A Combined Dynamic Causal Modeling and Functional MRI Study to Assess Visuospatial Symmetry Judgment in Healthy Subjects

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Introduction: Functional MRI (fMRI) studies aim to identify network components that are selectively engaged by a specific cognitive task. Analysis of effective connectivity between the brain regions identified in an fMRI task can be performed with techniques such as Dynamic Causal Modeling (DCM). In the present study, we focused on applying DCM to assess the functional connectivity between maximally activated brain regions in a visuospatial symmetry judgment task. Bilateral activations were observed in the brain regions associated with visuospatial cognition with more activity in the left hemisphere. Although right-hemisphere specialization for visuospatial processing has been suggested in literature, the exact neural mechanisms of asymmetry have not been deciphered yet and hemispheric specialization remains controversial. Thus a DCM analysis was carried out by our group to assess the asymmetry of visuospatial processing task administered in our fMRI study.

Materials & Methods: Eight right handed healthy controls (30–50 years) were chosen for the study. The fMRI task paradigm comprised two conditions run in a block design. In the resting phase, subjects focused at the centre of a crosswire placed on a slide and responded by pressing a button as and when a red circle appeared at the crosswire centre. In the activation phase, a 10-by-10 grid divided into two equal halves with a vertical blue line was projected onto a slide each second. Any two of the squares in the grid, one on either side of the central vertical line, were presented in red. Subjects had to judge symmetry in the position of the two red squares and respond by pressing the button when the squares were symmetrically positioned on the grid. The task was supposed to invoke 16 correct responses in each block. The subject's response was monitored with the help of in-house fabricated four-button feedback response device.

fMRI was carried out using 1.5 Tesla whole-body MRI system (Magnetom Vision, Siemens, Germany) with a circularly polarized head coil and 25 mT/m actively shielded gradient system. 33 oblique slices covering entire brain were acquired using gradient echo based interleaved EPI sequence with TE = 64ms and field of view = 230 x 230mm^2. 65 sequential image volumes (belonging to six cycles + one baseline for eliminating T_1 saturation effects and acclimatization of the patient to the gradient noise) were taken with an optimized inter-scan interval of 7.2 seconds. Pre-processing and post-processing were performed using SPM5 software. Single subject analysis was done with FWE corrected $p \leq 0.001$. One-sample 't' test for group analysis within task (FDR corrected $p \leq 0.01$, extent threshold 'k' = 50 voxels) was also performed. The anatomical representation of the clusters was related to cytoarchitectonic maps as implemented in the SPM Anatomy Toolbox [1]. The group results were then used for choosing the regions of interest (ROIs) for the effective connectivity analysis. Subject-specific ROI's were drawn for all eight subjects according to the nearest local maxima in relation to the group coordinates. Twelve models were hypothesized, analyzing the direct effect of input on each of the components of the model along with its modulatory effect on the effective connectivity between the regions in both hemispheres. In the absence of input, bidirectional connectivity was assumed between the regions as that model showed the maximum strength in a prior analysis for the best model for intrinsic connectivity.

Results & Discussion: BOLD activations were observed in the Superior and Inferior Parietal Lobule (SPL (7A) and SPL (7P)); Extrastriate visual cortical areas (Area 18, hOC3v (v3v) and hOC4v (v4)); Middle Frontal and Precentral Gyrus (predominantly Area 6); Inferior Frontal Gyrus (p. Opercularis) (Area 44), Thalamus and Cerebellum for visuospatial symmetry judgment task. These regions are known to play a critical role in the execution and implementation of spatial cognition skills [2]. The dorsal stream of the visual cortex was chosen to be the primary network for visuospatial processing and three important regions namely extrastriate visual cortical area left hOC4v(v4) and right MOG, posterior parietal cortical area SPL(7A) and secondary motor area BA 6 were chosen in each hemisphere for an effective connectivity analysis using DCM. Using the Bayesian Model Selection procedure, we found that out of the 12 models, the model analyzing the effect of the task on SPL (7A) and the connectivity between SPL (7A) and BA 6 was optimal at the group level for both hemispheres. DCM clearly demonstrates the critical role the posterior parietal cortex plays in visuospatial processing. The parietal cortex receives somatosensory and visual inputs, uses them to determine the position of the target in space thereby producing internal models of the movement to be made, prior to the involvement of the rostral part of Brodmann Area 6 in the updating of spatial information and decision making [2, 3]. Although the effect of the task was greater in right SPL; the connectivity in the presence of the task was excitatory in the left hemisphere and inhibitory in the right hemisphere (Figure 1). This in turn highlights the greater involvement of the left hemisphere in visual symmetry assessment which is also evident from the larger number of voxels activated in the left hemisphere as revealed by fMRI analysis (Table 1).

Conclusion: Our preliminary findings indicate the contrasting nature of the effective connectivity between the posterior parietal cortex and secondary motor area between the two hemispheres in response to the same task. It will be interesting to study dynamic causal models connecting right SPL to left BA6 and vice versa to better assess hemispheric asymmetries. DCM is thus a novel way of using fMRI to address functional hemispheric differences in a cognitive task that shows bilateral representation.

References:

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Table 1: Extent of activation in the regions chosen for DCM analyses in each hemisphere for the subject group.

Hemisphere	Region	Number of Voxels
Left	SPL(7A)	976.3
Right	SPL(7A)	632.8
Left	hOC4v(v4)	396.3
Right	MOG	267.6
Left	MFG (BA 6)	53.8
Right	MFG (BA 6)	62.1

Figure 1: DCM analyses of visuospatial symmetry judgment in each hemisphere for the healthy subject group (* Connection strength in Hz; p = posterior probability).