Research article

Usefulness of a psychomotor function test as a cognitive function scale for patients with schizophrenia: A pilot study

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1. Introduction

Symptoms of schizophrenia progress slowly and gradually and include the following: 1) positive symptoms, such as hallucinations, delusions, and significant thought disorders, 2) negative symptoms, including a lack of motivation, autistic tendencies, and apathy, and 3) cognitive impairments, such as memory deficits and concentration difficulties (Tandon et al., 2013). Although pharmacological treatment using antipsychotics is the most common therapeutic strategy for schizophrenia, there are currently no effective treatments that specifically target cognitive impairment (Pu et al., 2016). Cognitive function plays an important role in the development of social skills, as well as the ability to develop daily routines (Brüne et al., 2011). Thus, impairments in cognitive function may lead to a wide range of dysfunctions, such as in language, working memory, information processing, attention, and executive function. In addition, previous studies suggested that patients who present with severe cognitive impairment in the early phase of schizophrenia are more likely to develop chronic and severe forms of the disease (Bralet et al., 2008; Hoe et al., 2012). Therefore, the severity of cognitive impairment significantly affects the daily lives of patients and their ability to reintegrate into society.

Patients with schizophrenia have a low level of social and occupational functioning because cognitive impairment significantly affects their working capacity and interpersonal relationships (Bowie et al., 2008). Therefore, the aim of treatment for schizophrenia is the reintegration of patients into society such that they may independently participate in social activities. Improvements in cognitive function have been associated with high-level functional outcomes, including employment (Lexèn et al., 2016). Therefore, an accurate assessment of cognitive function is essential for supporting the reintegration of patients with schizophrenia into society. Among several scales of cognitive function, the Brief Assessment of Cognition in Schizophrenia (BACS) is a commonly used scale worldwide (Bralet et al., 2008; Keefe et al., 2004). BACS enables an objective measurement of cognitive impairment, and is used to assess areas of cognitive function, including verbal memory, verbal fluency, working memory, motor speed, attention, and executive...
The Japanese version (BACS-J), developed by Kaneda et al. (2007), was introduced to help diagnose based on the DSM-IV criteria for schizophrenia and had been taking antipsychotics for at least 3 months at the Okehazama Hospital Fujita Kokoro Care Center between March 2017 and March 2018. Patients with organic central nervous system disorders, drug or alcohol addiction, severe cognitive deficiency, or mental retardation were excluded. The purpose and significance of the present study were explained to all patients in a written format, and consent was obtained from the patients themselves. The present study was approved by the Institutional Review Board of the Okehazama Hospital Fujita Kokoro Care Center (H29-003).

2.2. Study procedures

2.2.1. Baseline and outcome measures

The following baseline measures were collected from each patient: age, sex, years of education, time from diagnosis, and the type and amount of medications currently used. Nine out of 20 patients were on monotherapy with atypical antipsychotics (clozapine: n = 7, olanzapine: n = 2), and 10 were on combination therapy with multiple antipsychotics. The combination of antipsychotics varied among patients. The remaining patient did not take antipsychotics during the study period. The amount of antipsychotics was calculated using the chlorpromazine (CP) equivalent method. Psychiatric symptoms were evaluated using the Positive and Negative Syndrome Scale (PANSS), and severity was assessed by the Clinical Global Impression (CGI) scale. The level of social functioning was evaluated using the Global Assessment of Functioning Scale (GAF), and side effects associated with antipsychotics were assessed by the Drug-Induced Extrapyramidal Symptoms Scale (DIEPSS). Psychomotor function was evaluated using a battery of tests (CRT and CTT) (Kamei et al., 2003, 2012), and cognitive function was assessed by BACS-J (Kaneda et al., 2007).

2.2.2. Test procedures

Psychomotor function tests (CRT and CTT) were performed primarily using computers, and included the assessment of concentration and judgement (Kamei et al., 2003, 2012). The content of each item of the test and how to provide the answers were explained to the patients, and they were given the opportunity to practice the test once prior to the actual test. The practice was performed using training software, which consisted of fewer tasks for CTT than the actual test. Actual measurements were taken after confirming that the patients understood the rules and were fully competent to perform the test. The psychomotor function test and BACS-J were performed on the same day, and lasted for approximately 20 and 50 min, respectively.

