participants responded yes/no with a left or right button press to indicate whether the probe appeared in the remembered location plus the rotation angle. In +00 trials, participants pressed the button if the probe appeared in the same location as the target. On 50% of trials, the probe was in the predicted location and, on the remaining 50% of trials, it was in a location ±30° away from the correct location. A variable ITI uniformly varying between 1.5 and 5 s followed, during which the +++ remained at the center of the screen. The scan also included 30 s rest periods at the beginning and end of each session. All participants underwent two 7-min sessions of this task for a total of 96 trials. Participants practiced this task outside the scanner immediately before the scan, until they were able to complete the task with at least 80% accuracy, and reported being able to comfortably fixate the center of the screen throughout the task. The +00 trials required fixating the center of the screen while covertly attending the location of a previously flashed target; this condition required that this spatial position be maintained in WM and will be referred to throughout as WM maintenance. The trials that involved mentally shifting the target location by a given angle will be referred to as spatial WM manipulation.

**Behavioral Analyses**

Accuracy measures were calculated and response times averaged for manipulation and maintenance trials, and for each angle of rotation (30°, 45°, 60°, 75°). These measures were entered into repeated-measures ANOVAs (rm-ANOVAs) with rotation angle as a within-subjects factor.

**Working Memory Manipulation Task Neuroimaging Analysis**

Functional MRI data from this task were preprocessed and analyzed using SPM8. fMRI preprocessing included manual alignment to the AC-PC, slice time correction, realignment to the first image in the first scan, and coregistration to the individual 3D SPGR anatomical scan. For ROI analyses, images were left in native space and smoothed with a 4-mm FWHM Gaussian kernel. This smoothing kernel was chosen in order to increase the accuracy of fitted parameter estimates while minimally blurring spatial boundaries. For whole-brain group analyses, images were normalized to MNI coordinate space using participant-specific normalization parameters derived from the segmentation of the anatomical scan. Images were then smoothed with an 8-mm FWHM Gaussian kernel.

For each participant, a general linear model was defined with regressors for the 3 maintenance conditions, corresponding to the hemifield of target presentation (right: 45°, 0°, −45°; top/bottom: −90°, 90°; left: −135°, 180°, 135°—relative to right horizontal), and 3 regressors corresponding to manipulation trials in the right, top/bottom, and left hemifield, at the time of the manipulation-angle cue. Locations refer to both target and probe hemifield, which were always the same; any targets
that crossed from one hemifield over to the other during rotation were grouped with the top/bottom manipulation regressor. Regressors were constructed as impulse functions convolved with the canonical hemodynamic response function (HRF). The model also included the motion parameters calculated during realignment as nuisance regressors, and a high-pass filter of 128 s was applied. Contrasts comparing targets in the left and right hemifields, as well as left and right manipulation versus maintenance were calculated for each participant. Random-effects analyses were conducted by entering these contrasts into one-sample t-tests at the group level. For whole-brain analyses, inferences were drawn at peak intensities of \( P < 0.05 \) familywise error (FWE) corrected over the whole brain, unless otherwise stated.

**IPS Region-of-Interest Analyses**

ROI analyses were run for each of the IPS subregions (0–4), defined by the visuotopic mapping analysis. Parameter estimates for each condition from the general linear model were extracted using within-subject masks for each ROI. These values were averaged over all voxels included in the mask (independent of statistical threshold) and entered into a rm-ANOVA, with within-subject factors of condition (manipulation/maintenance), IPS ROI (0–4), target location (ipsilateral) IL/CL, and hemisphere (left/right), to determine if there were significant differences between IPS regions in responses to WM maintenance or manipulation conditions. Post hoc paired t-tests were used to investigate effects of interest.

WM, manipulation, and mental rotation tasks have previously been shown to engage large areas along bilateral IPS. We investigated the extent to which activation during spatial WM manipulation and maintenance was located within visuotopic IPS regions. To do this, we asked whether the dorsal occipital/parietal cortex voxel (constrained using a FreeSurfer-derived mask) showing the greatest response to WM maintenance and manipulation fell within visuotopic IPS, and if so, in which IPS region.

**Functional Connectivity Analyses**

In order to test for functional interactions between visuotopic IPS regions during WM manipulation, a psychophysiological interaction analysis (PPI; Friston et al. 1997) was performed using individually defined IPS masks as seed regions. For this analysis, a general linear model was constructed which included 1) regressors modeling the difference between manipulation and maintenance trials for targets pooled across target locations (psychological variable), 2) a regressor for the timecourse of activation in the seed region, extracted as the eigenvariate over voxels in the seed region and adjusted for nuisance effects (physiological variable), 3) regressors modeling the interaction between the seed region timecourse and the psychological variable (psychophysiological interaction term), generated as the product of the deconvolved timecourse and condition vector (Gitelman et al. 2003), which were then reconvolved with the HRF. A second model was run splitting the trials into hemifields (right, left, top/bottom). Parameter estimates from these models were analyzed within individual IPS ROIs using rm-ANOVAs with ROI, hemisphere, and location (IL/CL target) as factors. Whole-brain voxelwise analyses were also conducted. In order to test for changes in connectivity with regions of prefrontal cortex, spherical ROIs (12 mm radius) were generated around group-level peaks in the prefrontal cortex for the spatial WM

