Subjectively-assessed cognitive impairment and neurocognition associations in schizophrenia inpatients

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博 士 論 文

Subjectively-assessed cognitive impairment and

neurocognition associations in schizophrenia inpatients

（統合失調症入院患者の主観的な認知機能障害と神経認知との相関）

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Abstract

 Cognitive impairment affects real-world functioning in people with schizophrenia who often face difficulties in their activities of daily living. Subjectively-assessed cognitive impairment can be evaluated through data on the patient's daily difficulties, as reported by the patient. However, the specific neurocognitive functions responsible for these cognitive impairments have not been clarified. We examined cognitive functioning in patients with schizophrenia using the Schizophrenia Cognition Rating Scale Japanese version (SCoRS-J) and the Brief Assessment of Cognition in Schizophrenia Japanese version (BACS-J). This study aimed to investigate the relationship between subjectively-assessed cognitive impairment and objectively assessed neurocognition in patients with schizophrenia. The results showed that patients' global rating scores of the SCoRS-J were significantly correlated with the BACS-J attention scores ($r = -0.376$, $p < 0.008$), which indicates that the difficulties patients perceived in their daily lives are due to deficits in attentional functioning, as measured by neurocognitive testing. Thus, our findings indicate that improving attentional functioning may also alleviate difficulties in patients' daily lives.

Keywords
SCoRS; Schizophrenia; Cognition; BACS; Cognitive Impairment

1 Introduction

 Schizophrenia is characterized by psychiatric symptoms such as hallucinations, delusions, and cognitive impairments. Cognitive impairments affect real-world functioning, which make the patient's life difficult (Bowie et al., 2010). Neurocognitive functions, including verbal memory, immediate memory, executive functioning, and vigilance, are related to functional outcomes such as daily activities, social problem-solving, and psychosocial skill acquisition (Green et al., 2000). Cognitive impairment is associated with functional outcome severity in patients with schizophrenia (Green et al., 2000). Neuropsychological test batteries such as the MATRICS Consensus Cognitive Battery (Nuechterlein et al., 2008) and the Brief Assessment of Cognition in Schizophrenia (BACS; Keefe et al., 2004) are often used to assess such cognitive impairment. However, it is difficult to assess which cognitive functions affect patients' lives only by using a neurocognitive test. Patients' reported difficulties in their daily lives, such as remembering or concentrating, or subjectively-assessed cognitive impairment, are also crucial. It is important to address patients' perceptions of their functioning during psychiatric rehabilitation mainly focusing on their lives. Studies on self-reported cognitive impairment and objective assessment of cognitive functioning in patients with

schizophrenia have reported contradictory results (Harvey et al., 2007; Moritz et al., 2004; Medalia et al., 2008; Chan et al., 2008; Durand et al., 2015).

The Schizophrenia Cognition Rating Scale (SCoRS; Keefe et al., 2006) can be used in addition to a neurocognitive test. It assesses cognitive impairment and the degree to which it affects real-world functioning through interviews. The SCoRS comprises three forms, one each for the patient, informant, and interviewer. The patient's form is assessed based on an interview with the patient and reflects more subjective difficulties caused by cognitive impairments than the other forms as it reflects the patient's experience. In this study, we defined these impairments as subjectively-assessed cognitive impairments based on SCoRS patient form scores.

Currently, no improvement methods for specific cognitive functions in psychiatric rehabilitation practice exist. A focus on specific cognitive impairments may enable the mitigation of patients' functional difficulties, making it necessary to determine the domains of cognitive functioning responsible for patients' difficulties. However, the SCoRS has no subscales, making such an assessment difficult. Evaluating patient interviews of the SCoRS and comparing them to the subscales of the neurocognitive functions measured by the BACS, can help us determine the domains of cognitive functioning affected by the patients' difficulties. Identifying the neurocognitive function responsible for the patient's cognitive impairment can help alleviate their everyday functional difficulties.

This study aimed to investigate the relationship between subjectively-assessed cognitive impairment and objectively assessed neurocognition in patients with schizophrenia. The findings will allow professionals to provide rehabilitation tailored to the patient's life circumstances by clarifying the relationship between their subjectively-assessed cognitive impairment and objectively assessed neurocognition.

2 Methods

2.1 Participants

Inpatients with schizophrenia were recruited from a psychiatric hospital in Japan. Inclusion criteria were patients aged 18-65 years with a diagnosis of schizophrenia according to the International Classification of Diseases-10 (F20). Exclusion criteria were a diagnosis of mental retardation, dementia, substance use, or history of neurological disorders. The study took place from January 30th to February 10th, 2017. Demographic profiles were collected from clinical records: age, gender, age of onset, total length of hospital stays, number of hospital stays, and antipsychotic drugs and dosages.

