### Regular Article

# Measurement and Treatment Research to Improve Cognition in Schizophrenia Consensus Cognitive Battery: Validation of the Japanese version

Yasuhiro Kaneda, MD, PhD,<sup>1\*</sup> Tetsuro Ohmori, MD, PhD,<sup>2</sup> Yuko Okahisa, MD, PhD,<sup>3</sup> Tomiki Sumiyoshi, MD, PhD,<sup>4</sup> Shenghong Pu, MD,<sup>5</sup> Yoshinori Ueoka PhD,<sup>2</sup> Manabu Takaki, MD, PhD,<sup>3</sup> Kazuyuki Nakagome, MD, PhD<sup>6</sup> and Ichiro Sora, MD, PhD<sup>7</sup>

<sup>1</sup>Department of Psychiatry, Iwaki Clinic, <sup>2</sup>Department of Psychiatry, Institute of Health Bioscience, The University of Tokushima Graduate School, Tokushima, <sup>3</sup>Department of Neuropsychiatry, Okayama University Graduate school of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, <sup>4</sup>Department of Neuropsychiatry, University of Toyama Graduate School of Medicine and Pharmaceutical Sciences, Toyama, <sup>5</sup>Division of Neuropsychiatry, Department of Brain and Neuroscience, Tottori University Faculty of Medicine, Tottori, <sup>6</sup>National Center of Neurology and Psychiatry, Tokyo, and <sup>7</sup>Department of Biological Psychiatry, Tohoku University Graduate School of Medicine, Miyagi, Japan

Aim: This preliminary study was performed to test the reliability and validity of the Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) Consensus Cognitive Battery (MCCB), developed by the National Institute of Mental Health MATRICS initiative, as an assessment tool in a Japanese-language version (MCCB-J).

Methods: The subjects for the present study were 37 patients with schizophrenia. Each subject gave written informed consent to participate in the research. In order to examine the validity of the MCCB-J, the correlation between the MCCB-J and the Japanese-language version of the Brief Assessment of Cognition in Schizophrenia (BACS) was determined.

Results: Cronbach's alpha for the MCCB-J was 0.72. The MCCB-J composite score was significantly correlated with all subtests of the MCCB-J. There was a significant correlation between the MCCB-J and the BACS composite score.

Conclusion: This preliminary study indicates that the MCCB-J has good psychometric properties and validity.

**Key words:** cognitive function, Japanese version, Measurement and Treatment Research to Improve Cognition in Schizophrenia Consensus Cognitive Battery, psychometrics, schizophrenia.

THE ASSESSMENT OF cognitive function is an important step in evaluating patients with schizophrenia because of the extensive evidence that cognitive impairment is a core feature of schizophrenia,  $^{1,2}$  as well as a key determinant of functional outcome.  $^{3,4}$ 

Cognitive domains that show differential impairment in schizophrenia include attention (vigilance), executive function, long-term and learning memory, working memory, and verbal fluency.<sup>3-7</sup> The long-term and learning memory and attention, in particular, have been shown to predict functional outcome better than positive and negative symptoms.<sup>3,4</sup>

For assessing cognitive function in schizophrenia, an extensive neuropsychological test battery (NTB), usually consisting of 8–12 tests tapping each of several tests for the putative neurocognitive domains,

<sup>\*</sup>Correspondence: Yasuhiro Kaneda, MD, Department of Psychiatry, Iwaki Clinic, 11-1 Kamimizuta, Gakubara, Anan, Tokushima 774-0014, Japan. Email: kaneday-tsh@umin.ac.jp Received 5 September 2012; revised 25 January 2013; accepted 2 February 2013.

has been employed. These NTB are, however, timeconsuming, technically difficult, and costly. Moreover, differences in NTB chosen for various studies make a direct comparison across studies difficult. Thus, the availability of a quick and efficient tool for measuring cognition in patients with schizophrenia would be extremely useful for clinicians in considering an indication of rehabilitation, as well as for researchers implementing clinical trials to assess cognitive improvement. In this regard, we introduced the Brief Assessment of Cognition in Schizophrenia (BACS), and prepared the Japanese-language version (BACS-J).9