---

**Figure 2.** Examples of topographic maps in 2 participants (S1 top, S2 bottom). Color legend half-circles on the left and right indicate phase values, represented on inflated surfaces. Dashed white lines indicate borders between adjacent regions, at phase reversals. On flattened maps, IPS regions 0–4 are shown, as well as V1 and extrastriate regions V2v, V3v, V2d, V3d, and V3A/B. On inflated maps (lateral) only V3A/B and IPS0–4 are marked. LH, left hemisphere; RH, right hemisphere.
manipulation versus maintenance contrast across all target locations (DLPCS: [−50 10 32] and [50 8 28], near putative human FEF: [−28 2 58] and [26 2 60], and putative SMA [−2 20 48]). These ROIs were used to perform small-volume correction in connectivity analyses.

Control Task 1: Covert Attention Shifts
This task was used to measure activation related to covert attention shifts, and included trials with cued 0°, 30°, and 75° within hemifield attention shifts around a circle. The main difference between this task and the spatial manipulation task is that here attention shifts were cued to a particular location, whereas, in the manipulation task, participants had to mentally shift a remembered position by a given angle. Participants were asked to fixate the center of the screen throughout this task. The background on the screen was identical to the spatial-manipulation task (Fig. 1c). All trials started with the appearance of “+++” at the center of the screen. Next, a white target flashed on the background circle for 250 ms at 1 of 8 peripheral locations equally distributed around the circle. All targets and subsequent probes spanned the width of the background circle (0.5°), and subtended 5° of visual angle. Target locations were randomly distributed around the circle at (left hemifield: 75°, 30°, −30°, −75°; right hemifield: 105°, 150°, −105°, −150°—relative to right horizontal), with a random jitter of ±5°. Participants were asked to maintain central fixation while covertly attending to the target location, during a delay period of 1.75 s. Following the delay, for 250 ms, the +++ changed to −−− on 50% of trials, or one of (−−+, −++, −−−) on the remaining 50% of trials. This cued participants to maintain attention (−−−) or shift attention to the location cued by the arrow (0° or 180° relative to right horizontal). After 1.5 s, a blue probe flashed for 250 ms and participants responded yes/no with a left or right button press to indicate whether the probe appeared at the attended location. On 50% of trials, the probe was in the correct location and in the remaining 50% of trials it was in a location ± 30° away from the correct location. A variable ITI uniformly varying between 1.5 and 5 s followed, during which the +++ remained at the center of the screen. Scans included 30 s rest periods at the beginning and end of each session. All participants underwent two 7-min sessions of this task for a total of 96 trials. All participants practiced this task outside the scanner immediately before the scan, until they were able to complete the task with 80% accuracy, and reported being able to comfortably fixate the center of the screen.

Behavioral Analysis
Accuracy measures and reaction times for this task were entered into rm-ANOVAs with effects of task (arithmetic/maintenance) and probe (expected/unexpected number). Accuracy values were also compared with the spatial manipulation task.

Control Task Neuroimaging Analyses
Data were preprocessed in the same manner as the spatial WM manipulation task. Tasks were modeled separately in both native space and MNI space with 4 regressors: left hemifield-maintenance, left-arithmetic (or attention shift), right-maintenance and right-arithmetic (or attention shift), modeled as delta functions convolved with the canonical HRF, and motion regressors included as nuisance effects. At the group level, random-effects analyses were conducted by entering the contrast of arithmetic (or attention shift) versus maintenance (averaged over left and right hemispheres) in one-sample t-tests. In this smaller sample, inferences were drawn at $P < 0.001$ uncorrected, with cluster-level correction for multiple comparisons at $FWE P < 0.05$. Follow-up analyses in individual IPS ROIs were conducted identically to the spatial WM task.

Eye Position
Eleven participants completed 2 runs of 2 of the 3 tasks (WM manipulation, arithmetic, attention shifts), randomly assigned and in counterbalanced order. Two participants completed only one task, and data from a total of 10 runs from 5 participants were excluded due to excessive noise. Data from 7 participants were analyzed for the WM manipulation task, 7 for the attention-shift task and 5 for the arithmetic task. Tasks were practiced until participants reached an accuracy of 80% and reported being able to comfortably fixate the center of the screen throughout the task. This was similar to the prescan training; eye movements were not recorded during practice, and no feedback about eye movements was given. Participants then completed 2 runs of each task. For these measurements, eye position was monitored using an eye tracker (Eyelink 1000; SR Research, Kanata, ON, Canada), while tasks were presented on a computer screen; responses were collected using a standard keyboard. A chin rest was used to stabilize head position. Participants sat 65 cm from the screen, which subtended ~16° of visual angle and had a resolution of 1024 × 768. Eye position data were collected at 1 kHz and analyzed off-line using MATLAB. After blinks were removed, the center position was calculated from the median position of the 30 s fixations at the beginning and end of each run. Eye position data, relative to center, were averaged during the initial maintenance period of trials in each hemifield. To determine whether there was a bias toward the cue being maintained, left and right hemifield trials were compared within subjects using nonparametric Wilcoxon rank-sum tests. In order to assess whether manipulation, attention shifts or arithmetic were associated with an increase in eye movements relative to maintenance, the standard deviation of eye position was calculated during the initial maintenance period, and subtracted from the standard deviation during the period following the manipulation cue (for non-zero manipulation trials). These values were compared against a median of zero using a nonparametric Wilcoxon signed-rank test. The total proportion of time spent fixating within 1° of the center was also calculated for each participant.

