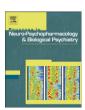
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#### Quality of life and cognitive dysfunction in people with schizophrenia

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#### ABSTRACT

The main purpose of the present study was to examine the relationship between quality of life (QOL) and cognitive dysfunction in schizophrenia. Subjects were 61 stabilized outpatients. Quality of life and cognitive function were assessed using the Quality of Life Scale (QLS) and the Brief Assessment of Cognition in Schizophrenia (BACS), respectively. Clinical symptoms were evaluated with the Positive and Negative Syndrome Scale (PANSS) and the Calgary Depression Scale for Schizophrenia (CDSS). The BACS composite score and the BACS Verbal memory score were positively correlated with the QLS total score and two subscales. The BACS Attention and speed of information processing score had positive correlation with the QLS total and all the subscales scores. The PANSS Positive and Negative syndrome scores also had significant correlations with the QLS total score and all of the subscales. In addition, the CDSS score was negatively correlated with the QLS total score and some of the subscales. Stepwise regression analysis showed that the BACS Attention and speed of information processing score was an independent predictor of the QLS total score but it was less associated with the QLS than the PANSS Negative syndrome score and the CDSS score. The results suggest that negative and depressive symptoms are important factors on patients' QOL and also support the view that cognitive performance provides a determinant of QOL in patients with schizophrenia.

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#### 1. Introduction

Quality of life (QOL) is thought to be one of the key outcome variables in the treatment of schizophrenia (Matsui et al., 2008), and the importance of evaluating it has been increasing in patient care and clinical research. Previous studies have revealed that several clinical factors such as negative and positive symptoms, depressive symptoms, and extrapyramidal adverse effect are associated with lowered QOL (Browne et al., 1996; Dickerson et al., 1998; Smith et al., 1999; Norman et al., 2000; Fitzgerald et al., 2001; Rocca et al., 2005; Strejilevich et al., 2005; Bozikas et al., 2006; Hofer et al., 2006; Tomotake et al., 2006; Aki et al., 2008; Yamauchi et al., 2008). Moreover, Yamauchi et al. (2008) reported that QOL correlated with dose of antipsychotics, and Xiang et al. (2007) and Browne et al. (1996) demonstrated that number of hospitalizations and duration of illness were associated with QOL.

Recently, cognitive dysfunction has been paid much more attention because they may lead to poor social functioning. Cognitive dysfunction is thought to be a core feature of schizophrenia (Kraus and Keefe, 2007), and it has been reported that cognitive functions of schizophrenia patients are of the order of one to two standard deviations below the mean of healthy controls in several cognitive dimensions, particularly memory, attention, verbal fluency, and executive function (Heinrichs

Abbreviations: BACS, the Brief Assessment of Cognition in Schizophrenia; CDSS, the Calgary Depression Scale for Schizophrenia; DIEPSS, the Drug-Induced Extrapyramidal Symptoms Scale; PANSS, the Positive and Negative Syndrome Scale; QLS, the Quality of Life Scale: OOL, quality of life.

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and Zakzanis, 1998; Gold, 2004; Kraus and Keefe, 2007; Savilla et al., 2008)

Previous research groups have studied the relationship between QOL and cognitive function in people with schizophrenia, and reported the significant correlations between QOL and some domains of cognitive function such as verbal memory, vocabulary, fluency performance, attention, social knowledge, and executive function (Dickerson et al., 1998; Addington and Addington, 2000; Bozikas et al., 2006; Ritsner, 2007; Matsui et al., 2008; Savilla et al., 2008). Although, considering the results of previous studies, it is clear that cognitive dysfunctions and some clinical symptoms are significantly correlated with lowered QOL in schizophrenia patients, it seems to remain unclear how much impact these factors have on patients' QOL. Some studies demonstrated that cognitive dysfunction has a greater influence on patients' QOL than do positive symptoms (Breier et al., 1991; Green, 1996; Ho et al., 1998). On the other hand, some reported that neuropsychological function had a little impact on patients' QOL in the presence of some clinical symptoms (Wegener et al., 2005; Matsui et al., 2008). The discrepancy among these studies might have been caused by differences of sample population, sample size, cognitive tests, and QOL scales (Breier et al., 1991; Green, 1996; Wegener et al., 2005; Matsui et al., 2008).

The purpose of the present study was to elucidate clinical determinants of QOL in schizophrenia patients with a special reference to cognitive dysfunction. Using a schizophrenia disease-specific QOL measure, we have already studied and reported significant correlations between QOL and negative factor, cognitive factor, and emotional discomfort factor which derived from the Positive and Negative Syndrome Scale (PANSS). But we did not assess cognitive function with a real neuropsychological battery in the study (Yamauchi et al., 2008). Hofer et al. (2007) demonstrated that clinical assessment of cognitive deficits on PANSS is not a viable alternative to neuropsychological testing to obtain information about cognitive functioning in schizophrenia. Therefore, in the present study, we assessed cognitive function using the Brief Assessment of Cognition in Schizophrenia (BACS) (Keefe et al., 2004; Kaneda et al., 2007) that is a newly developed neuropsychological battery for assessing cognitive function of schizophrenia patient.