Meanwhile, the National Institute of Mental Health Measurement and Treatment Research to Improve Cognition in Schizophrenia (NIMH-MATRICS) initiative, created to stimulate the development of cognition-enhancing drugs for schizophrenia, 10 developed a consensus cognitive battery for clinical trials of cognition-enhancing treatments for schizophrenia through a broadly based scientific evaluation of measures: the MATRICS Consensus Cognitive Battery (MCCB). The MCCB has been recommended as the standard battery for clinical trials of cognitionenhancing interventions for schizophrenia by the US Food and Drug Administration (FDA). Therefore, for its clinical application, we prepared the Japaneselanguage version (MCCB-J). The aim of this study was to test psychometric properties and validity of the MCCB-J for the evaluation of cognitive function in schizophrenia.

#### **METHODS**

#### Translation of the MCCB

In order to have an approved translation of the MCCB, the following translation methodology was used: two independent forward translations, reconciliation, two independent back translations, and pilot testing on five people with schizophrenia. The author of the scale checked the back-translation. In addition, we have adjusted two sub-tests (Letter-Number Span [LNS] and Mayer-Salovey-Caruso Emotional Intelligence Test: Managing Emotions [MSCEIT]) to Japanese language/culture.

#### **Subjects**

Thirty-seven patients with chronic schizophrenia were recruited for the present study. The diagnosis

**Table 1.** Demographic information (n = 37)Age (years) 38.4 (11.2) Sex (F/M) 14/23 Education (years) 13.3 (2.0) BPRS (total) 41.0 (7.1) Data are given as mean (SD). BPRS, Brief Psychiatric Rating Scale.

was based on DSM-IV criteria for schizophrenia, 11 a detailed clinical interview, and review of the prior records. In the subjects, hepatic and renal functions were normal, and subjects were excluded if they presented with any organic central nervous system disorder, significant substance abuse, or mental retardation. The study was approved by the relevant ethics committees and was performed in accordance with the Declaration of Helsinki II. The ethics committees of each institution were as follows: the Ethics Committee of University of Tokushima, the Ethics Committee of Okayama University Graduate School of Medicine, the Committee on Medical Ethics of Toyama Medical and Pharmaceutical University, and the Ethics Committee of the Tottori University Faculty of Medicine. The patients who gave informed consent to the research participated in this study. Table 1 shows the demographic characteristics of the subjects.

Twenty of the 37 patients were being treated with a single second-generation antipsychotic medication (aripiprazole, n = 3; blonanserin, n = 2; olanzapine, n = 7; perospirone, n = 1; quetiapine, n = 1; risperidone, n = 6), four with a single first-generation antipsychotic medication (haloperidol, n = 3; zotepine, n = 1), nine with a combination of antipsychotic drugs, and two without antipsychotic medications. The medications for two of 37 patients were unknown, because a site could not obtain the information.

#### Assessment procedures

The MCCB-J comprises 10 tasks that measure speed of processing (BACS Symbol-coding [BACS SC]; Category Fluency Animal Naming [Fluency]; Trailmaking Test Part A [TMT-A]), attention/vigilance (Continuous Performance Test-Identical Pairs), working memory (Wechsler Memory Scale-Third Edition Spatial Span; LNS), verbal learning (Hopkins Verbal Learning Test-Revised), visual learning (Brief Visuospatial Memory Test-Revised), reasoning and problem solving (Neuropsychological Assessment Battery Mazes), social cognition (MSCEIT). A composite score was calculated by averaging all z-scores of the 10 subtests from the MCCB-J.

In order to examine the validity of the MCCB-J, the correlation between the MCCB-J and the BACS-J was determined. The BACS-J takes approximately 30 min, and is devised for easy administration and scoring by non-psychologists. It is specifically designed to measure treatment-related improvements. The BACS-I has high test-retest reliability, and is as sensitive to cognitive dysfunction in schizophrenia as standard 2.5-h NTB. The BACS-J includes brief assessments of verbal memory (Verbal Memory), working memory (Digit Sequencing), motor speed (Token Motor), verbal fluency (Verbal Fluency), attention and processing speed (Symbol-coding), and executive function (Tower of London), and its composite scores are calculated by averaging all z-scores of the six subtests from the BACS-J. The 18-item Brief Psvchiatric Rating Scale (BPRS, 12 1-7 score) was completed by trained psychiatrists along with the MCCB -J and BACS-J.

