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Selective impairment of attentional networks of orienting and executive control in schizophrenia

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Abstract

Background: Difficulty attending is a common deficit of schizophrenic patients. However, it is not known whether this is a global attentional deficit or relates to a specific attentional network.
Method: This study used the attention network test to compare schizophrenic patients ($N=77$) with controls ($N=53$) on the efficiency of three anatomically defined attentional networks: alerting, orienting, and executive control.
Results: Schizophrenic patients showed a large and highly significant deficit in the executive network and a smaller but significant deficit in the orienting network as well as in overall RT and accuracy. There was no deficit in the alerting network.
Conclusion: These results suggest some specificity in the attentional networks influenced by the disorder. The executive attention network has been shown in normal subjects to activate the anterior cingulate and lateral prefrontal areas. Previous data using neuroimaging with schizophrenic patients has shown abnormal control by the anterior cingulate. Our findings support this previous research by indicating that the major attentional deficit in schizophrenic patients is in a network that includes the anterior cingulate.

Keywords: Schizophrenia; Attention; Attentional networks; Alerting; Orienting; Executive control

1. Introduction

Recent theories have conceptualized attention as comprising three anatomically defined brain networks (Fan et al., 2003b; Posner and Petersen, 1990). The attentional component of alerting involves the ability

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to maintain the alert state tonically and the phasic response to a warning signal. It involves the cortical projection of the norepinephrine system (Marrocco and Davidson, 1998). The orienting network involves the selection of information from among numerous sensory inputs. The temporal parietal junction, superior parietal lobe and frontal eye fields are involved (Corbetta and Shulman, 2002). Blocking cholinergic input to the superior parietal lobe influences the ability to shift attention to cues (Davidson and Marrocco, 2000). Executive control of attention is involved in self-regulation of cognitions and emotions. It is most frequently measured by requiring a response to one aspect of a stimulus while ignoring a more dominant aspect. For example, to name the color a word is written in when the word spells a different color. The executive network involves the anterior cingulate cortex and lateral prefrontal cortical regions and is modulated by dopamine (Benes, 2000), with individual variations in executive attention related to genetic polymorphisms in genes related to dopamine (Diamond et al., 2004; Fan et al., 2003a; Fossella et al., 2002).

In various studies schizophrenic patients have been found to have a deficit in one or another of these attentional systems. Classical studies by Zahn et al. (1963) found that schizophrenic patients have trouble in responding well to warning signals, indicating an alerting deficit. In studies involving using cues to direct orienting to various locations it was shown that first break schizophrenic patients showed a specific deficit in orienting to stimuli on the right (Posner et al., 1988). Functional imaging studies have indicated a deficit in executive attention and abnormalities in activation of the dorsal anterior cingulate (Carter et al., 1997; Fletcher et al., 1999). These findings are with different patients and used different assays to probe the attentional deficit.

A method has been developed to assay the three attention networks within one experiment (Fan et al., 2002). The attention network test (ANT) provides a survey of the efficiency of the alerting, orienting and executive attention networks. Since the networks have been related to specific anatomy and neuromodulators, it would be useful to compare the performance of schizophrenic and control subjects in each of the networks using the attention network test. Accordingly we examined hospitalized patients with chronic schizophrenia on various neuroleptics with the attention network test in order to determine whether they would show generalized deficits in all attentional networks, or show specific deficits limited to the orienting and executive attention networks. We also examined the relationship between any deficits observed and variation on the patients' demographic and clinical characteristics, such as age, number of positive and negative symptoms, and duration of the disorder.

2. Methods

2.1. Participants

The current study included 77 hospitalized schizophrenic participants who met DSM-III-R criteria for schizophrenia (American Psychiatric Association, 1987). They were recruited from Hefei Psychiatry Hospital affiliated with Anhui Medial University, the largest provincial psychiatric facility located in Anhui Province, China. The following inclusion criteria were met by all participants: (a) no demonstrable brain disease other than schizophrenia (i.e. no history of loss of consciousness and no history of neurological conditions such as epilepsy, Parkinson's disease or brain injury), (b) no history of mental retardation, and (c) no evidence of current substance (including alcohol) abuse. Fifty-three normal adults were recruited from the same region as the control group. They also met the same inclusion criteria as the patient group and were matched in age and education level. All participants had normal vision and hearing and were able to understand the procedures of the experiment. Written informed consent was obtained from all participants.

