Motor impairment in schizophrenics: A combined fMRI and VBM study

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Introduction: Schizophrenia is a chronic and psychotic mental disorder, characterized by disturbances of thought, behaviour and social interactions. Previous neuropsychological and functional imaging studies, showed deficits in long-term memory, verbal memory, psychomotor speed, executive functioning and vigilance consistently and usually associated with poor functional outcome (1- 4). Various studies have also shown structural changes in schizophrenics using Voxel based morphometry (VBM). But the relation between structural and functional alterations in schizophrenia remains unclear. Therefore, the present study sought to investigate whether functional alterations in schizophrenia are also associated with structural brain aberrations, directly in related brain regions or in anatomically closely connected areas, using a simple motor task.

Materials and Methods: 16 right handed healthy subjects (mean age± SD = 32.63±7.64 years) and 16 schizophrenic patients (mean age± SD =34.06±9.89 years) were chosen for the study. All patients were on antipsychotic medications at the time of scan. The functional and structural data were collected in the same session on a 3 Tesla whole-body MRI system (Magnetom Skyra, Siemens, Germany). For structural images, high-resolution MR images were obtained with a T1- weighted 3D gradient echo sequence (MPRAGE: Magnetization Prepared Rapid Acquisition Gradient Echo, 160 sagittal slices, slice thickness = 1 mm, field of view = 256 mm, TR = 1900 ms, TE = 2.07 ms). In addition, a T2-weighted turbo spin echo (TE=100 ms, flip angle=150°, field of view=220mm) scan with 25 axial 4mm slices and 1.2 mm gap of the whole brain was acquired for neuro-diagnostic evaluation to rule out any other neurological problem. Functional images were acquired using echo-planar T2*-weighted sequence. Each brain volume consisted of 36 interleaved 3 mm thick slices with 0.6 mm interslice gap and parallel to AC-PC axis (TE = 36 ms; TR = 3000 ms; FOV = 210 mm; flip angle = 90°; voxel size = 3.3 X 3.3 X 3 mm). Block paradigm (BABABABA….) with alternating phases of activation (A) and baseline (B) was chosen. 110 sequential image volumes (belonging to five cycles + one baseline for eliminating T1 saturation effects and acclimatization of the patient to the gradient noise) were taken. In the fMRI experiment, subjects performed a discrete tapping task with the right index finger at tapping rate of 120 taps/min. Each cycle consisted of 10 measurements for activation and rest phase, resulting in a total of 110 measurements for complete study. Visual Stimuli were presented using fMRI hardware from NordicNeuroLab http://www.nordicneurolab.com/Products_and_Solutions/nordic_fMRI_solution/index.aspx) as a cue for finger tapping rate. Pre-processing and post-processing of MRI scans were performed using SPM8 (Wellcome Department of Cognitive Neurology) implemented in MATLAB R2008a (version 7.6.0 (Mathworks, Sher- born, MA)). For functional analysis, a one-sample t-test was performed for group analysis with $p<0.05$ (FWE corrected) and voxel threshold of 50 voxels. For structural analysis, the normalized, segmented, smoothed and modulated data sets were assessed using 'Two-sample t-test' , threshold at $p<0.001$, uncorrected, to find morphological changes in the brain tissue composition of schizophrenic subjects relative to the control groups. The anatomical representation of the clusters was related to cytoarchitectonic maps as implemented in the SPM Anatomy Toolbox [4].

Results: The fMRI study showed relatively less activation in the left precentral and postcentral gyrus and right cerebellum in schizophrenic patients as compared to controls during finger tapping task (Figure 1). On the other hand, VBM revealed grey matter decreases in the left precentral, postcentral gyrus and left middle frontal gyrus while white matter decreases in the right cerebellum and right inferior temporal gyrus of schizophrenics as compared to controls (Table I and II).

Discussion: This study emphazises the correlation of functional and structural changes in schizophrenic patients. In fMRI study, group analysis showed reduced activation in motor areas i.e., the left precentral and postcentral gyrus and right cerebellum in schizophrenic patients as compared to controls during finger tapping task. Similarly VBM results also showed grey matter loss in the left precentral and postcentral gyrus and white matter decreases in the right cerebellum in schizophrenics. Although postcentral gyrus is associated with sensory function while precentral gyrus is related to movement. However, movement is also accompanied by activation of the postcentral gyrus and somatosensory stimuli activate the precentral gyrus (5). Since the primary motor cortex is responsible for the direct production of movements via its outputs to the pyramidal tract, any grey or white matter loss in this area will produce a motor deficit in the corresponding parts of the body. Whereas cerebellum provides a route by which information from sensory, motor, and cognitive domains influences the generation and control of movement at the level of primary motor cortex (6). Therefore, any white matter reduction in the cerebellum can result in the cerebellar and cognitive deficits comprising of executive, motor, attention, visuospatial and linguistic impairments. Our VBM results are well supported by fMRI results that have shown motor function deficit in schizophrenic patients as compared to the healthy subjects in the execution of the same motor task. In addition, grey matter loss in middle frontal gyrus and white matter reduction in temporal gyrus as revealed by VBM, might be associated with deficits in attention, problem-solving and decision making and high-level visual processing of complex stimuli and memory functions respectively in schizophrenics (7).

Conclusion: The study suggests motor impairment in schizophrenic subjects as compared to healthy controls using simple motor task. The grey and white matter changes prominently in motor cortex and cerebellum may account for the motor deficit in schizophrenic subjects as compared to controls. Our VBM results very well support fMRI findings in schizophrenic patients.

References:

1. Am J Psychiatry 1996; 153: 321-330.
2. Psychiatry 1997; 60: 281-291.
3. Prog Neuropsychopharmacol Biol Psychiatry. 2002 Apr; 26(3):421-6.
4. Schizophrenia Research 2007; 89: 191-197.
5. Stroke 2000; 31: 668-671.
6. The Journal of Neuroscience 2003; 23(23): 8432- 8444.
7. Atlas of functional neuroanatomy. In Taylor and Francis Groups. 2006: 40-60.

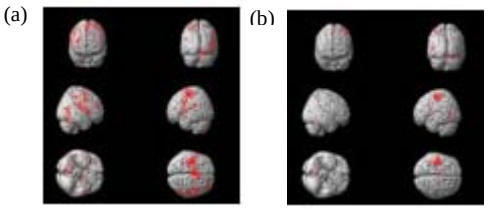

Figure 1: 3D rendered view showing group analysis of BOLD activation pattern in the brain of (a) healthy controls and (b) schizophrenic patients corresponding to 120taps/min.

Table I

Localization of peak voxels	Cluster Size
Controls versus Schizophrenic Subjects Contrast	
Left middle frontal gyrus	275
Left postcentral gyrus	
Left precentral Gyrus	104

Table II

Localization of peak voxels	Cluster Size
Controls versus Schizophrenic Subjects Contrast	
Right cerebellum	429
Right inferior temporal gyrus	360

Table I and II shows grey and white matter, volume loss in schizophrenics as compared to controls in VBM analysis.