Altered brain activation in schizophrenia during visually guided motor selection revealed by fMRI

Dear Editors

Recent advances in functional neuroimaging technology have revealed some evidence of altered brain activation during cognitive processes in patients with schizophrenia. We previously conducted a functional magnetic resonance imaging (fMRI) study in normal volunteers during a visually guided motor selection task based on the ‘janken game’ (‘paper-scissors-stone’ game), which involves several cognitive processes including visual shape discrimination, attentional set-shifting for motor selection rules as well as motor preparation and execution (Omori et al., 1999). The results demonstrated that the task activated the ventral visual pathway, prefrontal cortex and frontal motor fields. Since several forms of deficit in visual processing as well as frontal dysfunction have been shown in schizophrenia (Park and Holzman, 1992; O'Donnell et al., 1996), the difference in brain activation while performing the above-mentioned task was examined by fMRI between six right-handed medicated patients with DSM-IV schizophrenia (three men and three women, mean age 27.0 ± 6.1 years, mean duration of illness 4.9 ± 4.8 years, mean chlorpromazine equivalent dose 353.3 ± 371.9 mg) and six age-matched normal controls (three men and three women, mean age 22.0 ± 2.0 years) under conditions of matched performance levels across the groups. All subjects gave their written informed consent for the study.

Each subject had two experimental sessions; each session consisted of four rest and four task periods. Each period was 18 s long, and the rest and task periods alternated. During the rest periods, no task was required other than keeping eyes on the screen. During the task periods, one of three janken hand-shapes (stone, scissors or paper) was randomly projected every 1.5 s on the screen as a visual cue. The subjects were instructed to make the hand-shape that beats the first visual cue with their right hand and to make the losing hand-shape in response to the second cue, alternating winning and losing: the win rule alternated with the lose rule at each visual cue. Since reciprocal conversion between the win and lose rules of janken was carried out, this task requires set-shifting of rules for motor selection.

In each subject whole brain functional images [T2*-weighted; TR/TE = 3.6 s/50 ms, a flip angle = 90°, a field of view = 220 mm, 64 × 64 matrix and 12 slices (voxel size = 3.44 × 3.44 × 10 mm)] were acquired with a 1.5 T MRI system (GE, USA). The images were realigned, normalized and spatially smoothed using SPM96 (Wellcome Department of Cognitive Neurology, London, UK) (Friston et al., 1995). The analysis involved subtraction of the rest condition from the task condition for schizophrenics and controls, followed by direct comparisons of these subtractions between the two groups. The statistical threshold was set at P < 0.05 (corrected, Z > 3.09) for height and P < 0.05 (corrected) for extent. To avoid the potential contribution of relative deactivation in one group to the between-group analysis, the results from the subtraction were masked by activations in the corresponding subtraction for both groups (masking threshold was set at P = 0.05). Other details of the experimental procedures have been described in our previous paper (Omori et al., 1999).

There was no significant difference in task performances between the schizophrenic and control groups (percent error, 5.38 ± 9.26% and 3.99 ± 4.34%, respectively; P = 0.747, Mann-Whitney U test: reaction time, 471.7 ± 86.8 ms and 391.6 ± 81.3 ms, respectively; P = 0.078).
Both groups showed approximately the same pattern of significant activations in the left prefrontal cortex including the middle (Brodmann area [BA] 46) and inferior (BA 44) frontal gyri, the supplementary motor area (SMA; BA 6), the left premotor (PMC; BA 6) and sensorimotor cortex (SMC; BA 4), the left inferior parietal lobe (BA 40) and precuneus (BA 7), and bilateral ventral visual cortices, mainly the fusiform (BA 19) and lingual (BA 18) gyri during the task condition compared to the rest condition. The right inferior frontal gyrus (BA 44) and PMC (BA 6) were significantly activated only in the schizophrenics (Fig. 1A–D). Group comparison showed that schizophrenics demonstrated greater activation in the right inferior frontal gyrus (BA 44) and SMA (BA 6) but less activation in the bilateral ventral visual cortices (BA 18 and 19), left SMC (BA 4) and precuneus (BA 7) compared to that in controls (Fig. 1E–H). Percentage signal changes in the right inferior frontal gyrus [Talairach coordinates (Talairach and Tournoux, 1988) x=44, y=8, z=20] and SMA (x=0, y=12, z=52) of the patient group were significantly greater than those in the control group (inferior frontal, 0.35±0.23 and 0.12±0.07, respectively; P<0.0001, t-test: SMA, 0.29±0.36 and 0.05±0.25, respectively; P=0.0014).

These results may suggest a reduction in processing efficiency in the ventral visual areas of schizophrenia with secondary increased utilization of the frontal cortex to compensate for such insufficiency, as reported in the visual processing of old normal subjects compared to young subjects (Grady et al., 1994).

Another possibility is that the cognitive capacity of the frontal cortex in schizophrenia may be primarily impaired. The rostral SMA and right inferior frontal gyrus are active in the movement decision-making process (Humberstone et al., 1997) or response inhibition (Kawashima et al., 1996; Konishi et al., 1998). Our janken task also includes such processes, in which the subject needs to select an appropriate hand-shape in response to the present rule (win or lose) and to inhibit another response to the opposing rule. Thus, insufficient processing capacity of the frontal cortex in schizophrenia may result in inappropriate overactivation or recruitment of cortices less activated in normal subjects to accurately complete the present motor selection task, with reciprocal inhibition of the visual cortices (Bench et al., 1993).

Since these are just preliminary results with a small number of subjects who were on neuroleptic medication, further studies are needed to confirm our speculation.

Fig. 1. Statistical parametric maps showing areas activated during the task condition relative to the rest condition for the control group (A, B) and schizophrenic group (C, D). They are also showing areas of greater task-related activations in the schizophrenic group compared to the control group (E, F) and in the control group compared to the schizophrenic group (G, H). Views are shown from the right (A, C, E, G) and above (B, D, F, H).
References


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