The association between cognitive deficits and depressive symptoms in at-risk mental state: A comparison with first-episode psychosis

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A B S T R A C T

Cognitive deficits and a high prevalence of depressive symptoms have been reported in at-risk mental state (ARMS) for psychosis, but the relationships between these variables remain unclear. The Brief Assessment of Cognition in Schizophrenia (BACS) was administered to 50 individuals with ARMS, 50 with first-episode psychosis (FEP), and 30 healthy controls (HC). Clinical symptoms were assessed by the Positive and Negative Syndrome Scale (PANSS) and the Beck Depression Inventory-2nd edition (BDI-II). Composite z-scores in BACS were compared between the three groups. Pearson correlations between composite z-scores on the BACS and indices of clinical symptoms were compared in the ARMS and FEP groups. The mean composite z-scores on the BACS for the ARMS (-2.82) and FEP (-2.85) groups were significantly lower than the HC group ($P < 0.001$); no differences between the ARMS and FEP groups emerged ($P = 0.995$). Cognitive deficits and depressive symptoms were significantly correlated in the ARMS group (PANSS depression: $r = -0.36$, $P = 0.010$; BDI-II: $r = -0.34$, $P = 0.02$), while the correlation between cognitive deficits and negative symptoms was significant in the FEP group ($r = -0.46$, $P = 0.001$) and approached significance in the ARMS group ($r = -0.25$, $P = 0.08$). The correlation between cognitive deficits and depressive symptoms significantly differed between the ARMS and FEP groups (PANSS depression: $Z = 2.50$, $P = 0.012$; BDI-II: $Z = 1.96$, $P = 0.0499$). Thus, a relationship between cognitive deficits and depression appears to be specific to ARMS compared to FEP.

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1. Introduction

Cognitive impairment has been known to be present in individuals with at-risk mental state (ARMS) for psychosis (Fusar-Poli et al., 2012a). Specifically, significant neurocognitive deficits in ARMS have been recorded in general intelligence, attention, executive function, verbal fluency, working memory, verbal memory, and visual memory, but not processing speed domains.

However, high clinical heterogeneity is inherent in the ARMS population, with only a subgroup of this population transitioning to psychosis (Fusar-Poli et al., 2013a). Therefore, Fusar-Poli et al. (2012b)

suggested that some attenuated psychotic symptoms exhibited by ARMS participants may reflect the emergence of an underlying "core" psychotic process, while some symptoms may be "clinical noise" or epiphenomena associated with a non-psychotic clinical condition; and some symptoms may be normal variations among the general population.

The research is mixed regarding the magnitude of cognitive disturbance in ARMS participants, with some reports of significant differences compared to controls and others reporting no differences (Brewer et al., 2006; Fusar-Poli et al., 2012a). Moreover, the profile of neurocognitive impairments has varied across studies. These findings suggest that heterogeneity in ARMS participants is observed in both psychopathology and cognition.

Cognitive impairment in individuals with ARMS has largely been investigated in comparison to patients with schizophrenia (Brewer et al., 2006), and some studies report relationships between cognitive deficits and positive (Frommann et al., 2011) and/or negative symptoms (Frommann et al., 2011; Meyer et al., 2014). Others report no association with positive (Niendam et al., 2006; Meyer et al., 2014) or negative

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symptoms (Niendam et al., 2006). Moreover, little attention has focused on the relationship between cognitive deficits and processes other than psychotic or negative symptoms in ARMS.

ARMS can be comorbid with depression. In previous research (Fusar-Poli et al., 2012b), 40% of ARMS participants had a depressive disorder, and a comorbid diagnosis was associated with impaired global functioning. Additionally, significant cognitive disturbances have been reported, and correlations between those deficits and depression have been shown in young adults with major depressive disorder (Egeland et al., 2003; Lee et al., 2012; Merriam et al., 1999; Trivedi and Greer, 2014). These findings suggest the possibility that cognitive deficits observed in ARMS participants can be associated with participants' depressive symptoms. Moreover, affective dysregulation has an assumed association with reality distortion and the formation of psychotic experiences (van Rossum et al., 2011). It also appears that only one study has investigated the association between cognition and depression in ARMS, and no association was found (Frommann et al., 2011). Therefore, it seems important to clarify the relationship between cognitive deficits and depressive symptoms in ARMS participants.

In the current study, we compared cognitive performance in ARMS and first-episode psychosis (FEP); we also examined if cognitive deficits were associated with clinical symptoms. We hypothesized that cognitive deficits and depressive symptoms would be correlated in ARMS participants, while negative symptoms associated with biological processes in schizophrenia (Baare et al., 1999; Sanfilipo et al., 2000; Roth et al., 2004) would be correlated with FEP participants' cognitive deficits.