# Statistical analysis

The data analyses were conducted using JMP-8.0.2.J for Mac software (SAS Institute Inc., Cary, NC, USA). Descriptive statistics were used to report the patients in terms of sociodemographic and clinical data. Cronbach's alpha<sup>13</sup> was used to determine the internal consistency of the MCCB-J and BACS-J. The relations among the MCCB-J and BACS-J measures were determined by calculating Pearson correlations among the scores. To test the construct validity, Pearson correlation coefficients (r) were used between the MCCB-J and BACS-J scores. The factor structure of the scores was determined by performing a principal component analysis with varimax rotation. The level of significance was set at P < 0.05 (two-tailed).

#### **RESULTS**

Table 2 lists the means and standard deviations for all of the measures from the MCCB-J and BACS-J. The MCCB-J required a mean of 80.0 min (SD = 13.8) to complete, while the BACS-J required 35.4 min (1.9).

Table 2. Mean (SD) of MCCB-J and BACS-J-tests

Tests	Raw scores
MCCB-J	
Trail-making Test Part A (time in s)	38.4 (15.5)
BACS Symbol-coding	49.6 (11.8)
Hopkins Verbal Learning Test-Revised	21.7 (4.8)
Wechsler Memory Scale-Third Edition	15.7 (3.6)
Spatial Span	
Letter-Number Span	10.7 (3.2)
Neuropsychological Assessment Battery	17.1 (7.0)
Mazes	
Brief Visuospatial Memory Test-Revised	22.0 (6.9)
Category Fluency Animal Naming	17.8 (5.2)
Mayer-Salovey-Caruso Emotional	80.8 (8.5)
Intelligence Test Managing	
Emotions (branch score)	
Continuous Performance Test-Identical	2.6 (0.6)
Pairs (d-prime)	
BACS-J	
Verbal Memory	37.2 (11.6)
Digit Sequencing	17.6 (4.6)
Token Motor Task	68.4 (18.7)
Verbal Fluency	38.3 (9.9)
Symbol-coding Task	51.3 (13.2)
Tower of London	16.6 (3.9)

Data are given as mean (SD).

BACS-J, Brief Assessment of Cognition in Schizophrenia Japanese-language version, MCCB-J, Measurement and Treatment Research to Improve Cognition in Schizophrenia Consensus Cognitive Battery Japanese-language version.

#### Reliability

#### Internal consistency

Cronbach's alpha was 0.72 for the MCCB-J, and 0.78 for the BACS-I.

# Intercorrelations between MCCB-J/BACS-J subtests and composite score

Table 3 presents the correlations among the MCCB-J subtests and composite score. The MCCB-J composite score was significantly correlated with all primary MCCB-J measures. In addition, Table 4 presents the correlations among the BACS-J subtests and composite score, and the BACS-J composite score was also significantly correlated with all primary BACS-J measures.

<b>Table 3.</b> Pearson correlations among MCCB-J me	easures	
--	---------	--

				WMS-III		NAB			MSCEIT	
	TMT-A	BACS SC	HVLT-R	SS	LNS	Mazes	BVMT-R	Fluency	ME	CPT-IP
Composite Score	-0.62***	0.67***	0.71****	0.55***	0.75****	0.67****	0.73****	0.51**	0.39*	0.75****
CPT-IP	-0.34*	0.52**	0.37*	0.39*	0.61****	0.37*	0.38*	0.39*	0.33*	_
MSCEIT ME	-0.11	0.05	0.26	0.01	0.34*	-0.01	0.29	0.15	-	_
Fluency	-0.22	0.15	0.29	0.15	0.26	0.22	0.40*	-	-	_
BVMT-R	-0.38*	0.37*	0.53***	0.33*	0.55***	0.46**	-	-	-	-
NAB Mazes	-0.60****	0.43**	0.44**	0.34*	0.35*	_	-	-	-	_
LNS	-0.20	0.47**	0.56***	0.46**	-	_	-	-	-	-
WMS-III SS	-0.17	0.38*	0.32	-	-	_	-	-	-	-
HVLT-R	-0.40*	0.35*	-	-	-	_	-	-	-	_
BACS SC	-0.57***	-	-	-	-	-	-	-	-	_

<sup>\*</sup>P < 0.05, \*\*P < 0.01, \*\*\*P < 0.001, and \*\*\*\*P < 0.0001.