Results

IPS Mapping
IPS0–4 were successfully mapped in 26 participants (except one IPS4 which could not be reliably defined in 1 participant). Examples from 2 participants are shown in Figure 2 (examples from 5 additional participants are shown in Supplementary...
Fig. 1). ROI masks were normalized to the MNI template in order to calculate the mean center of mass for each ROI (Table 1). The locations of these regions are consistent with previously published reports (Swisher et al. 2007; Sheremata et al. 2010; Szczepanski et al. 2010). We additionally defined visual areas V1, V2v, V3v, V2d, V3d, V3A/B, also shown in Figure 2. Maps in the prefrontal cortex were not reliably identified using this procedure.

Spatial Working Memory Manipulation

Behavior

The average accuracy for the manipulation (rotation) and maintenance trials was 82% and 95%, respectively; participants were significantly more accurate on the maintenance trials ($t_{(29)} = 7.3, P < 0.001$). Accuracy for each of the rotation angles was 95% (0), 86% (30), 83% (45), 81% (60), and 77% (75). A rm-ANOVA confirmed a significant effect of angle within the rotation trials ($F_{(1,29)} = 10.8, P < 0.01$), indicating that rotating greater angles was less accurate. Reaction time data indicated that participants were significantly faster to respond on the maintenance, relative to the manipulation trials ($t_{(29)} = 9.1, P < 0.001$). However, within the manipulation trials, there was no effect of rotation angle ($F_{(1,29)} = 2.8, P = 0.1$). This was expected as participants would have completed the mental rotation by the time the probe cued them to respond.

Functional Imaging

Working Memory Maintenance Preferentially Engages Contralateral IPS

Group-level analyses of left versus right hemifield maintenance showed activation in regions of the occipital cortex and PPC CL to the remembered location (Fig. 3a). WM in the right hemifield engaged left parieto-occipital regions (peaks at $[-34 -90 18], [-16 -100 18], [-38 -74 16], N = 1175, Z = 5.6, 5.54, 5.35$). WM in the left hemifield engaged right superior parietal ($[24 -60 70], N = 197, Z = 5.3$), parieto-occipital ($[28 -80 22], N = 138, Z = 5.1$), and lateral occipital ($[46 -72 6], N = 2, Z = 4.6$) regions.

Follow-up ROI analyses in individual IPS regions were conducted to examine differential involvement of IPS regions in the WM maintenance task (Fig. 3b–e). An rm-ANOVA on the maintenance regressor with ROI (IPS0-4), hemisphere (left/ right), and location (IL/CL) showed significantly greater activation in the left hemisphere ($F_{(1,24)} = 8.8, P < 0.05$), for CL targets ($F_{(1,24)} = 219, P < 0.001$), and a significant effect of ROI ($F_{(4,96)} = 11.1, P < 0.001$). Post hoc t-tests showed that overall during maintenance responses in IPS2 and 3 were not significantly different, but responses in IPS2 were significantly greater than adjacent IPS1 ($t_{(25)} = 4.6, P < 0.001$) and responses in IPS3 greater than adjacent IPS4 ($t_{(24)} = 3.9, P < 0.001$). The location × ROI ($F_{(4,96)} = 6.4, P < 0.001$), and hemisphere × ROI ($F_{(4,96)} = 3.4, P < 0.05$) interactions were significant, indicating greater CL bias in more posterior IPS ROIs and greater differences between ROIs in the right hemisphere. The hemisphere × location × ROI interaction was also significant ($F_{(4,96)} = 2.8, P < 0.05$). However, follow-up paired t-tests showed that the CL bias did not reach significance in IPS0 or IPS1 in the left versus right hemisphere ($P = 0.2$ and 0.27).