2.2. Procedures and measures

The demographic and illness-related information of patients were determined by staff psychiatrists at the Hefei Psychiatry Hospital. Symptoms were assessed with the Scale for Assessment of Negative Symptoms (SANS) (Andreasen, 1983) and Scale for Assessment of Positive Symptoms (SAPS) (Andreasen, 1984). After giving informed consent, each of the study participants completed neuropsychological tests and the ANT.

2.3. Neuropsychological background tests

The Wechsler Adult Intelligence Scale-Revised Chinese Version (WAIS-RC) (Gong, 1992) was administered for measuring intelligence. The Wechsler Memory Scale-Chinese Version (WMS-C) (Gong, 1989) was employed to quantify memory function. The Word Fluency Test, to name animals with four legs within 1 min (Wang et al., 2002), was used to measure semantic function.

2.4. Attention network test

Participants viewed the stimuli shown on a computer screen and responses were collected via two response buttons. Stimuli consisted of a row of five visually presented horizontal black lines, with arrowheads pointing leftward or rightward, against a gray background where the target was a leftward or rightward arrowhead at the center. This target was flanked on either side by two arrows in the same direction (congruent condition), or in the opposite direction (incongruent condition), or by nothing (neutral condition). The participants' task was to identify the direction of the centrally presented arrow by pressing one button for the left direction with index finger of left hand and a second button for the right direction with index finger of right hand. Cues consisted of a 100 ms asterisk presented 400 ms before the target. There were four cue conditions: (1) no-cue, participants were shown a cross which was the same as the first fixation for 100 ms; (2) central-cue, which was at the central fixation point; (3) double-cue, in which cues were presented on the two possible target locations simultaneously (both above and below the fixation point); and (4) spatial-cue, in which the cue was presented on the target location (either above, below the central fixation point). ANT consisted of a 24-trial practice block and three experimental blocks of trials. Each experimental block consisted of 96 trials (48 conditions: 4 cue types $\times$ 2 target locations $\times$ 2 target directions $\times$ 3 congruencies, with two repetitions). The presentation of trials was in a random order. Participants were instructed to focus on a centrally located fixation cross throughout the task, and to respond as fast, and as accurately as possible.

2.5. Calculation of attention network efficiencies

ANT uses differences in reaction times (RT) derived from the different experimental conditions to measure the alerting, orienting and executive control networks. Values for attention network efficiency were calculated from the raw reaction time data as described below. To avoid the influence of the outliers, raw RTs with correct responses were clipped with a 100–1700 ms window. RTs outside this window were excluded. Standard deviations (SD) were calculated for each condition and RTs outside 2 SD of each condition were excluded. Then medians were calculated for each test condition (12 conditions in total: 4 cue types by 3 target types). The alerting effect was calculated by subtracting the mean of median RTs of the conditions with double cue from the mean of median RTs of the conditions with no cue. Since neither of these conditions provides information on the spatial location of the target, the subtraction gives a measure of alerting. The orienting effect was calculated by subtracting the mean of median RTs of the conditions with spatial cue from the mean of median RTs of the conditions with center cue. In both conditions the subject was alerted but only the spatial cue provided spatial information on where to orient. The conflict (executive) effect was calculated by subtracting the mean of median RTs of the conditions with congruent flankers from the mean of median RTs in the conditions with incongruent flankers.

3. Results

3.1. Demographic and clinical data

Schizophrenic patients aged between 17 and 57 years (mean = 28 years, 46 female and 31 male, 74 with right handedness and 3 left with handedness), and were educated for 5–15 years. Fifty-three normal controls were aged from 19 to 57 years (mean = 29 years, 27 female and 26 male, 51 with right handedness and 2 with left handedness) and educated for 5 to 15 years. There were no significant differences in age or years of education between the patient and the control groups. The mean duration of illness of schizophrenia was 4.3 years (from 0.5 to 15 years). The mean of SAPS for patients was 8.36 (SD, 3.66), whereas the mean of SANS for patients was 5.57 (SD,