BACS SC, BACS Symbol-coding; BVMT-R, Brief Visuospatial Memory Test-Revised; CPT-IP, Continuous Performance Test-Identical Pairs; Fluency, Category Fluency Animal Naming; HVLT-R, Hopkins Verbal Learning Test-Revised; LNS, Letter-Number Span; MCCB-J, Measurement and Treatment Research to Improve Cognition in Schizophrenia Consensus Cognitive Battery Japanese-language version.; MSCEIT ME, Mayer-Salovey-Caruso Emotional Intelligence Test Managing Emotions; NAB Mazes, Neuropsychological Assessment Battery Mazes; TMT-A, Trail-making Test Part A; WMS-III SS, Wechsler Memory Scale-Third Edition Spatial Span.

# **Validity**

#### Correlations between MCCB-J and **BACS-I** measures

Table 5 shows the Pearson correlations between corresponding subtests from the MCCB-J and BACS-J. Because the BACS-J includes only four of the seven cognitive domains nominated by the MCCB, we examined correlations of corresponding subtests in only these four domains. The MCCB-J subtests in working memory, verbal learning, and reasoning and problem-solving were significantly correlated with relevant subtests. In speed of processing, BACS SC was significantly correlated with all three relevant BACS subtests, MCCB Fluency was correlated with BACS Verbal Fluency, and TMT-A with Symbol-coding Task. In addition, the MCCB-J composite score was significantly correlated with BACS-J composite score.

#### Factor analysis for MCCB-J/BACS-J subtests

Tables 6 and 7 show the factor loadings for the MCCB-J and BACS-J, respectively. For both MCCB-J and BACS-J, a factor accounts for more 40% of the

Table 4. Pearson correlations among BACS-J measures

	Verbal Memory	Digit Sequencing	Token Motor Task	Verbal Fluency	Symbol-coding Task	Tower of London
Composite Score	0.76****	0.75****	0.58***	0.63***	0.66****	0.80****
Tower of London	0.53 * * *	0.60***	0.35*	0.42**	0.42*	_
Symbol-coding Task	0.37*	0.46**	0.33*	0.41*	-	-
Verbal Fluency	0.40*	0.44 * *	0.12	_	_	_
Token Motor Task	0.39*	0.17	_	_	_	_
Digit Sequencing	0.43 * *	_	_	_	_	_

<sup>\*</sup>P < 0.05, \*\*P < 0.01, \*\*\*P < 0.001, and \*\*\*\*P < 0.0001.

BACS-J, Brief Assessment of Cognition in Schizophrenia Japanese-language version.

Cognitive domains	MCCB-J	BACS-J	r
Speed of processing	BACS SC	Symbol-coding Task	0.87***
		Verbal Fluency	0.42 * *
		Token Motor Task	0.37*
	Fluency	Symbol-coding Task	0.14
		Verbal Fluency	0.63****
		Token Motor Task	0.19
	TMT-A	Symbol-coding Task	-0.50**
		Verbal Fluency	-0.24
		Token Motor Task	-0.25
Attention/Vigilance	CPT-IP	-	_
Working memory	WMS-III SS	Digit Sequencing	0.57***
	LNS	Digit Sequencing	0.66****
Verbal learning	HVLT-R	Verbal Memory	0.67****
Visual learning	BVMT-R	_	_
Reasoning and problem-solving	NAB Mazes	Tower of London	0.38*
Social cognition	MSCEIT ME	_	_
Composite score			0.76***

<sup>\*</sup>P < 0.05, \*\*P < 0.01, \*\*\*P < 0.001, and \*\*\*\*P < 0.0001.