Table 1

<table>
<thead>
<tr>
<th></th>
<th>V3A/B</th>
<th>IPS0</th>
<th>IPS1</th>
<th>IPS2</th>
<th>IPS3</th>
<th>IPS4</th>
</tr>
</thead>
<tbody>
<tr>
<td>LH Mean (mm)</td>
<td>-25.6</td>
<td>-24.8</td>
<td>-20.7</td>
<td>-18.9</td>
<td>-22.3</td>
<td>-24.4</td>
</tr>
<tr>
<td>LH SD</td>
<td>4.35</td>
<td>4.45</td>
<td>5.55</td>
<td>6.65</td>
<td>7.75</td>
<td>7.106</td>
</tr>
<tr>
<td>RH Mean (mm)</td>
<td>29.3</td>
<td>26.8</td>
<td>22.9</td>
<td>19.8</td>
<td>24.7</td>
<td>28.6</td>
</tr>
</tbody>
</table>
| RH SD   | 4.23  | 4.24 | 4.34 | 5.44 | 6.65 | 6.74 

LH = left hemisphere, RH = right hemisphere.
The difference between CL and IL maintenance regressors in all visuotopically mapped ROIs are shown in Figure 3d,e. Among visuotopically mapped occipital and parietal regions, V3A/B showed the strongest CL bias during attention. Within subjects, peaks in parieto-occipital regions for right versus left maintenance contrasts were tested for overlap with visuotopic regions. Of 52 peaks (26 participants × 2 hemispheres), 47 were within 1–2 voxels of a visuotopic mask. The majority, 24, were in V3A/B, 10 were in IPS0, and 5 in V3d.

**Bilateral IPS is Engaged During WM Manipulation**

A contrast was calculated to determine the general manipulation response, independent of target location (contrast: all 3 manipulation vs. all 3 maintenance regressors). This contrast showed widespread activation in the frontoparietal attention network (Fox et al. 2005; Toro et al. 2008), including bilateral IPS ([−26 −76 30], N = 2697, Z = 6.5; [22 −64 54], N = 3773, Z = 6.9), near putative human FEF ([−28 −2 −58], N = 822, Z = 6.5; [26 2 60], N = 739, Z = 6.5), anterior insula ([−34 20 −4], N = 685, Z = 5.24; [34 22 2], N = 13, Z = 4.7), DLPFC ([−50 10 32], N = 205, Z = 5.3; [50 8 28], N = 96, Z = 5.3), and ventral striatum ([−12 12 −2], N = 685, Z = 5.7; [10 16 −4], N = 526, Z = 5.6), as well as putative SMA ([−20 48], N = 898, Z = 6.3), left inferior frontal gyrus ([−40 42 2], N = 86, Z = 5.3), and right middle frontal gyrus ([44 34 20], N = 300, Z = 5.8) (Fig. 4a). Manipulation responses to targets in the left- and right-hemifields overlapped with this network, and there were no significant differences for the interaction contrasts comparing manipulation to maintenance in the left and right hemifield, at a whole-brain corrected threshold.

A follow-up analysis was performed in individual IPS subregions. Parameter estimates for the manipulation and maintenance regressors are shown in Figure 4b,c, and the contrast of manipulation-maintenance in Figure 4d,e. Focusing on manipulation specific activation, a rm-ANOVA was performed on the manipulation-maintenance contrast with effects of IPS ROI (0–4), location (IL/CL), and hemisphere. The results showed a significant main effect of ROI (F_{4,96} = 23.78, P < 0.001). This analysis showed that some IPS subregions showed a greater relative increase during manipulation trials. Post hoc t-tests showed that the manipulation-maintenance response, averaged over conditions, was significantly greater in IPS1 than IPS0 (t_{(25)} = 9.9, P < 0.05) and IPS3 (t_{(25)} = 3.8, P < 0.05), but not IPS2 (t_{(25)} = 1.3, P > 0.05) (Bonferroni-corrected for multiple comparisons). We additionally verified the location of the peak of this response in relation to visuotopic IPS regions. Peaks were identified in the left and right hemisphere from the overall manipulation-maintenance contrast. Of 52 peaks (26 participants × 2 hemispheres), 50 fell within 1–2 voxels of an IPS mask. The majority, 19, were in IPS1, 10 were in IPS0, and 11 in IPS2.