Table 1
Demographic, clinical data and neuropsychological background tests scores and SD of schizophrenic patients and normal controls

	Schizophrenic patients	Normal controls
N	77	53
Age (years)	28.47(8.07)	29.42(12.63)
Gender	46f/31m	26f/27m
Education levels (years)	10.38(2.80)	10.25(2.93)
Handedness	74 R/3 L	51 R/2 L
Duration of disease	5.28(4.79)	
Global rating for symptom		
Scale for Assessment of Positive Symptom (SAPS)	8.36(3.66)	
Scale for Assessment of Negative Symptom (SANS)	5.57(5.56)	
Wechsler Adult Intelligence Scale-Revised Chinese (WAIS-RC)	102.25(8.89)	104.45(7.98)
Wechsler Memory Scale-Chinese (WMS-C)	101.92(8.02)	101.79(6.40)
Word fluency test	15.21(3.47)	16.28(3.02)

5.56). All but one patient was on maintenance atypical antipsychotic medicine.

3.2. The neuropsychological background data

There were no significant differences in mean level of intelligence, memory or semantic function between the two groups as shown in Table 1.

3.3. The efficiencies of three networks

The means and standard errors are summarized in Table 2. Across the whole test, the schizophrenic group had a longer overall mean reaction time than the control group ($t(128)=3.88$, $P<0.01$, two-tailed). Patients were also significantly less accurate than controls ($t(128)=2.88$, $P<0.01$, two-tailed). The data showed that patients took longer to resolve conflict (less efficient executive attention than controls) ($t(128)=4.30$, $p<0.01$). The differences between groups for alerting and orienting network scores were not significant ($t(128)=0.28$, $t(128)=1.60$ respectively, P's>0.05, two-tailed), although the data showed a trend reduced orienting scores for patients in comparison with controls.

Fig. 1 shows the frequency of patients and controls separately with various conflict scores. For controls, the numbers peaked in the 51–100 ms range. However, for the patients, it peaked in the 101–150 ms range and showed greater variability. It is clear that the patient group had both a larger mean score and a wider distribution of scores than the controls although there is a substantial overlap between the patient and control population.

Since RTs are generally longer in patients, it is useful to use the ratio to examine specific effects that are not influenced by overall reaction time. Table 2 also shows the ratio scores. In addition to the significant difference on conflict resolution ($t(128)=3.41$, $p<0.01$), the orienting network also showed a significant difference, $t(128)=2.73$, $p<0.01$ based on ratio scores. Comparing the patient and control groups, the difference based on ratio score of alerting effect was not significant ($t(128)<0.21$, $p>0.05$). We also used covariance to partial out the contribution of the overall RT to the network scores. The pattern shown above was the same using this approach. This result demonstrates that schizophrenic patients have selective impairments

Table 2
Attention network scores (in RT and ratio score) and accuracy (%) of schizophrenic and controls

	Schizophrenic patients (*N*=77)		Normal controls (*N*=53)	
	Mean	SE	Mean	SE
Alerting (ms) RT	32	4.10	31	3.52
Ratio	.042	.005	.044	0.005
Orienting (ms) RT	44	4.41	54	3.45
Ratio	.057**	.006	.078	0.004
Conflict (ms) RT	153**	10.03	99	4.33
Ratio	.193**	.011	.144	0.006
Mean RT(ms)	803**	19.85	696	16.78
Accuracy (%)	95**	0.92	98	0.33

*$p<.05$; **$p<.01$.

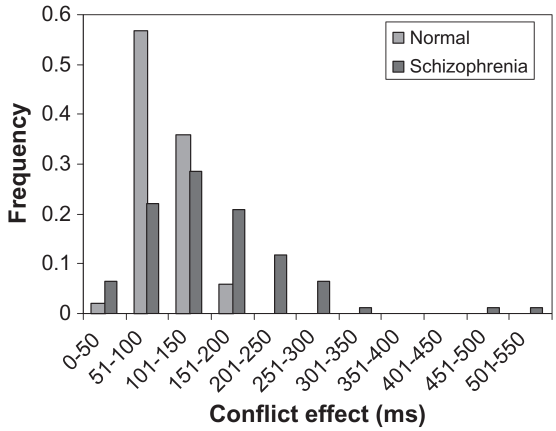

Fig. 1. The frequency of patients and normal controls within each conflict 50 ms score range. For normal controls, the numbers peaked in the 51–100 ms range. However, for the patients, it peaked in the 101–150 ms range and showed greater variability.

of the orienting and executive networks, while the alerting network is spared.