2. Methods

2.1. Participants

Participants included 50 individuals with ARMS, 50 patients with FEP, and 30 healthy control (HC) participants who were Japanese-speaking and between 14 and 35 years of age. The exclusion criteria were as follows: (i) serious risk of suicide or violence due to a personality disorder, (ii) current substance dependence, (iii) intellectual disability (IQ < 70), or (iv) neurological disorder, head injury, or any other significant medical conditions associated with psychiatric symptoms.

Participants in the ARMS and FEP groups were recruited from the Sendai At-Risk Mental State and First Episode (SAFE) clinic at Tohoku University Hospital, which is a specialized clinic for early psychosis (Mizuno et al., 2009; Katsura et al., 2014). They were referred to the SAFE clinic by health providers or self-referral. Trained psychiatrists and psychologists assessed them with the clinical and cognitive measures described below.

Participants who met the criteria for ARMS or FEP were evaluated during a baseline examination for future comparative studies examining the clinical follow-up of patients. The data reported herein are baseline data from the ARMS or FEP participants who consented to participation.

The ARMS group was assessed using the Japanese version of the Comprehensive Assessment of At-Risk Mental States (CAARMS-J; Miyakoshi et al., 2009), and diagnosis was confirmed by the clinical team. Participants had no history of DSM-IV psychotic disorders and met one or more of the following criteria for ARMS developed by the

Personal Assessment and Crisis Evaluation (PACE) Clinic in Melbourne, Australia (Yung et al., 2004). This procedure has been widely used as standard criteria of ARMS (Fusar-Poli et al., 2012c) and includes the following: (i) attenuated psychotic symptoms (APS), (ii) brief limited intermittent psychotic symptoms (BLIPS; a psychotic episode that resolves within 1 week), and (iii) state and trait risk factors (e.g., a recent decline in functioning, plus either a first-degree relative with psychosis or a schizotypal personality disorder). The distribution of the fulfilled criteria in the ARMS group and their comorbid diagnoses for DSM-IV Axis I are summarized in Table 2. Nine of the ARMS participants made a transition during the follow-up period and were included in the analyses. The mean duration of follow-up was 39.4 months (SD = 18.1, median 40.3).

Participants included in the FEP group met the CAARMS-J criteria for psychosis and had a Positive and Negative Syndrome Scale (PANSS; Kay et al., 1987) score of 4 or more on the items for delusion, hallucinatory behavior, grandiosity, suspiciousness, or unusual thought content for more than 1 week. Although participants were experiencing their first episode and had not fully remitted at the time of the neuropsychological examination, they were all sufficiently stable to undergo neuropsychological examination. The distribution of baseline diagnosis in the FEP group is summarized in Table 2.

The HC participants were recruited from a local university. All participants reported that they had never been diagnosed with a psychiatric disorder.

The study was conducted with the authorization of the Ethics Committee of Tohoku University Graduate School of Medicine and Tohoku University Hospital. Written informed consent was obtained from participants 18 years of age or older and from the parents of participants under 18, with written assent from the participants.

2.2. Measures

2.2.1. Clinical assessments

Psychopathology (positive symptoms, negative symptoms, depression, and anxiety) was assessed with the PANSS. Subjective severity of depression was assessed with the Beck Depression Inventory-2nd edition (BDI-II, Beck et al., 1996). Global functioning was assessed with the Global Assessment of Functioning (GAF, American Psychiatric Association, 1994). Social functioning was assessed with the Japanese version of the Social Functioning Scale (SFS, Birchwood et al., 1990; the Japanese version of SFS, Nemoto et al., 2008). Estimated premorbid IQ was assessed using the Japanese version of the National Adult Reading Test (NART, Nelson, 1982; JART, Matsuoka et al., 2006).

2.2.2. Cognitive assessments

The Japanese version of the Brief Assessment of Cognition in Schizophrenia (BACS) was used in the current study (Kaneda et al., 2007). The BACS (Keefe et al., 2004) consists of six subtests of verbal memory, working memory, motor speed, verbal fluency, attention/processing speed, and executive function. All study participants were administered the BACS and raw subtest scores were standardized by creating z-scores. The HC group's means and standard deviations were set to 0 and 1 respectively (Keefe et al., 2004). A composite z-score was calculated by averaging the z-scores from all six subtests and then dividing

Table 1
Demographic data.

	ARMS (n = 50)	FEP (n = 50)	HC (n = 30)	Statistic value	P
Number of males (%)	18 (36.0)	15 (30.0)	13 (43.3)	Exact test	0.49
Age in years at testing, M (SD)	20.1 (4.3)	23.2 (5.9)	21.3 (1.0)	F = 5.83	0.004
Years of education, M (SD)	12.0 (2.1)	12.7 (2.1)	14.4 (0.8)	H = 27.2	<0.001
Premorbid IQ, M (SD)	100.1 (10.5)	99.2 (7.9)	111.9 (6.6) [a]	F = 22.0	<0.001

ARMS: At-Risk Mental State; FEP: First-Episode Psychosis; HC: Healthy Control; premorbid IQ was measured by the Japanese version of the National Adult Reading Test (JART).

[a] Data missing for 1 participant.