BACS-J, Brief Assessment of Cognition in Schizophrenia Japanese-language version; BACS SC, BACS Symbol-coding; BVMT-R, Brief Visuospatial Memory Test-Revised; CPT-IP, Continuous Performance Test-Identical Pairs; Fluency, Category Fluency Animal Naming; HVLT-R, Hopkins Verbal Learning Test-Revised; LNS, Letter–Number Span; MCCB-J, MATRICS Consensus Cognitive Battery Japanese-language version; MSCEIT ME, Mayer–Salovey–Caruso Emotional Intelligence Test Managing Emotions; NAB Mazes, Neuropsychological Assessment Battery Mazes; TMT-A, Trail-making Test Part A; WMS-III SS, Wechsler Memory Scale-Third Edition Spatial Span.

total variance, and thus a single-factor solution was indicated.

# **DISCUSSION**

Overall, the results of this study indicate that the MCCB-J is a useful tool to evaluate cognitive function in schizophrenia. In addition, some of the psychometric properties of the BACS-J are replicated. More importantly, this was the first study to compare the MCCB and BACS directly.

The MCCB-J required a mean of 80.0 min to complete, whereas the BACS-J required a mean of 35.4 min. This was easily predicted, as the MCCB-J covered much more cognitive domains than the BACS-J.

As for internal consistency, Cronbach's alpha was 0.72 for the MCCB-J, and 0.78 for the BACS-J, which is in the acceptable range for internal consistency (>0.60). In addition, the intercorrelations between MCCB-J/BACS-J subtests and composite score indicate that the MCCB-J and BACS-J are reliable.

Pearson correlations between corresponding subtests from the MCCB-J and BACS-J provide evidence of good construct validity for all four domains, speed of processing, working memory, verbal learning, and reasoning and problem-solving. In addition, the MCCB-J composite score was significantly and strongly correlated with BACS-J composite score.

Data from the factor analyses show, for both MCCB-J and BACS-J, that a factor accounts for more than 40% of the total variance. According to guidelines regarding the proportion of explained variance, <sup>14</sup> a single-factor solution is the only appropriate solution when any factor accounts for more than 40% of the total variance, regardless of the size of additional factors. Presence of a single factor underlying the baseline cognitive data in both batteries may indicate that a single composite index is appropriate.

The definitive validation of the MCCB-J will require further study. First, further comparisons need to be made for temporal stability. Second, the

<b>Table 6.</b> Factor loadings of MC	CB-1 measures
---------------------------------------	---------------

	(	Componen	t
	1	2	3
TMT-A	-0.88	-0.01	-0.16
BACS SC	0.59	0.51	0.03
HVLT-R	0.40	0.37	0.49
WMS-III SS	0.13	0.84	-0.06
LNS	0.12	0.74	0.47
NAB Mazes	0.78	0.28	0.08
BVMT-R	0.41	0.34	0.56
Fluency	0.27	0.01	0.58
MSCEIT ME	-0.17	0.05	0.79
CPT	0.26	0.58	0.46
Eigenvalue	4.2	1.2	0.9
Percentage of variance	42.5	12.9	9.8

BACS SC, BACS Symbol-coding; BVMT-R, Brief Visuospatial Memory Test-Revised; CPT-IP, Continuous Performance Test-Identical Pairs; Fluency, Category Fluency Animal Naming; HVLT-R, Hopkins Verbal Learning Test-Revised; LNS, Letter-Number Span; MCCB-J, MATRICS Consensus Cognitive Battery (MCCB) Japanese-language version; MSCEIT ME, Mayer-Salovey-Caruso Emotional Intelligence Test Managing Emotions; NAB Mazes, Neuropsychological Assessment Battery Mazes; TMT-A, Trail-making Test Part A; WMS-III SS, Wechsler Memory Scale-Third Edition Spatial Span.

MCCB-J will need to be assessed in various populations of patients with schizophrenia. It is also important to determine whether the MCCB-I is sensitive to cognitive changes during clinical trials.