2.2 Clinical and neuropsychological assessments

The SCoRS-J and BACS-J were used to assess cognitive functioning of the patients. The Positive and Negative Syndrome Scale (PANSS) was used to assess patients' symptoms.

The Global Assessment of Functioning (GAF) was used to assess social functioning.

2.2.1 SCoRS-J

The SCoRS-J is a 20-item interview-based assessment of cognitive impairments that evaluates the degree of their effects on real-world functioning. Each item focuses on the degree of impairment and the degree to which the deficit impairs real-world functioning and is rated on a 4-point Likert scale. A higher rating means a greater degree of impairment. SCoRS-J interviews include the patient and their informant who has the most regular contact in everyday situations. The interviewer's rating reflects a combination of the interviews with both participants. The global ratings are scored on a scale of 1-10. All informants in this study were primary care nurses because the participants were inpatients. All of the interviewers were occupational therapists.

2.2.2. BACS-J

The BACS-J is a performance-based cognitive assessment battery for schizophrenia. The BACS-J assesses six cognitive domains: Verbal memory, working memory, motor speed, verbal fluency, attention, and executive function. Each of the six measures is standardized by z-scores. A lower score means greater cognitive impairment. Assessments are carried out by trained occupational therapists.

2.2.3. PANSS

The PANSS assesses the severity of psychotic symptoms. The PANSS is a 30-item rating scale to assess the severity of the positive and negative symptoms of schizophrenia. Each item is rated on a 7-point Likert scale. A higher rating indicates more psychotic symptoms. Assessments are carried out by psychiatrists.

2.2.4. GAF

The GAF assesses social functioning. The GAF measures a patient's psychological, social, and occupational functioning. Scores on this scale range from 1-100. A lower score means lower functioning. Assessments are carried out by psychiatrists caring for the patients.

2.3 Study's flow chart

The study's flow chart is described in Figure 1. The study recruited 129 inpatients who met the inclusion criteria, of which, 61 declined to participate and 68 agreed to participate. A total of 18 participants were excluded: 15 for declining assessments and 3 for worsening medical condition. Finally, the data of 50 participants were analyzed.

2.4 Statistical analysis

Data were analyzed with BellCurve for Excel. Spearman's correlation was performed to

find the associations between the SCoRS-J global ratings and the BACS-J scores. The significance level was set at $p < 0.008$ as correction for multiple correlations.

3 Results

3.1 Demographic profile

Table 1 shows the demographic and clinical characteristics of the patients. Table 2 shows the SCoRS-J and BACS-J scores. Overall, patients' global rating score was 5.32±2.95, informants' global rating score was 3.98±2.03, interviewers' global rating score was 5.08±1.96, and the composite score for BACS-J was -3.58±1.55.

3.2 Correlations between SCoRS-J and BACS-J

Table 3 shows the correlations between SCoRS-J and BACS-J. Patients' global rating scores were significantly correlated with BACS-J attention scores ($r = -0.376$, $p < 0.008$). Informants' global rating scores were significantly correlated with BACS-J scores, except for verbal memory and verbal fluency. The interviewer's global rating score was significantly correlated with the composite score and working memory and attention scores on the BACS-J.

4 Discussion

Patients with schizophrenia account for the majority of inpatients in Japanese psychiatric hospitals, being over half of the psychiatric inpatient population (Ministry of Health, Labour and Welfare, 2017), and therefore, were the target of this study. The current study found a similar correlation between interviewers' global SCoRS-J ratings and composite BACS-J scores as previous studies (Keefe et al., 2006; Keefe et al., 2015; Harvey et al., 2019). In terms of the correlation between global SCoRS-J ratings and the BACS-J subscale scores, the present results showed that the informants and interviewer had a common correlation in assessing cognitive functioning, which did not correlate with patients' assessments in a previous study (Keefe et al., 2015; Harvey et al., 2019). Corresponding correlations between the interviewer and informants were found for attention and working memory; patients' global SCoRS-J rating and BACS-J attention score were also weakly correlated. In other words, patients with schizophrenia who experienced general difficulties in their daily lives that required cognitive functioning had lower attentional functioning, as measured by the BACS-J. These results indicate that everyday difficulties requiring cognitive functioning as assessed by the SCoRS-J are related to attentional functioning as assessed using performance-based measures, with stronger correlations found for the interviewer and weaker for the patient. A previous study showed that patients' global SCoRS ratings did not correlate with z-scores in any of the BACS domains (Poletti et al., 2012). Although Harvey et al. (2007) found patients' self-reports to be inconsistent with objective assessments, subjectively-assessed cognitive impairments are not necessarily inconsistent with objectively-assessed cognitive

impairments, as the current results showed a correlation with attention. The current correlation between subjectively-assessed cognitive impairment and BACS-J may be because of participants' heterogeneity, unlike many previous studies.