2.3. Assessment scales

2.3.1. Assessment of psychomotor function

Psychomotor function test is typically used to evaluate dysfunctions in the central nervous system, such as sedation and hypnosis caused by multiple antihistamines (Kamei et al., 2003, 2012). These effects are used to obtain objective measurements of psychomotor function (Hindmarch et al., 2002). The 2 sub-tests (CRT and CTT) that comprise the psychomotor function test are described below.

2.3.1.1. CRT. CRT is used as an indicator of sensorimotor function and assesses the ability to focus on and react to a critical stimulus (Kamei et al., 2003, 2012). The instrument was equipped with a start button in the middle, as well as 6 reaction buttons aligned in a fan-shape at equal intervals. Each reaction button had red and green lights that were also aligned in a fan-shape, and the green light turned on prior to the red light. After placing the index finger onto the start button, patients were asked to use the green light as a warning in order to react quickly when the red light turned on. Patients were asked to press the reaction button next to the red light as soon as it lit up in order to turn it off. The number of warning green lights gradually increased (1, 3, and 6 light(s) in this order) and decreased (6–3 and then 1 light(s) in this order) during the test. The task was performed 8 times at each level. Therefore, measurements were taken 48 times in a single test. The time between the red light coming on and the finger being released from the starting button was taken as CRT. Low scores reflected a rapid reaction to the task, indicating a high level of attention.

2.3.1.2. CTT. CTT is composed of the following two tasks:

- Tracking task (TT)

TT evaluates the ability to react to and track an object (Kamei et al., 2003, 2012). In TT, subjects were asked to track a round object that appeared on the computer screen. The object moved along a straight line in a random manner, and subjects were asked to place the cursor in the middle of the object using a computer mouse and track its movement for 9 min. The distance between the center of the object and the cursor was measured in pixels, and performance was evaluated as the mean distance between the two points for samples randomly selected during the 9-minute test. Low scores indicated the ability to accurately track the object.

- Peripheral awareness task (PAT)

PAT was performed at the same time as TT, ensuring that it did not interfere with TT. PAT evaluates peripheral awareness (Kamei et al., 2003, 2012) and lasts for 9 min, similar to TT. In PAT, 100 stimuli...
In order to evaluate the applicability of the psychomotor function tests (CRT and CTT) to the assessment of patients with schizophrenia, the outcomes of these tests were compared with the sub-score and total score of BACS, and the outcomes of psychiatric assessments using Pearson's correlation coefficient. A multiple regression analysis was performed to clarify the relationship between psychomotor function tests and the total BACS score, which correlated with most of the components of the psychomotor function tests.

All statistical analyses were performed using SPSS (version 24; IBM Co., Armonk, NY, USA), and \( p < 0.05 \) was considered to be significant.

3. Results

3.1. Patient characteristics

The baseline characteristics and psychiatric symptoms of the 20 patients enrolled in the present study are summarized in Table 2. There were 10 male (50%) and 10 female (50%) patients, with 17 (85.0%) being inpatients and the remaining 3 (15.0%) being outpatients. The age of patients was 45.4 ± 11.7 (mean ± SD) years. On average, patients received 12.2 ± 1.5 years of education, had been diagnosed for 18.5 ± 7.5 years, and were taking 964.3 ± 453.9 mg of CP daily.

The mean scores for positive, negative, and general psychopathological symptoms measured by PANSS were 22.4 ± 3.0, 21.8 ± 2.8, and 47.3 ± 5.8, respectively, with a total PANSS score of 91.9 ± 10.1. The mean CGI and GAF scores for social functioning were 5.0 ± 1.1 and 38.3 ± 17.6, respectively.