Table 7. Factor loadings of BACS-J measures

	Component		
	1	2	
Verbal Memory	0.55	0.53	
Digit Sequencing	0.81	0.10	
Token Motor Task	0.04	0.94	
Verbal Fluency	0.79	-0.02	
Symbol-coding Task	0.61	0.36	
Tower of London	0.71	0.38	
Eigenvalue	3.0	0.9	
Percentage of variance	50.2	15.7	

BACS-J, Brief Assessment of Cognition in Schizophrenia Japanese-language version.

#### Conclusion

The present study indicates that the MCCB-J is a promising tool for assessing the major constructs of cognition that have been found to be most impaired and strongly correlated with outcome in patients with schizophrenia.

#### **ACKNOWLEDGMENTS**

This work was supported by the following grants: Health Labor Sciences Research Grant; Research on Psychiatric and Neurological Diseases and Mental Health from MHLW; the Global COE Program 'Basic & Translational Research Center for Global Brain Science' from MEXT and the Research Group for SCHIZOPHRENIA, Japan.

The authors are grateful to the research staff at the four performance sites: Tokushima University (Tsunehiko Tanaka, Masahito Tomotake, and Takeo Tominaga), Okayama University (Hiroshi Ujike, Masafumi Kodama, Yutaka Mizuki, and Shinji Sakamoto), Toyama University (Shimako Nishiyama, Yuko Higuchi, Tomonori Seo, Hidemasa Takagi, and Michio Suzuki), and Tottori University (Satoshi Ikezawa).

None of the authors has any conflict of interest to declare.

#### REFERENCES

- 1. Mohamed S, Paulsen JS, O'Leary D, Arndt S, Andreasen N. Generalized cognitive deficits in schizophrenia: A study of first-episode patients. Arch. Gen. Psychiatry 1999; 56: 749-
- 2. Saykin AJ, Shtasel DL, Gur RE et al. Neuropsychological deficits in neuroleptic naive patients with first-episode schizophrenia. Arch. Gen. Psychiatry 1994; 51: 124-131.
- 3. Green MF. What are the functional consequences of neurocognitive deficits in schizophrenia? Am. J. Psychiatry 1996; 153: 321-330.
- 4. Green MF, Kern RS, Braff DL, Mintz J. Neurocognitive deficits and functional outcome in schizophrenia: Are we measuring the 'right stuff'? Schizophr. Bull. 2000; 26: 119-
- 5. Pantelis C, Maruff P. The cognitive neuropsychiatric approach to investigating the neurobiology of schizophrenia and other disorders. J. Psychosom. Res. 2002; 53: 655-
- 6. Rund BR, Borg NE. Cognitive deficits and cognitive training in schizophrenic patients: A review. Acta Psychiatr. Scand. 1999; 100: 85-95.

- Sharma T, Antonova L. Cognitive function in schizophrenia. Deficits, functional consequences, and future treatment. *Psychiatr. Clin. North Am.* 2003; 26: 25– 40
- 8. Keefe RS, Goldberg TE, Harvey PD, Gold JM, Poe MP, Coughenour L. The brief assessment of cognition in schizophrenia: Reliability, sensitivity, and comparison with a standard neurocognitive battery. *Schizophr. Res.* 2004; 68: 283–297.
- 9. Kaneda Y, Sumiyoshi T, Keefe R, Ishimoto Y, Numata S, Ohmori T. Brief assessment of cognition in schizophrenia: Validation of the Japanese version. *Psychiatry Clin. Neurosci.* 2007; **61**: 602–609.
- 10. Buchanan RW, Davis M, Goff D *et al*. A summary of the FDA-NIMH-MATRICS workshop on clinical trial design for neurocognitive drugs for schizophrenia. *Schizophr. Bull.* 2005; 31: 5–19.
- 11. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV)*. American Psychiatric Association, Washington, DC, 1994.
- 12. Overall JE, Gorham DR. The brief psychiatric rating scale. *Psychol. Rep.* 1962; **10**: 799–812.
- 13. Cronbach LJ. Coefficient alpha and the internal structure of tests. *Psychometrika* 1951; **16**: 297–334.
- Gorsuch RL. Factor Analysis, 2nd edn. Lawrence Earlbaum, Hillsdale, 1983.