Effective connectivity analysis of visual-motor network in patients with schizophrenia

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Introduction: Previous work has shown that effective connectivity (EC) can be used to map connections between brain areas in auditory-motor tasks in healthy controls (HC) [1]. Previous work in schizophrenia has shown low-level abnormalities in perceptual processing of visual stimuli [2] and also motor function [3]. Although there is information about altered functional connectivity in the visuo-motor pathway, the directionality of the altered connections, which is critical given the known causal flow of information between visual and motor cortices, is unknown. In our current study, we have used fMRI to study the EC between visual and motor cortices in HC and patients with schizophrenia (SZ). We investigated if there was altered connectivity of paths originating from the visual cortex and projecting to motor areas in schizophrenia participants compared to the healthy controls.

Methods: Functional magnetic resonance imaging (fMRI) data was collected on a 3T head-only (Siemens Allegra) scanner in 21 off-medication SZ and 20 healthy control (HC) subjects. During the performance of the fMRI task, subjects were shown a series of words and after each, asked to press a button with their left or right index finger to indicate if the word was novel or previously seen. The functional data were acquired using the gradient recalled echo-planar imaging (EPI) sequence (TR 2.1 s, 4-mm slice thickness, 1-mm gap, 26 axial slices). All data were preprocessed using SPM 8. Five regions of interest (ROI) were chosen based on the activation maps and the mean percent signal change time series were extracted. The resulting time series were temporally normalized and deconvolved using a cubature Kalman filter [4] and input into a dynamic multivariate autoregressive (dMVAR) [5,6,7] model to obtain connectivity between every pair of ROIs as a function of time. Based on the causal connectivity values we obtained the dominant directional influence score for each path. For example, if the connectivity strength of a path from ROI A to ROI B is greater than ROI B to ROI A, then the path ROI A to ROI B will be assigned an influence score of (path weight of ROI A to ROI B) - (path weight of ROI B to ROI A) and the influence score of path ROI B to ROI A will be set to zero. The obtained influence scores during the task of interest (when the participant gave a correct answer) were then populated into different samples for both HC and SZ participants separately. Then a right tailed t-test was performed on the sample to obtain the paths that were significantly ($p<0.05$) greater than zero for both the groups (HC and SZ). These paths were illustrated by using the brainnet viewer toolbox [8].

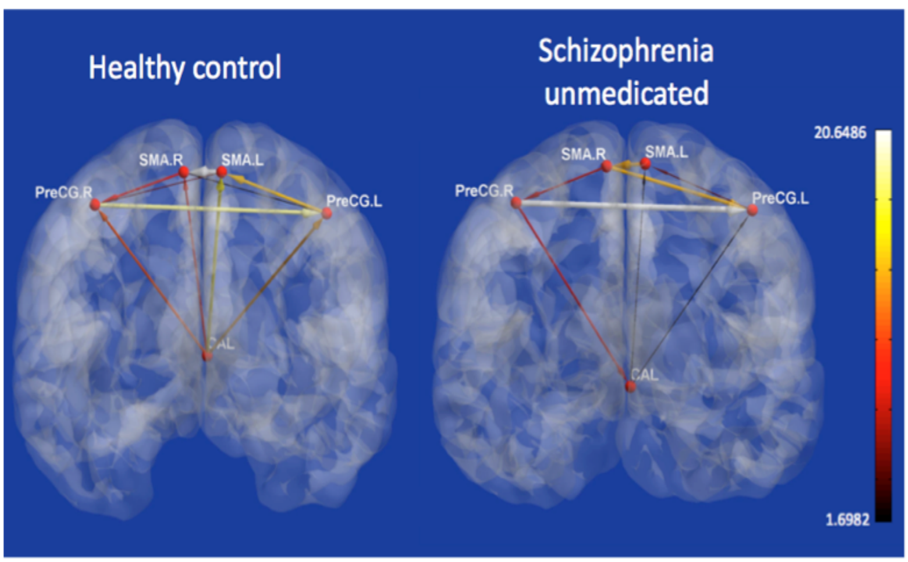

Figure 1. Paths that were significant within the visual-motor network in healthy controls (n = 20) and unmedicated patients with schizophrenia (n = 21). CAL, calcarine sulcus; PreCG.L, left precentral gyrus; PreCG.R, right precentral gyrus; SMA.L, left supplementary motor area; SMA.R, right supplementary motor area. Color bar indicates *t* values.

Results: Figure 1 shows the paths that were significantly greater than zero for both HC and SZ participants. We found that, HC did show strong unidirectional connections that originated from the calcarine sulcus and projected to the bilateral precentral gyrus (PreCG) and bilateral supplementary motor areas (SMA). However, SZ participants showed less robust projections from calcarine sulcus to bilateral PreCG and SMA.

Discussion: These results were consistent with previous work showing that in a visual-motor task, neural information proceeds from visual cortex to motor and supplementary motor areas [1]. Also, it shows a novel finding that the visual-motor deficits seen in schizophrenia may stem from altered connectivity within and between these networks. The effective connectivity method utilized was able to map connectivity within the visual-motor system in healthy controls and patients with schizophrenia. Also, this work showed that patients with schizophrenia have low-level disruption of visual-motor connectivity, which adds to a growing body of literature that schizophrenia is characterized by disrupted connectivity within multiple neural networks, some which are not traditionally associated with Schizophrenia.

References: [1] Abler, B., et al. Magnetic Resonance Imaging, 2006; 24(2): 181-185. [2] Vinckier, F., et al. Neuropsychologia 2013; doi: http://dx.doi.org/10.1016/j.neuropsychologia.2013.10.004. [3] Walther, S., et al. Neurobiology of Disease, 2011; 42(3): 276-283. [4] M Havlicek, et al, NeuroImage 2011, 56(4): 2109-2128. [5] Lacey et al, NeuroImage 2011, 55:420–433. [6] Sato et al, NeuroImage, 31:187–196, 2006. [7] Sathian K, et al. J Neurosci. 2013; 33(12): 5387–5398. [8] Xia M, et al. PLoS ONE 2013;8(7): e68910.