The participants of this study were Japanese, long-term hospitalized patients with severe cognitive impairment and other symptoms, taking high dosages of antipsychotic drugs. The mean age of patients in this study was 53.5 years. Previous studies using both SCoRS and BACS involved participants within the age range of 19.4-42.6 years (Keefe et al., 2006, Chia et al., 2010, Higuchi et al., 2017). Cognitive impairments assessed by the BACS-J had a composite score of -3.58±1.55 (mean ± SD), compared to previous studies where scores ranged from -2.03 to -0.60 (Keefe et al., 2004). Thus, the cognitive impairments of patients in this study were more severe. The antipsychotic medication dosage in the present study was 949.9±542.2 mg, compared to previous studies using the SCoRS (133.3 mg to 750.0 mg; Harvey et al., 2011). The patients in this study were taking higher dosages of medication. Hori et al. (2006) reported that patients who take high dosages of antipsychotics or polypharmacy have more severe cognitive impairment than those receiving monopharmacy. Patients in this study were hospitalized for 172.90±122.50 months. The average length of hospital stay for patients with schizophrenia was 531.8 days in Japan (Ministry of Health, Labour and Welfare, 2017). The participants in this study spent longer time in the hospital compared to the average length of other patients with schizophrenia in Japan. The patients in this study showed characteristic psychiatric symptom severity. The results differed from those of previous studies, but no clear cause has been identified.

One of the subtypes of schizophrenia is deficit schizophrenia, which is characterized by persistent and primary (i.e., not explained by other factors such as medication effects, depression, positive symptoms, and anxiety) negative symptoms (Carpenter et al., 1988), and indicates a patient with severe psychiatric symptoms. The psychiatric symptoms of this study were more severe compared to previous studies investigating deficit schizophrenia (Sum et al., 2018), and the total score of the PANSS was 99.44±19.87 vs 39.617±7.93~67.2±13.2. Sum et al. (2018) showed that there is a negative correlation between the score for deficit schizophrenia based on the PANSS score and cognitive functioning including attentional functioning. A study investigating neurocognitive impairment in deficit schizophrenia (Bora et al., 2017) showed that deficit schizophrenia has more severe cognitive impairment than non-deficit schizophrenia. Bora et al. (2017) state that verbal memory, executive functioning, and processing speed contribute to the effect size of the difference in cognitive domain between deficit schizophrenia and non-deficit schizophrenia. Therefore, in deficit schizophrenia, the overall severity of cognitive impairment is affected by the severity of impairment in processing speed. Attention in the BACS assesses processing speed (Keefe et al., 2004) and indicates that the severity of attentional impairment affects the overall severity of cognitive impairment. The severity of psychiatric symptoms in this study was greater compared to deficit schizophrenia. This

suggests that attentional functioning affects the overall severity of cognitive impairment, as shown in previous study (Sum et al., 2018). The weak correlation between a patient's global rating of the SCoRS-J and attentional functioning of the BACS-J indicates that the difficulties patients perceived in their daily lives are due to attentional functioning, as measured by the neurocognitive test. The current results suggest that improved attentional functioning may decrease patients' subjective everyday difficulties, opening the door for a renewed focus on subjectively-assessed cognitive impairments and attentional functioning in Japanese patients with severe cognitive impairment and symptoms.

4.1 Conclusion

The results showed that inpatients who experienced general difficulties in activities of daily living that require adequate cognitive functioning had lower attentional functioning as measured by the BACS-J. It is possible to improve patients' difficulties in their daily lives, if an approach focused on attentional functioning is successfully introduced. The subjects of this study were Japanese, older, long-term hospitalized patients with severe cognitive impairment, severe psychiatric symptoms, and taking high dosages of medication.