**Functional Connectivity with IPS Regions During Manipulation**

Functional connectivity analyses were performed to investigate how interactions with the IPS changed from the maintenance to manipulation conditions. PPI models were run with each of the 5 IPS seed regions individually, as well as in a model that included all 5 regions, to enable comparisons of connectivity patterns between IPS ROIs. PPI models are designed to test for changes in connectivity with a seed region under different conditions, while controlling for the main effects of task conditions and seed timecourse. In models testing interactions separately for each seed, all 5 IPS regions showed significant connectivity changes with SMA, either at a whole-brain or small-volume corrected threshold (peak P < 0.001 uncorrected, cluster correction at P < 0.05 FWE-corrected) (IPS0: [−10 10 54], N = 444, Z = 4.3; IPS1: [−8 6 52], N = 759, Z = 4.41; IPS2: [−6 8 56], N = 105, Z = 3.7; IPS3: [−10 8 46], N = 17, Z = 3.5; IPS4: [−8 6 48], N = 13, Z = 3.4). The IPS1 cluster extended into left FEF ([−20 −8 58], Z = 4.14), and is shown in Figure 5a. IPS2 and IPS3 also showed significant connectivity changes with left FEF (IPS2: [−26 −6 60], N = 129, Z = 3.8; IPS3: [−26 −12 58], N = 9, Z = 3.2). Results using left hemisphere seeds showed a similar pattern and are reported in Supplementary Table 1. When all 5 IPS regions were modeled together, right IPS showed significantly greater connectivity changes, relative to IPS1,2,3,4 with left DLPFC ([−48 20 38], N = 18, Z = 3.15) and middle frontal gyrus ([−16 32 32], N = 221, Z = 4.3), and right IPS1 showed significantly greater connectivity changes relative to IPS0,2,3,4 with a peak in the left
hemispheres, with IPS1 seeds from the opposite hemisphere. An rm-ANOVA on these data, with hemisphere, ROI (V3A/B, IPS0-4), and location (targets CL or IL to the given hemisphere), showed functional connectivity changes were significantly greater for targets in the opposite hemisphere ($F_{1,24} = 24.8, P < .001$), and there were connectivity differences between IPS regions ($F_{2,120} = 2.7, P < .05$). The location × IPS ROI ($F_{1,24} = 3.0, P < .05$) interaction was also significant. These results suggest that during the manipulation of spatial information in WM, IPS IL to the manipulated target is engaged through interactions with the opposite hemisphere (CL to the target), which is preferentially engaged during WM maintenance. We report connectivity using IPS1 as a seed, however these results indicate that interhemispheric connectivity is not unique to IPS1 and extends across the IPS, therefore a similar pattern would be expected using adjacent IPS regions as seeds (see Supplementary Fig. 2).

**Control Task 1: Covert Attention Shifts**

This task was run in a subset of participants to test the effects of covert attention shifts, in the absence of spatial WM manipulation.

**Behavior**

Mean accuracy for trials where attention was maintained or shifted was 95% and 97.5%, respectively, and these were not significantly different ($t_{(9)} = 1.18, P = 0.1$). Reaction times showed that participants were significantly faster to respond when the probe came up at the expected location, relative to unexpected, for both the maintenance ($t_{(9)} = 2.9, P < 0.01$) and shift ($t_{(9)} = 3.7, P < 0.05$) conditions, suggesting compliance with task instructions.

**Neuroimaging**

Whole-brain group normalized analyses comparing attention shifts to maintenance (contrast: (left + right hemifield shift) – (left + right hemifield maintenance)) showed engagement of frontal and parietal regions, similar to the WM manipulation task (Fig. 6a, yellow). These included SMA ([6 ± 2 ± 72] Z = 3.86), bilateral FEF ([32 ± 16 ± 64] N = 831, Z = 4.5; [−18 ± 2 ± 68] N = 614, Z = 4.2), a large cluster in bilateral superior parietal cortex (peaks at [38 ± 40 ± 56] Z = 4.4, and [−36 ± 36 ± 56] Z = 4.3, N = 2066), bilateral dorsal occipital ([36 ± 64 ± 18] N = 1137, Z = 4.6; [−34 ± 74 ± 36] N = 75, Z = 3.5), left lingual gyrus ([−38 ± 62 ± 8] N = 982, Z = 4.5), and right precenral gyrus ([56 ± 14 ± 50] N = 270, Z = 4.6). Supplementary Figure 3 shows the overlap between the manipulation, attention-shift and arithmetic tasks (results reported below) in a single participant, along with topographic labels.

Within IPS regions, shift versus maintenance effects for IL and CL targets in the left and right hemispheres are shown in Figure 6d,e (Fig. 6b,c shows parameter estimates from the spatial manipulation task in the same 10 participants for comparison). An rm-ANOVA compared spatial manipulation with attention shifts (both relative to maintenance), within subjects. This analysis showed main effects of task ($F_{1,9} = 21.7, P < 0.05$), IPS ROI ($F_{1,5} = 10.6, P < 0.05$) and a task × IPS ROI interaction ($F_{1,5} = 8.4, P < 0.05$). Post hoc t-tests indicated that the response in IPS1 was significantly higher for spatial manipulation than attention shifts across all 4 conditions (LHipsi: $t_{(9)} = 2.5$; RHipsi: $t_{(9)} = 4.5$; LHcontra: $t_{(9)} = 4.3$; RHcontra: $t_{(9)} = 3.3$; all $P < 0.05$). These results suggest that though the
Figure 6. Attention shift and arithmetic control tasks. (a) Inflated left and right hemisphere maps of significant group-level activation in all 3 tasks (red = spatial WM manipulation, yellow = attention shift, light orange = arithmetic, pink = attention shift + arithmetic, green = spatial WM manipulation + attention shift, dark orange = arithmetic + spatial WM manipulation, white = all 3 tasks), in 10 participants, displayed at P < 0.001 uncorrected. (b–g) Parameter estimates from first-level SPM models were averaged within each participants’ IPS regions and across participants. Plots show task-maintenance contrasts for contralateral (CL) and ipsilateral (IL) trials, relative to the hemisphere shown. (b,c) Left and right hemisphere, spatial WM manipulation-maintenance in 10 participants who returned for the control tasks, (d,e) Left and right hemisphere attention shifts. (f,g) Left and right hemisphere arithmetic. Plots show means with error bars indicating standard errors.
spatial WM manipulation task included a covert attention shift, attention shifts alone are unlikely to account for the observed pattern of activity in the IPS.

