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Assessing Weight-Related Quality of Life in Persons with Schizophrenia

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ABSTRACT

Background: Weight gain by antipsychotic medicines may result in adverse physical and psychosocial consequences.

Objectives: This preliminary study was performed to examine weight-related quality of life (QOL) in persons with schizophrenia using the Impact of Weight on Quality of Life-Lite (IWQOL-Lite) questionnaire. Psychometric properties of the IWQOL-Lite were evaluated for persons with schizophrenia (n = 37).

Methods: In this cross-sectional study, the IWQOL-Lite was administered together with other self-report measure, the Schizophrenia Quality of Life Scale (SQLS), to assess validity. Psychopathology was assessed using the Brief Psychiatric Rating Scale.

Results: Internal consistency reliability of the five subscales of the IWQOL-Lite (Physical Function, Self-Esteem, Sexual Life, Public Distress, and Work) ranged from 0.84 to 0.95 and was 0.96 for the total IWQOL-Lite score. Correlations between the IWQOL-Lite and SQLS supported the construct validity of the IWQOL-Lite. Psychopathology rather than body mass index was more importantly correlated with the IWQOL-Lite scores.

Conclusions: The IWQOL-Lite appears to be a unique and clinically practical measure of QOL even in persons with schizophrenia. However, a further prospective study would be needed before using the IWQOL-Lite as a weight-related QOL measure in this population.

KEY WORDS

antipsychotic agents, quality of life, schizophrenia, body weight, questionnaires

INTRODUCTION

Quality of life (QOL) in persons with schizophrenia is an area of major concern to both researchers and clinicians. Since atypical (second generation) antipsychotic agents are considered to have favorable risk-benefit profiles, they are expected to improve QOL in persons with schizophrenia. Meanwhile, some antipsychotic agents including second generation ones are known to be often associated with weight gain (Vanina *et al.*, 2002), and weight gain is reported to affect QOL scores (Kolotkin *et al.*, 2001), even in persons with schizophrenia (Allison *et al.*, 2003).

Kolotkin *et al.* (1997; 1995) developed the Impact of Weight on Quality of Life (IWQOL) to assess QOL in obesity. Eight areas of functioning are assessed by the IWQOL: health, social/interpersonal, work, mobility, self-esteem, sexual life, activities of daily living, and comfort with food. The IWQOL has been shown to be a reliable and valid instrument for measuring posttreatment changes in health-related QOL. Later, a brief version of the IWQOL (IWQOL-Lite) that is more convenient for use as an outcome measure was developed (Kolotkin *et al.*, 2001). The IWQOL-Lite is a 31-item questionnaire, and provides scores on five scales (Physical Function, Self-Esteem, Sexual Life, Public Distress, and Work).

The IWQOL-Lite was shown to be psychometrically sound and clinically sensitive in both non-psychiatric (Kolotkin *et al.*, 2001) and psychiatric samples (Kolotkin *et al.*, 2006). This preliminary study was performed to examine weight-related QOL in Japanese persons with schizophrenia, and to test the validity and value of the Japanese IWQOL-Lite in this population.

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Table 1. Demographic Characteristics of Subjects

N	Age	Duration of illness	BMI	BPRS	Dosage	IWQOL-Lite[a]					SQLS				
(Female/ Male)	(yrs)	(yrs)	(kg/m^2)	(Total)	(mg/d)[b]	Physical Function	Self-Esteem	Sexual Life	Public Distress	Work	Grand Total	Psycho-social	Motivation/ energy	Symptoms/ side effects
	Mean ±SD	Mean ±SD	Mean ±SD	Mean ±SD	Mean ±SD	Mean ±SD	Mean ±SD	Mean ±SD	Mean ±SD	Mean ±SD	Mean ±SD	Mean ±SD	Mean ±SD	Mean ±SD
37 (15/22)	54.5± 13.5	27.4± 10.7	24.8± 4.5	41.8± 9.5	12.1± 14.0	64.2± 25.1	67.0± 30.4	80.6± 23.5	77.8± 23.2	72.9± 28.7	71.3 ± 21.2	43.9± 21.5	48.4± 18.6	32.1± 20.3

BPRS = Brief Psychiatric Rating Scale; IWQOL-Lite; = Impact of Weight on Quality of Life-Lite; SQLS = Schizophrenia Quality of Life Scale.
[a]Transformed Score (0 to 100).
[b]Haloperidol-equivalents.

METHODS

Subjects

In this cross-sectional study, subjects were 37 medicated chronic inpatients with schizophrenia. The diagnosis was based on Diagnostic and Statistical Manual (DSM)-IV (American Psychiatric Association, 1994) criteria for schizophrenia, a detailed clinical interview, and review of the prior records. We chose the subjects at random from the larger pool of inpatients. Only patients who gave informed consent participated in the study. Subjects were excluded if they presented with any organic central nervous system disorder, significant substance abuse, and mental retardation. Table 1 shows demographic characteristics of the subjects.

