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Impaired processing speed and attention in first-episode drug naive schizophrenia with deficit syndrome

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ABSTRACT

Although first-episode drug naive patients with schizophrenia are known to show cognitive impairment, the cognitive performances of these patients, who suffer deficit syndrome, compared with those who suffer non-deficit syndrome is undetermined. The aim of this study was to compare cognitive performances in first-episode drug-naive schizophrenia with deficit syndrome or non-deficit syndrome. First-episode drug naive patients (n = 49) and medicated patients (n = 108) with schizophrenia, and age, sex, and education matched healthy controls (n = 57 for the first-episode group, and n = 128 for the medicated group) were enrolled. Patients were divided into deficit or non-deficit syndrome groups, using the Schedule for Deficit Syndrome. Cognitive performance was assessed using the CogState computerized cognitive battery. All cognitive domains in first-episode drug naive and medicated patients showed significant impairment compared with their respective control groups. Furthermore, cognitive performance in first-episode drug naive patients was significantly worse than in medicated patients. Interestingly, the cognitive performance markers of processing speed and attention, in first-episode drug naive patients with deficit syndrome, were both significantly worse than in equivalent patients without deficit syndrome. In contrast, no differences in cognitive performance were found between the two groups of medicated patients. In conclusion, this study found that first-episode drug naive schizophrenia with deficit syndrome showed significantly impaired processing speed and attention, compared with patients with non-deficit syndrome. These findings highlight processing speed and attention as potential targets for pharmacological and psychosocial interventions in first-episode schizophrenia with deficit syndrome, since these domains are associated with social outcomes.

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1. Introduction

Deficit syndrome in schizophrenia has been proposed as a distinct pathophysiological subtype, defined by severe primary negative symptoms (Carpenter et al., 1988). Sufferers are characterized by enduring, idiopathic negative symptoms, including restricted affect, diminished emotional range, poverty of speech, curbing of interest, diminished sense of purpose and diminished social drive (Carpenter et al., 1988; Kirkpatrick et al., 1989). These features are constantly present during periods of clinical stability and are primary symptoms, that is, they are not the result of depression, anxiety, medication side effects, positive symptoms, substance abuse or psychosocial deprivation (Kirkpatrick et al., 2001; Carpenter, 2007; Kirkpatrick and Galderisi, 2008; Réthylyi et al., 2012). However, preliminary studies of both psychosocial and pharmacological treatment suggest that some therapies which are effective for negative symptoms in patients with non-deficit syndrome are less effective or ineffective, in patients with deficit syndrome (Kopelowicz et al., 1997, 2000; Kirkpatrick, 2014).

Cognitive impairment is a core feature of schizophrenia, often persisting even when psychotic symptoms have been treated successfully (Green, 1996; Elvevag and Goldberg, 2000; Harvey and Keefe, 2001; Keefe and Harvey, 2012). First-episode patients with schizophrenia are known to suffer cognitive impairment (Saykin et al., 1994; Mohamed et al., 1999; Bilder et al., 2000; Mesholam-Gately et al., 2009). Furthermore, studies on adolescents and young adults at high risk for developing psychosis have demonstrated cognitive impairment before the onset of psychotic symptoms (Lencz et al., 2006; (Simon et al., 2007; Frommann et al., 2011; Carrión et al., 2011; Fusar-Poli et al., 2012). Compared with non-sufferers, deficit syndrome appears to be associated with cognitive impairment (Réthelyi et al., 2012; Buchanan et al., 1994; Putnam and Harvey, 2000; Bryson et al., 2001). A meta-analysis, including 13 neuropsychological studies, showed that patients with deficit syndrome displayed greater global impairment compared with non-sufferers,

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although the effect sizes were small (Cohen et al., 2007). Subsequent meta-analysis of 47 published studies showed that patients with deficit syndrome exhibited less severe mood symptoms and slightly more severe disorganization symptoms (Cohen et al., 2010). However, there are no reports showing comparisons between cognitive impairment in first-episode drug-naive schizophrenia with and without deficit syndrome.

The purpose of this study was to investigate cognitive performance in first-episode drug naive patients and medicated patients with deficit syndrome or non-deficit syndrome. First, we assessed cognitive performance in first-episode drug naive patients and medicated patients, using the Chinese language version of the CogSate battery (Zhong et al., 2013), a sensitive, computer based cognitive assessment instrument, suitable for schizophrenia (Maruff et al., 2009; Pietrzak et al., 2009a; 2009b; Yoshida et al., 2011; Murthy et al., 2012). Second, we assessed cognitive performance in first-episode drug naive and medicated patients, with deficit syndrome or non-deficit syndrome.