**Control Task 2: Mental Arithmetic**

This task was run to control for general effects of task difficulty, and involved performing cued mental arithmetic on remembered 2-digit numbers.

**Behavior**

Average accuracy for number maintenance and mental arithmetic was 90% and 82%, respectively; these were significantly different \((t_{10} = 4.2, P < 0.05)\). Accuracy was compared between the arithmetic and spatial WM manipulation tasks using a rm-ANOVA, with task (spatial vs. arithmetic) and manipulation (vs. maintenance) factors. This analysis showed only a significant main effect of manipulation \((F_{1,9} = 23.6, P < 0.05)\) and probe (correct vs. incorrect) \((F_{1,9} = 15.1, P < 0.05)\).

**Neuroimaging**

Whole-brain group normalized analyses comparing arithmetic to number-maintenance (contrast: [left + right hemifield arithmetic] − [left + right hemifield maintenance]) showed engagement of frontal and parietal regions, similar to the spatial WM manipulation task, but with a leftward bias particularly in the prefrontal cortex (Fig. 6a, orange). These included a midcingulate \((l[28 8 30], N = 5401, Z = 5.0)\) and bilateral caudate \((-16 12 18, Z = 4.47; [14 14 18], Z = 4.8)\) cluster, bilateral anterior parietal \((-50 −36 44), N = 560, Z = 4.5; [48 −32 44], N = 548, Z = 4.0\), left anterior calcarine sulcus \((-18 −62 2), N = 142, Z = 7.7)\), bilateral parieto/occipital \((-28 −62 30), N = 484, Z = 6.7; [-28 −68 30], N = 360, Z = 3.8)\), precuneus \((8 −64 48), N = 129, Z = 6.5)\), left inferior frontal gyrus \((-44 34 16), N = 162, Z = 3.8)\), and a cluster including SMA and bilateral FEF peak \(([18 4 44], N = 1121, Z = 6.2)\).

Within IPS regions, arithmetic versus maintenance effects for IL and CL numbers in the left and right hemispheres are shown in Figure 6f/g. A rm-ANOVA compared spatial WM manipulation (vs. maintenance) with arithmetic (vs. maintenance), within subjects. This analysis showed main effects of IPS ROI \((F_{4,36} = 6.7, P < 0.05)\), and a task × IPS ROI interaction \((F_{4,36} = 12.3, P < 0.05)\). Post hoc contrasts indicated that the response in IPS1 was significantly higher for spatial WM manipulation (vs. maintenance) than arithmetic (vs. maintenance) averaged over all 4 conditions \((t_{9} = 3.6, P < 0.05)\). Differences in IPS3, where the arithmetic responses peaked, were not significant \((P=0.4)\). These results demonstrate that the pattern of activation observed during the spatial WM manipulation task is not general to all challenging WM tasks that engage fronto-parietal regions.

**Eye Position**

For the WM-manipulation task \((N = 7)\), participants spent an average of 97% of the time within 1° of center (range 93–99%). Six of 7 participants showed no systematic bias in eye position toward the maintained hemifield \((P >0.15)\); 1 participant showed a bias toward the remembered hemifield \((P =0.01)\); however, this effect was only apparent in the first of 4 sessions, suggesting an improvement with practice. No participants showed a significant increase in the standard deviation of eye position during the manipulation phase of trials relative to maintenance \((all P > 0.2)\). Results were similar for the control tasks. For the attention-shift task \((N = 7)\), participants spent an average of 96% of the time within 1° of center (range 93–99%). Participants showed no systematic bias in eye position toward the maintained hemifield \((all P >0.15)\). There was no increase in eye position variability during attention shifts relative to the initial maintenance period \((all P >0.2)\). For the arithmetic task \((N = 5)\), participants spent an average of 97% of the time within 1° of center (range 93–99%). Participants showed no systematic bias in eye position toward the maintained hemifield \((all P >0.15)\), or increased eye position variability during mental arithmetic \((all P >0.2)\).

**Discussion**

In this study, we investigated the involvement of visuotopic regions along the IPS in the maintenance and manipulation of spatial information in WM. The task we employed was designed to preferentially engage IPS CL to a presented target during WM maintenance, and test whether manipulation would affect IPS activation in a lateralized fashion, as well as whether IPS regions 0–4 would be differentially engaged by this task. We found that during manipulation, activity increased in bilateral IPS regions and, in most participants, this response peaked in IPS1. Functional connectivity analyses showed that during manipulation IPS regions increased connectivity to prefrontal regions such as SMA and FEF, relative to maintenance. We also found evidence for target-location-dependent increases in interhemispheric IPS and dorsal visual connectivity. These findings suggest that visuotopic IPS plays a role in the spatial manipulation of information in WM.