3.2. Outcomes of psychomotor function and cognitive function tests

The results from the psychomotor function test battery and BACS in schizophrenia patients are shown in Table 3. The scores for psychomotor functions assessed in the present study were as follows: \( 8.00 \times 10^{-5} \pm 1.03 \) for CRT, \(-1.00 \times 10^{-5} \pm 1.03 \) for CTT-PAT (a component of CTT), and \( 4.00 \times 10^{-5} \pm 1.03 \) for CTT-PAT (a component of CTT). In BACS, scores between -0.5 to -1.0 indicate mild cognitive impairment, -1.0 to -1.5 moderate cognitive impairment, and below -1.5 severe cognitive impairment. The mean BACS scores for cognitive function in 20 schizophrenia patients were -2.8 ± 1.4 for verbal memory, -1.2 ± 1.0 for verbal fluency, -2.0 ± 1.4 for working memory, -2.5 ± 1.2 for motor function, -2.3 ± 1.3 for attention, and -2.5 ± 2.4 for executive function, with a total mean score of -2.2 ± 1.0.

3.3. Correlation between psychomotor function tests (CRT and CTT) and BACS

The relationships between the results from psychomotor function tests (CRT and CTT) and cognitive function assessed by BACS are summarized in Table 4. The total BACS score for cognitive function

| Background | Gender | Male 10 (50.0%) | Female 10 (50.0%) |
|------------|--------|----------------|------------------|
| Inpatient  | 17 (85.0%) |                |                  |
| Outpatient | 3 (15.0%)  |                |                  |
| Age (years)| 45.4 ± 11.7 |               |                  |
| Years of education (years) | 12.2 ± 1.5 |               |                  |
| Time from diagnosis (years)  | 18.5 ± 7.5  |               |                  |
| Total dose of antipsychotics (CP equivalent mg/day) | 964.3 ± 453.9 |               |                  |

| Psychiatric symptoms | PANSS (total) | Positive symptoms | Negative symptoms | General psychopathological symptoms | CGI | GAF |
|----------------------|--------------|------------------|------------------|------------------------------------|-----|-----|
|                      | 91.9 ± 10.1  | 22.4 ± 3.0       | 21.8 ± 2.8       | 47.3 ± 5.8                          | 5.0 ± 1.1 | 38.3 ± 17.6 |

Values are expressed as the mean ± SD. CP: Chlorpromazine, PANSS: Positive and Negative Syndrome Scale, CGI: Clinical Global Impression, GAF: Global Assessment of Functioning Scale.
negatively correlated with CRT ($r = -0.506, p = 0.023$), CTT-TT ($r = -0.463, p = 0.040$), and CTT-PAT ($r = -0.609, p = 0.004$). The correlation was negative because high CRT, CTT-TT, and CTT-PAT and low BACS scores indicate reduced cognitive function. A correlation was observed between attention in BACS and CRT ($r = -0.633, p = 0.003$), motor speed ($r = -0.486, p = 0.03$), and attention ($r = -0.716, p < 0.001$) in BACS.

4. Multiple regression analysis with BACS scores as outcome variables

A multiple regression analysis was performed to clarify the relationship between psychomotor function tests and the total BACS score because it correlated with the majority of components in the psychomotor function tests. The total BACS score was defined as the outcome variable, and CRT, CTT-TT, and CTT-PAT scores as explanatory variables (Table 5). CTT-PAT was independently associated with the total BACS score ($\beta = -0.609, p = 0.004$) with an $R^2$ of 0.37 (Table 5).

5. Discussion

Cognitive function assessments play an important role in the accurate and objective evaluation of functional impairment in schizophrenia patients aiming for social reintegration. Due to the relationship between cognitive function tests and psychomotor function tests, we attempted to clarify the applicability of psychomotor function tests for the assessment of cognitive function.

Patients with schizophrenia often have impaired cognitive function, including verbal memory, working memory, attention and alertness, reasoning and problem solving, and information processing, as well as impairments in the functions required for social interactions, such as the ability to recognize facial expressions (Tandon et al., 2013). Cognitive impairments are common and associated with a lack of motivation and the worsening of patient-physician relationships and long-term treatment outcomes. Cognitive function assessed by BACS (Keeke, 2008) was 1.5-2-fold lower in patients with schizophrenia than in healthy volunteers. Patients in the present study had moderately impaired verbal fluency with a Z score of -1.2 as well as severely impaired verbal learning, working memory, motor function, attention, and executive function with Z scores below -2.0. The overall score was -2.2, suggesting that the patient population had moderate to severe cognitive impairment.