#### 2. Methods

#### 2.1. Subjects

Clinical data were collected at Department of Psychiatry, Tokushima University Hospital from 1 October 2007 to 31 March 2009. Treating psychiatrists consecutively asked 77 stabilized outpatients with a DSM-IV diagnosis of schizophrenia to participate in this study every weekday for the first 6 months and a particular day of the week for another 12 months. Subjects were excluded if they presented with any organic central nervous system disorder, epilepsy, mental retardation, severe somatic disorder, drug dependence, or alcohol dependence. Of 77 patients, 62 gave us written informed consent to participate in this study. As one subject did not complete all the assessments, data from 61 were used for analysis. This study was approved by the Ethics Committee of University of Tokushima.

All subjects had been regularly receiving outpatient treatment. The information on patients was obtained from both patients and family members living with them by treating psychiatrists. Their mean age was 40.1 years (SD = 12.2), ranging from 20 to 60 years old. The subjects had never been hospitalized during the previous 6 months, including 13 who had never had inpatient treatment. 45 had followed the same antipsychotic regimen for at least 6 months before recruitment. Although 16 subjects had slight changes in regimen during the previous six months, the 16 were judged as clinically stabilized by the treating psychiatrists.

#### 2.2. Procedure

To assess QOL, we used the Quality of Life Scale (QLS) (Heinrichs et al., 1984, 2001). Cognitive function was evaluated using the BACS. Clinical symptoms were evaluated using the PANSS, the Calgary Depression Scale for Schizophrenia (CDSS), and the Drug-Induced Extrapyramidal Symptoms Scale (DIEPSS).

The QLS is a rating scale to assess QOL by means of semistructured interview. The ratings are based upon patients' self-report and observers' judgment about the functioning and life circumstances. This instrument includes four subscales measured by a total of 21 items, and each item is rated from 0 to 6. The four subscales are Interpersonal relations, Instrumental role, Intrapsychic foundation, and Common objects and activities. Higher scores indicate higher levels of QOL. Experienced psychiatrists who have been treating the patients for a long term and understood the patients' living conditions conducted the interviews according to the Evaluation Manual for the QLS (Heinrichs et al., 2001). They got information about the patients from family members and psychiatric social workers when it was necessary.

The BACS has been developed for clinical trials with a brief battery of tests for measuring cognition. It assesses the aspects of cognition that were found to be most impaired and most strongly correlated with outcome in patients with schizophrenia. The domains of cognitive function that are evaluated by the BACS are Verbal memory (List learning), Working memory (Digit sequencing task), Motor speed (Token motor task), Verbal fluency (Category instances and Controlled oral word association test), Attention and speed of information processing (Symbol coding), and Executive function (Tower of London). The BACS is fully portable, and is designed to be easily administered by a variety of testers, including nurses, clinicians, psychiatrists, neurologists, social workers, and other mental staff (Keefe et al., 2004; Kaneda et al., 2007). It was reported that the Japanese version of it was a reliable and practical scale to evaluate cognitive function in schizophrenia (Kaneda et al., 2007). In the present study, we used the Japanese version of the BACS and the BACS data were collected by clinical psychologists who were very experienced and well trained for the use of it.

The PANSS was originally designed as a rating scale that represents Positive, Negative and General psychopathology (Kay et al., 1987, 1991). The score ranges from 30 to 210 for the global score, and higher score indicates a greater level of symptom severity. Some of the authors who were all experienced psychiatrists conducted the interviews according to the Evaluation Manual for the PANSS (Kay et al., 1991).

The CDSS was specifically developed to distinguish depressive symptoms from positive and negative symptoms or antipsychotic-induced side effects. This scale is a 9-item questionnaire (depression, hopelessness, self-deprecation, guilty ideas of reference, pathological guilt, morning depression, early awakening, suicidality, and observed depression), and higher score indicates a greater level of depression. The reliability and validity of the scale have been verified (Addington et al., 1993; Kaneda et al., 2000).

The DIEPSS is composed of eight individual parameters (gait, bradykinesia, sialorrhea, muscle rigidity, tremor, akathisia, dystonia, and dyskinesia) and one global assessment constructed to assess extrapyramidal adverse effects, using 5-point scale that ranges from 0 to 4. Higher score indicates greater level of extrapyramidal adverse effects. In this study, the sum of eight individual parameters was considered the extrapyramidal symptoms score. Some of the authors assessed the drug-induced extrapyramidal symptoms according to the Rater's Manual for the DIEPSS (Inada, 1996).

#### 2.3. Statistical analysis

Spearman rank correlation coefficients were calculated to study the relationship between the QLS and other clinical variables including the BACS scores, the PANSS Positive syndrome score, the

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