Two control tasks were used to test the specificity of the observed effects. While the spatial WM manipulation task included a covert attention shift, we found that covert attention shifts alone engaged a pattern of activation in the IPS that was distinct from the spatial-manipulation task. This suggests that manipulation responses in the IPS were not driven by solely by attention shifts. We also used a similarly structured mental arithmetic task to control for general effects of task difficulty, and found a distinct anteriorly shifted pattern of IPS activation. Taken together, these control tasks show that IPS engagement peaking in IPS1 is not general to all tasks engaging the fronto-parietal attention network, as both control tasks engaged regions of this network as well. We also note that previous work has functionally dissociated mental arithmetic from spatial attention shifts and shown a similar functional pattern to that observed here (Simon et al. 2002, 2004).

The IPS has previously been implicated in the mental reordering of images (Champod and Petrides 2007), words (Champod and Petrides 2007), pitch information (Foster and Zatorre 2010), and melodies (Zatorre et al. 2010). This work suggests a domain general role for the IPS in tasks that require manipulation of information in WM. Our study adds to this work by showing bilateral IPS engagement, peaking in IPS1, during spatial WM manipulation. Interestingly, among visuotopic IPS regions, IPS1 shows stronger structural connections to dorsal visual regions, than anterior IPS regions (Greenberg et al. 2012; Bray et al. 2013a). It has been suggested that this parieto-occipital connectivity is important for the control of
visual attention (Greenberg et al. 2012). As we found that mental manipulation of numbers (arithmetic) showed a different pattern of IPS activation, posterior IPS may play a particular role in the manipulation of spatial information. Further work will be required to determine the specificity of this pattern during WM manipulation tasks in different domains.

Many previous investigations of functional connectivity changes during WM have focused on changes in fronto-parietal functional connectivity (Honey et al. 2002; Klingberg 2006; Ma et al. 2012). Here, we found significant connectivity changes between IPS seeds and SMA and FEF, which were not target-location dependent. We additionally found target-location-specific connectivity changes with IPS regions in the hemisphere opposite to the seed, during manipulation trials CL to the given hemisphere. These findings indicate that both fronto-parietal interactions and interhemispheric parietal interactions are important for spatial WM manipulation. Interhemispheric parietal functional connectivity has also recently been linked to numerical cognition (Park et al. 2013).

The peak WM maintenance response identified here was in IPS2–3. This peak was more anterior than a previous study that tested the effects of increasing visual short-term memory (VSTM) load, and found that VSTM primarily drives IPS0–2, relative to IPS3–4 (Sheremata et al. 2010). Differences could be due to differences in analytic approach; we used averaged parameter estimates rather than quantifying the proportion of significant voxel overlap, and as our task was event-related rather than a block design, differences may be related to sustained versus transient effects. Jerde et al. (2012) showed delay period activation, during a WM task similar to the one employed here (with a longer delay), that decreased from IPS3 to IPS0; this pattern of activation more closely resembles our findings.

In the spatial WM maintenance task, we found that while IPS2–3 showed the strongest overall engagement during maintenance, V3A/B showed the strongest lateralization of activity. V3A shows different properties from adjacent V3d including motion selectivity and larger receptive fields (Bartolomeo et al. 1994), and responses to stereopsis (Tsaø et al. 2003). During retinotopic mapping experiments, V3A responds similarly to early visual regions, showing sensitivity to stimulus alone, whereas more dorsal IPS regions are more strongly engaged when attention is maintained on the periodic mapping stimulus (Saygin and Sereno 2008). Previous work has implicated this region in WM encoding (Pessoa et al. 2002; Sneed et al. 2012). The task used in the current study was not designed to disentangle encoding relative to delay period effects in WM. However, our results suggest that V3A/B plays a role in spatial WM, and interacts with the IPS during spatial WM manipulation.

While tasks involving visuospatial imagery and WM typically show bilateral activity along the IPS, closer investigation has shown hemispheric asymmetry in responses in this region. Formisano et al. (2002) showed that the left PPC was engaged earlier than the right during a visual imagery task. Sack et al. (2002) also showed that TMS over right PPC significantly affected performance on this task, while TMS over left PPC did not. This suggests that while the left and right PPC show similar functional engagement during visuospatial tasks, the right PPC may be able to compensate for injury to the left, but not vice versa. Visuotopic IPS regions also show hemispheric asymmetries, for example, IPS1 and IPS2 show a stronger CL bias during spatial attention in the left hemisphere than in the right (Szczepanski et al. 2010). Similarly, maintaining an increasing number of items in visual short-term memory (VSTM) increased activation in the left IPS only for stimuli presented in the CL hemisphere, while the right increased activation for remembered stimuli in both ipsi- and contralateral hemifields (Sheremata et al. 2010). The task used here was designed to elicit asymmetric activation during maintenance, and probe differences in hemispheric recruitment during manipulation. Despite both pre- and postmanipulation target locations being in the same hemifield, we found bilateral IPS activation that was not significantly different between hemispheres. That we did not observe significant asymmetry during manipulation, or during an arithmetic control task, suggests that load-dependent asymmetry in IPS0–2 may be specific to VSTM and not general to tasks with increasing difficulty/cognitive load.