2. Methods

2.1. Subjects

Forty nine hospitalized, first-episode drug naive patients with schizophrenia were recruited from the First Hospital of Xi'an Jiaotong University, Xi'an, China (Table 1A), and 108 hospitalized, medicated patients with schizophrenia were recruited from the First Hospital of Xi'an Jiaotong University, Xi'an, China and Shanghai Mental Health center (SMHC), Shanghai, China (Table 1B). All patients satisfied the Diagnostic and Statistical Manual of Mental Disorders criteria (DSM-IV) for schizophrenia, according to the Structured Clinical Interview for DSM-IV (American Psychiatric Association, 1994). The inclusion criteria for this study included: (1) Chinese Han nationality; (2) written, informed consent; (3) more than nine years of education; (4) aged between 18 and 45 years and (5) normal or corrected-to-normal vision and hearing. The first-episode schizophrenia needed to satisfy two additional criteria: (1) Positive and Negative Syndrome Scale (PANSS) total score of ≥60 and (2) Clinical Global Impression Scale (CGI) score of ≥4. The exclusion criteria for this study included: (1) current or previous episodes of a mental disorder, including alcohol or drug dependence, but excluding schizophrenia; (2) traumatic brain injury, cerebrovascular disease, epilepsy, spasms or intellectual disability; (3) patients unable to follow the study protocol, due to severe aggressive behavior, suicidal tendencies and /or behavior; (4) treatment with cognitive enhancing drugs (e.g., donepezil) before 6 months of study entry; and (5) presence of cataracts or other ophthalmic diseases, or hearing impairment, which would compromise completion of the CogState battery. There were no other inclusion criteria based on specific medication for patient groups. Patients with schizophreniform disorders were included as first-episode patients.

A total of 57 age, sex, and education duration matched healthy controls for first-episode drug naive patients were recruited from the Xi'an community, China (Table 1A). In addition, 128 age, sex, and education duration matched, healthy controls for medicated patients were recruited from the Xi'an and Shanghai communities, China (Table 1B). These healthy controls were required to be free of any DSM-IV Axis I disorders and free of schizophrenia or affective disorder in their first degree family history. The inclusion and exclusion criteria for healthy controls were the same as those for patients.

This study was approved by the Institutional Review Board of the First Hospital of Xi'an Jiaotong University and SMHC, to ensure the highest standards of ethical consideration. Before enrollment, all subjects were given a full explanation of the study, and any potential risks and benefits of study participation. They then provided written, informed consent. Our study was performed in keeping with the Declaration of Helsinki II.

Table 1
Demographic and clinical characteristics of subjects.

A. First-episode drug naive patients and control subjects in Xi'an

	Controls (n = 57)	First-episode drug naive (n = 49)
Age	29.02 (8.037)	26.73 (7.011)
Male (female)	24 (33)	29 (20)
Smokers (non-smokers)	7 (49)	10 (39)
Years of education	14.09 (2.699)	14.41 (2.791)
Duration of illness (years)	–	1.06 (1.45)
Deficit syndrome (non-deficit syndrome)	–	17 (32)
CWRT	94.25 (5.780)	91.20 (9.524)
SASS	35.13 (5.089)	29.49 (6.384) ***
QOL	86.45 (10.166)	75.20 (12.38) ***
PANSS total	–	79.20 (16.12)
PANSS positive	–	20.20 (5.070)
PANSS negative	–	19.18 (6.016)
GAF	–	45.49 (16.00)

B. Medicated patients and control subjects in Xi'an and Shanghai

	Controls (n = 128)	Medicated patients (n = 108)
Age	30.45 (7.611)	29.70 (7.658)
Male (Female)	53 (75)	50 (58)
Smokers (Non-smokers)[a]	25 (102)	4 (93)
Years of education	13.55 (3.078)	13.56 (2.606)
Duration of illness (years)	–	6.31 (5.48)
Deficit Syndrome (Non-Deficit Syndrome)	–	52 (56)
CWRT	83.10 (17.486)	77.16 (18.02) **
SASS	35.94 (6.186)	33.87 (6.523) *
QOL	87.03 (10.151)	79.08 (12.31) ***
PANSS total	–	53.83 (13.06)
PANSS positive	–	13.43 (4.766)
PANSS negative	–	14.24 (5.086)
GAF	–	60.21 (14.24)

*p < 0.05, **p < 0.01, ***p < 0.001 when compared with the control group (Wilcoxon rank-sum test).
CWRT: Chinese Word Reading Test, SASS: Social Adaptation Self-evaluation Scale, QOL: Quality of Life,
PANSS: Positive and Negative Syndrome Scale, GAF: Global Assessment Function Scale.
[a] Data missing: There were data missing in the Smokers (Non-smokers) category for the Control (one case) and Medicated patient groups (11 cases).

2.2. Subtypes of deficit syndrome and non-deficit syndrome

Schedule for Deficit Syndrome (SDS) is an instrument for categorizing schizophrenic patients into groups with, or without deficit syndrome (Kirkpatrick et al., 1989). The severity of symptoms is rated on a 5-point scale ranging from no symptoms (0), through to moderate (2), and very severe (4) (Kirkpatrick et al., 1989). The first three specialist psychiatrists (CC, WJ, NZ) were trained to administer SDS, had achieved credentials as raters and showed high inter-rater reliability. Patients with deficit syndrome or non-deficit syndrome were divided using SDS.

2.3. Clinical variables

The Positive and Negative Syndrome Scale (PANSS) is a 30-item, clinician-rated instrument of positive, negative and general psychopathology symptoms (each item is scored from 1 = absent, to 7 = severe; with a total score ranging from 30 to 210) (Kay et al., 1987). The Clinical Global Impression Scale (CGI) is a widely used measure of global illness severity, scored on a seven-item scale by clinicians, with higher scores indicating more severe symptoms (Busner and Targum, 2007). The Global Assessment Function Scale (GAF) is intended to be a single measure of overall impairment, caused by mental factors (Jones et al., 1995). Its intended uses are to communicate the level of impairment, indicate the need for professional help and reflect improvement or change over time.

The Social Adaptation Self-evaluation Scale (SASS) is a 21-item, self-reporting scale, for evaluating broad areas of social functioning

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