There are several limitations to this study. First, this study was conducted in a single psychiatric hospital in a residential area in Japan, which may be different from city or rural settings, general or psychiatric hospitals, or patients outside of Japan. Second, about half of those who met the eligibility criteria did not agree to participate in the study, which may explain the current bias toward older, long-term hospitalized patients with severe psychiatric symptoms and cognitive impairment. Third, although we investigated SCoRS and neurocognition, we were not able to examine the relationship between SCoRS and social cognition or metacognition. Fourth, this was a pilot study with a small sample. Future research should include a comparable inpatient group without significant cognitive impairment to clarify the current results. Further studies are needed to reduce patients' everyday difficulties by focusing on attention rather than overall cognitive function.

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           │                    │  ・declining participation (n=61)       │
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│ Assessment    n=68          │
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           │                    │ Excluded n=18                          │
           │───────────────────▶│  ・declining assessments (n=15)         │
           │                    │  ・worsening medical condition (n=3)    │
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│ Statistical analysis    n=50│
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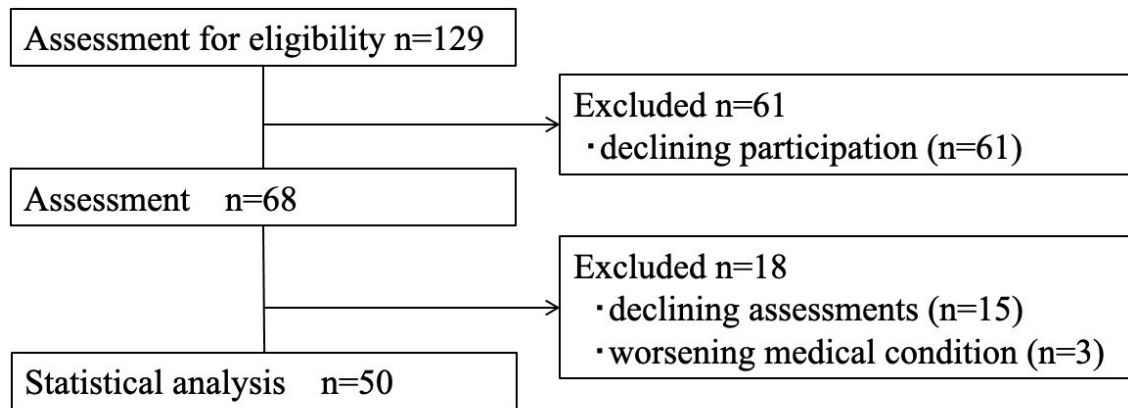
Fig. Study flow chart

Table 1. Patient characteristics

Age (years)	53.54	±	9.85
Gender (male/female)		20/30	
Age of onset (years)	20.77	±	5.82
Total length of hospital stays (months)	172.90	±	122.50
Number of hospital stays (times)	4.68	±	3.8
Antipsychotics dosage (mg/day, Chlorpromazine equivalent)	949.908	±	542.32
PANSS			
Positive	23.64	±	5.70
Negative	26.34	±	6.96
General psychopathology	49.46	±	11.27
Total	99.44	±	19.87
GAF	30.06	±	8.97

mean ± SD

PANSS: Positive and Negative Syndrome Scale

GAF: Global Assessment of Functioning

Table 2. SCoRS-J global ratings and BACS-J scores

SCoRS-J				
	Patient's global rating	5.32	±	2.95
	Informant's global rating	3.98	±	2.03
	Interviewer's global rating	5.08	±	1.96
BACS-J				
	Verbal memory	-2.50	±	1.26
	Working memory	-2.36	±	1.28
	Motor speed	-2.30	±	1.12
	Verbal fluency	-2.11	±	0.85
	Attention	-2.58	±	1.24
	Executive function	-1.63	±	1.51
	Composite score	-3.58	±	1.55

mean ± SD

SCoRS-J: Schizophrenia Cognition Rating Scale-Japanese version

BACS-J: The Brief Assessment of Cognition in Schizophrenia-Japanese version, z-score

Table 3. Correlations between SCoRS-J global ratings and BACS-J z scores

		BACS-J						
		Verbal memory	Working memory	Motor speed	Verbal fluency	Attention	Executive function	Composite score
SCoRS-J	Patient's global rating	0.005	-0.116	-0.277	-0.004	-0.376 *	0.074	-0.152
	Informant's global rating	-0.282	-0.529 *	-0.420 *	-0.216	-0.514 *	-0.377 *	-0.496 *
	Interviewer's global rating	-0.326	-0.494 *	-0.345	-0.303	-0.611 *	-0.346	-0.504 *

Spearman's correlation * $p < 0.008$

SCoRS-J: Schizophrenia Cognition Rating Scale-Japanese version

BACS-J: The Brief Assessment of Cognition in Schizophrenia-Japanese version