Patients with lesions to the parietal lobes often neglect or are unable to attend to stimuli presented in the hemifield CL to their injury. However, there is an apparent dissociation between injuries that cause perceptual neglect from injuries that cause neglect in visuospatial imagery (Bartolomeo et al. 1994; Coslett 1997). Here, we describe changes in activation in specific IPS subregions during manipulation, relative to maintenance, in WM. These data suggest some dissociation between regions involved in maintaining spatial attention from those involved in manipulating a spatial mental image, which could help to account for the observed double dissociation in perceptual and imagery neglect patients.

A network including bilateral IPS and FEF has been implicated in attentional orienting (Hopfinger et al. 2000), with recent work showing directed influences between these regions (Vossel et al. 2012). Here, we identified connectivity changes between the IPS and primarily left FEF during manipulation, that were independent of target location; this leftward bias may have been influenced by the right-handed motor response. However, a more precise characterization of target-location dependent IPS to FEF connectivity may have been possible with individually defined FEF regions (Hagler and Sereno 2006; Kastner et al. 2007). IPS2 has been suggested to be a potential homolog for macaque area LIP (Silver et al. 2005; Arcaro et al. 2011); a region known to make structural connections with FEF (Blatt et al., 1990; Anderson et al. 2011). A recent study highlighted both structural and functional connectivity between IPS2 and FEF believed to underlie spatial attention (Szczepanski et al. 2013).

There are several limitations associated with this study. The first is that eye-tracking was not performed concurrently with tasks in the scanner. However, the fact that we were able to uncover visuotopic maps in the mapping task, and hemispherically lateralized attention responses in the WM manipulation task, suggests that participants were generally compliant with central fixation. Additionally, a separate group of participants performed these tasks with eye-tracking outside the scanner; with a similar amount of practice, these participants were able to comply with central fixation. Several published reports have used eye-tracking to confirm that participants are able to comply with fixation during mapping scans (Szczepanski et al. 2010), and others have confirmed that visuotopic mapping is feasible with and without concurrent eye-tracking (Saygin and Sereno 2008; Sheremata et al. 2010). A second limitation is that with the current protocol we were unable to reliably delineate IPS5 or SPL1 regions, as have been identified in previous work (Szczepanski et al. 2010), or visuotopic regions in the prefrontal cortex (Hagler and Sereno 2006;
Kastner et al. 2007). Mapping these regions may be possible with a larger number of trials/scans or a different mapping paradigm [e.g., visually guided saccades (Szczepanski et al. 2010)]. Finally, during the spatial WM manipulation task, targets appeared in sequential order around the circle, which may have induced anticipation effects. Appearance of these targets was spatially jittered, the temporal delay between trials varied and event onsets were modeled at the time of the rotation cue; however, anticipation effects could nonetheless have affected parameter estimates.

In conclusion, we present here an investigation into the involvement of visuotopic IPS during the mental manipulation of spatial information. We found that while IPS CL to a remembered target was preferentially engaged by WM maintenance, a bilateral IPS response peaking in IPS1 was engaged for mental manipulation of spatial stimuli. IPS engagement during manipulation was related to increased functional interactions with SMA, FEF, V3A/B, and IPS 0–4 in the opposite hemisphere. This work adds to a growing body of knowledge about the functions of visuotopic IPS. Delineating these functions is important for understanding cognitive difficulties in disorders affecting the parietal lobes, such as stroke (Ptak and Schnider 2011), and developmental disorders such as Turner syndrome (Bray et al. 2011, 2013b), Williams syndrome (Meyer-Lindenberg et al. 2004) and Klinefelter syndrome (Bryant et al. 2011). Because lesions and developmental abnormalities often affect a relatively large cortical area, topographic mapping offers the possibility of better understanding and predicting which cognitive and perceptual functions are affected, and which are relatively spared (Konen et al. 2011).

**Supplementary Material**

Supplementary material can be found at: http://www.cercor.oxfordjournals.org/

**Notes**

The authors acknowledge the support of iCore, the Hotchkiss Brain Institute and the Seaman Family MR Centre at the University of Calgary, WestGrid and Compute/Calcul Canada computer resources, Chris Sears and Kristin Newman, as well as retinotopy stimuli from D. Samuel Schwarzkopf (http://sampendu.wordpress.com/retinotopy-tutorial/).

**Funding**

This work was supported by the Hotchkiss Brain Institute and the Seaman Family MR Centre at the University of Calgary, S.B. was supported by a Canadian National Science and Engineering Research Council (NSERC) PDF and iCore. G.I. and A.A. were supported by NSERC-735872.

**References**