We examined the relationship between psychomotor function tests (CRT and CTT) and BACS, and revealed a negative correlation between CRT and the BACS sub-score for attention. This result suggested that positive outcomes in CRT indicate a high level of attention. The correlation between CRT and BACS may be explained by CRT reflecting cognitive function for attention. PAT is a component of CTT and was associated with many of the sub-scores of BACS. PAT negatively correlated with attention and working memory. These results suggest that positive outcomes in PAT indicate high levels of attention and working memory in BACS. CTT consists of 2 tasks performed simultaneously, and PAT reflects the level of attention, as does CRT. Attention is the ability to focus on a target stimulus and maintain that level of attention while the stimulus is being processed. In addition to attention, subjects undergoing PAT will likely require working memory, which is needed to memorize actual tasks, which may explain the relationship between PAT and working memory in addition to attention. We also performed a multiple regression analysis with attention in BACS as the outcome and demonstrated that PAT was independently associated with the BACS score, indicating that PAT and CRT are effective measures of cognitive function. Cognitive function, such as attention and working memory, has a stronger impact on employment than psychiatric symptoms and the time from diagnosis (Kaneda et al., 2009). The magnitude of cognitive impairment has been shown to predict daily living abilities and real-world functioning to a greater extent than psychiatric symptoms (Green et al., 2000). A previous study that examined the relationship between cognitive function and employment in patients with schizophrenia revealed that working memory was a strong factor influencing the employment status and that improvements in working memory

### Table 3. Outcomes of psychomotor function tests and cognitive function tests.

| Test item   | Schizophrenia patients |
|-------------|------------------------|
| CRT         | 8.00 $\times$ 10^{-3}$ \pm$ 1.03 |
| CTT-TT      | -1.00 $\times$ 10^{-2}$ \pm$ 1.03 |
| CTT-PAT     | 4.00 $\times$ 10^{-3}$ \pm$ 1.03 |
| BACS total score | -2.24 $\pm$ 1.00 |
| Verbal memory | -2.78 $\pm$ 1.42 |
| Verbal fluency  | -1.22 $\pm$ 1.02 |
| Working memory  | -2.04 $\pm$ 1.44 |
| Motor speed    | -2.53 $\pm$ 1.20 |
| Attention       | -2.34 $\pm$ 1.35 |
| Executive function | -2.53 $\pm$ 2.50 |

Values are expressed as the mean $\pm$ SD.

### Table 4. Correlation between outcomes of psychomotor function tests and BACS in all patients.

| Psychomotor function tests | BACS |
|----------------------------|------|
|                            | Verbal memory | Verbal fluency | Working memory | Motor speed | Attention | Executive function | Total score |
| CRT                        | -0.176$^a$ | -0.391$^a$ | -0.422$^a$ | -0.272$^a$ | -0.521$^a$ | -0.286$^a$ | -0.506$^a$ |
|                            | 0.459$^b$ | 0.089$^b$ | 0.064$^b$ | 0.245$^b$ | 0.019$^b$ | 0.221$^b$ | 0.023$^b$ |
| CTT-TT                     | -0.101$^a$ | -0.173$^a$ | -0.484$^a$ | -0.257$^a$ | -0.344$^a$ | -0.394$^a$ | -0.463$^a$ |
|                            | 0.672$^b$ | 0.465$^b$ | 0.031$^b$ | 0.274$^b$ | 0.138$^b$ | 0.086$^b$ | 0.040$^b$ |
| CTT-PAT                    | -0.409$^a$ | -0.499$^a$ | -0.633$^a$ | -0.486$^a$ | -0.716$^a$ | -0.048$^a$ | -0.609$^a$ |
|                            | 0.074$^b$ | 0.025$^b$ | 0.003$^b$ | 0.030$^b$ | <0.001$^b$ | 0.839$^b$ | 0.004$^b$ |

BACS: Brief Assessment of Cognition in Schizophrenia (Japanese version), CRT: choice reaction time, CTT: compensatory tracking test, TT: tracking task, PAT: peripheral awareness task. $^a$ Pearson correlation coefficient, $^b$ p-value.