3.4. Correlations

An examination of the correlations between the networks shows that the scores for the three networks were not significantly correlated. We examined the relation of the scores for the attention network test with age, education IQ and word fluency. There was no evidence of correlations among these variables. Because hemispheric models of schizophrenia are common, we also examined whether left and right responses differed in patients and in controls. For patients mean RT was somewhat faster for right hand responses (796 ms) than for left hand responses (816 ms) and were also less accurate for right hand responses. For controls there were no significant differences.

4. Discussion

The attention network test appears to be very sensitive to attentional deficits in schizophrenic patients as it is in some other disorders (Fernandez-Duque and Black, in press; Posner, 2003; Posner et al., 2002; Sobin et al., 2004). The attention network test has the advantage of allowing for the comparison of the relative deficits in different attentional networks. In this sample of chronic, medicated schizophrenic patients there is a clear deficit in the executive network, related to the resolution of conflict, and a smaller deficit in orienting network for orienting of attention. Overall the patients were also slower and less accurate. The hypothesis that the deficit would extend to all attentional networks can be rejected because there is no evidence of any abnormality in the alerting network.

The patients showed smaller reaction time advantage when the cue is at the target location (44 ms) compared to the controls (54 ms). This difference in the orienting network was significant in the ratio scores. Previous work with first break schizophrenics showed much longer reaction time when they had to disengage from attending to the left visual field, and when the target went directly to the left hemisphere (right visual field) (Posner et al., 1988). This finding was associated with left parietal deficits. The attention network scores are in the opposite direction since the orienting scores of the patients are smaller than those of the normals. Whether this difference is due to the use of the vertical targets, to the fact that the spatial cue is 100% valid, or to the use in the current study of more chronic patients remains unknown.

The deficit found in schizophrenic patients in executive attention is not unique. A similar deficit, although somewhat smaller, was found in patients suffering from borderline personality disorder (Posner et al., 2002). It has also been reported that Alzheimer's patients showed a deficit in executive attention but not in the other attentional networks (Fernandez-Duque and Black, in press). Children below 7 years old also showed significantly longer executive attention scores than adults (Rueda et al., 2004). These findings indicate that the deficit observed in this study is not unique to schizophrenic patients. Furthermore, the degree of overlap between the patients and the normals also show that the attentional deficits are not diagnostic.

Recently, differences in the COMT gene have been related both to performance in a conflict related task similar to the congruence effect in the attention network test (Diamond et al., 2004) and to differences between normals and schizophrenic patients (Egan et al., 2001). The observed deficit in the executive network found in this study fits with the findings of Egan et al. In addition, two recent studies have shown that children with a deletion of the COMT gene (among other genes) have both an increased risk of schizophrenia and deficits in executive attention (Bish et al., 2005; Sobin et al., 2004). These difficulties with executive control can serve as a guide to the anatomical areas, neurochemicals, and genes involved in schizophrenia and may be useful in helping to guide remediation studies.

Executive attention involves the anterior cingulate, lateral prefrontal cortex and basal ganglia as parts of the network. This is a dopamine rich area of the brain and imbalances of dopamine have played a prominent role in the psychopharmacology of schizophrenia (Frith et al., 1995). Cellular abnormalities in the anterior cingulate have been reported in postmortem studies of schizophrenic brain (Benes, 1998). Imaging studies have shown that schizophrenia may involve reduced control of network activity by the anterior cingulate in schizophrenic patients (Fletcher et al., 1999) among other disorders (Bush et al., 1999). The anterior cingulate is known to play a role in tasks that involve word association, semantic priming and other tasks involving the kinds of cognitive processes frequently found to be disordered in schizophrenia (Spitzer, 1997). Disorder of the anterior cingulate has also been implicated in the alien hand sign, which is a disturbance of correct attribution of motor activity sometimes found in patients. These observations suggest an important role for areas of executive attention in relation to schizophrenia.

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