### Table 5. Multiple regression analysis with the total BACS score as the outcome variable.

| Unstandardized coefficient | Standardized coefficient | t-value | p-value |
|----------------------------|--------------------------|---------|---------|
| Constant                   | -2.235                   | -12.335 | <0.001  |
| CTT-PAT                   | -0.590                   | -0.609  | -3.258  | 0.004   |

R$^2$ = 0.37.

BACS: Brief Assessment of Cognition in Schizophrenia (Japanese version), CTT: compensatory tracking test, PAT: peripheral awareness task.
resulted in greater social functioning (Green et al., 2000). Therefore, the assessment of cognitive abilities related to daily-living skills or functional capacity is important to facilitate the development of novel therapies and improve daily-living functioning. The extent of on-job support and contact with employment specialists were predicted by the cognitive domains of attention and psychomotor speed (working memory) as well as by the severity of psychotic symptoms (McGurk et al., 2003). Collectively, these findings and the present results demonstrate that attention and working memory are both important functions for patients to reintegrate into society, and their assessment using psychomotor function tests including CRT and CTT may reflect the ability to achieve this goal.

In contrast to interviews in other cognitive tests, psychomotor function tests are simple to conduct because administrators are not required to ask questions to subjects and the tests are performed within a set amount of time. They also do not require specialized skills by administrators and are associated with a low risk of measurement errors. Therefore, they overcome the issues associated with BACS, specifically the need for administrators to obtain BACS certification. In addition, CRT and CTT may be performed within a shorter period of time than BACS. Cognitive function tests that are not time-consuming are preferred because they reduce stress in study subjects and are more efficient.

The present study has several limitations. The results obtained may not be generalizable because they were based on data collected from 20 patients with schizophrenia. Future studies are needed with a larger sample size to clarify the reliability of CRT and CTT measurements. Moreover, although antipsychotics are categorized into first and second generations with no significant differences in terms of their impact on cognitive function (Ayesa-Arriola et al., 2013), further studies are required to assess whether the dose and type of antipsychotics or any other factors influence the outcomes of psychomotor function tests.

Furthermore, we did not compare our psychomotor function tests with other cognitive function evaluations. The Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) trial showed that 93% of the variance observed in the cognitive composite score was accounted for by 6 tests that required only 35 min to complete (Keefe et al., 2006). Furthermore, in the CATIE trial, the Digit Symbol coding task, which takes less than 5 min to complete, accounted for more than 50% of the variance observed in the cognitive composite score (Gonzalez-Blanch et al., 2011). Our psychomotor function tests (CRT and CTT) required 20 min to complete. In measurements of cognitive function, it is important to consider not only the balance between brevity and comprehensiveness, but also the characteristics of cognitive function. Our tests are characterized by high sensitivity to attention and psychomotor speed (working memory), which are required to perform the relevant tasks (McGurk et al., 2003). In addition, since our tests use a computer and are easy to operate, they do not need to be performed by a specially trained clinician and the patient also does not require any special training. Additionally, in comparisons with the Screen for Cognitive Impairment in Psychiatry (SCIP), which predicts global cognitive impairment. Therefore, although our tests may be useful, they need to be directly compared with other test methods.

In conclusion, CRT and CTT constitute a battery of tests that objectively and easily assess psychomotor function. The present study demonstrated that CRT and CTT were effective for evaluating higher order cognitive function, such as attention, as well as working memory, which influence social functioning. Therefore, among psychomotor function tests, CRT and the CTT are applicable to the assessment of cognitive function in patients with schizophrenia in real-world clinical settings.

**Declarations**

**Author contribution statement**

Hiroyuki Kamei: Conceived and designed the experiments; Performed the experiments; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Ipppei Takeuchi: Performed the experiments; Contributed reagents, materials, analysis tools or data.

Yui Yamada: Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data.

Manako Hanya: Conceived and designed the experiments; Analyzed and interpreted the data.

Kiyoshi Fujita: Conceived and designed the experiments.

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**Data availability statement**

Data included in article/supplementary material/referenced in article.

**Declaration of interests statement**

The authors declare no conflict of interest.

**Additional information**

No additional information is available for this paper.

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