Data collection

The Japanese IWQOL-Lite was performed together with the Japanese Schizophrenia Quality of Life Scale (SQLS; Kaneda *et al.*, 2002). The SQLS, a brief self-report QOL measure specific to persons with schizophrenia, is a 30-item questionnaire, and provides scores on three subscales (psychosocial, motivation/energy, and symptoms/side effects). Although each of these questionnaires was designed as a self-administered instrument, the data collection was conducted by a trained interviewer, who provided assistance if needed. Psychopathology was assessed with the 18-item Brief Psychiatric Rating Scale (BPRS, 1-7 scores; Overall and Gorham, 1962). Based on previous groupings of BPRS symptoms (Guy, 1976), the following five BPRS factors were derived: anxiety/depression (AD), anergia (AN), thought disturbance (TD), activation (AC), and hostile/suspiciousness (HS). The same investigator carried out all the clinical investigations, and the QOL and clinical evaluations were performed on the same day.

Data analysis

Descriptive statistics were used to report the patients in terms of socio-demographic and clinical data. Internal consistency was calculated for all subscales using Cronbach's alpha (Cronbach, 1951). To test the construct validity, Spearman correlations were used between the IWQOL-Lite and SQLS.

RESULTS

Table 1 shows means and standard deviations of the IWQOL-Lite scales.

Reliability

Internal consistency

Cronbach's alpha was used to determine the internal consistency of five subscales and the total IWQOL-Lite

Table 2. IWQOL-Lite Scores and Correlation Coefficients

Scale and items	Score (Mean ± SD)	Cronbach's alpha	Item to total correlation	
Physical Function	64.2 ± 25.1[a]	0.92		
Picking up objects	2.6 ± 1.4		0.71	****
Tying shoes	2.3 ± 1.3		0.80	****
Getting up from chairs	2.2 ± 1.2		0.68	****
Using stairs	2.5 ± 1.3		0.86	****
Dressing	2.4 ± 1.3		0.79	****
Mobility	2.3 ± 1.4		0.76	****
Crossing legs	2.2 ± 1.4		0.76	****
Feel short of breath	2.5 ± 1.4		0.51	**
Painful stiff joints	2.2 ± 1.1		0.65	****
Swollen ankles/legs	2.1 ± 1.3		0.64	****
Worried about health	3.5 ± 1.5		0.31	
Self-Esteem	67.0 ± 30.4	0.95		
Self-conscious	2.8 ± 1.5		0.86	****
Self-esteem not what it could be	2.3 ± 1.4		0.82	****
Unsure of self	2.5 ± 1.5		0.85	****
Do not like myself	2.2 ± 1.3		0.89	****
Afraid of rejection	2.2 ± 1.4		0.74	****
Avoid looking in mirror	2.0 ± 1.3		0.83	****
Embarrassed in public	2.3 ± 1.4		0.84	****
Sexual Life	80.6 ± 23.4	0.92		
Do not enjoy sexual activity	1.6 ± 1.0		0.84	****
Little sexual desire	2.0 ± 1.2		0.79	****
Difficulty with sexual performance	1.7 ± 1.0		0.92	****
Avoid sexual encounters	1.7 ± 0.9		0.89	****
Public distress	77.8 ± 23.2	0.89		
Experience ridicule	2.2 ± 1.3		0.69	****
Fitting in public seats	1.9 ± 1.1		0.70	****
Fitting through aisles	1.9 ± 1.1		0.83	****
Worry about finding chairs	1.8 ± 1.1		0.75	****
Experience discrimination	1.8 ± 0.9		0.71	****
Work	72.9 ± 28.7	0.90		
Trouble accomplishing things	2.3 ± 1.4		0.70	****
Less productive than could be	2.1 ± 1.3		0.91	****
Do not receive recognition	2.0 ± 1.2		0.78	****
Afraid to go on interviews	1.9 ± 1.3		0.72	****

[a]Transformed Score (0 to 100) *p < .05, **p < .01, ***p < .001, and ****p < .0001 by Spearman rank correlations.

score. Cronbach's alpha values for individual scales were as follows: Physical Function, 0.92; Self-Esteem, 0.95; Sexual Life, 0.92; Public Distress, 0.89; and Work, 0.90, with the overall coefficient equaling 0.96 (Table 2). All of them reached the acceptable range for internal consistency (i.e., over 0.70; Cicchetti, 1994).

Corrected item to total correlation

Table 2 shows the correlations of items with their scale total. All items, with one exception ("Worried about health" in Physical Function) were significantly correlated with their own scale score (corrected to exclude the item being correlated).

Validity

Spearman's rank correlations showed that the IWQOL-Lite 'physical function' and 'self-esteem' scores were significantly correlated with the SQLS 'psychosocial' and 'symptoms/side effects' scores (Table 3). Meanwhile, the IWQOL-Lite 'sexual life' score was significantly correlated with the SQLS 'motivation/energy' score. The IWQOL-Lite 'public distress', 'work', and 'Grand Total' scores were significantly correlated with all SQLS subscale scores.

Table 3. Correlation Coefficients between Dimensions on IWQOL-Lite and SQLS

		SQLS		
		Psychosocial	Motivation/energy	Symptoms/side effects
IWQOL-Lite	Physical Function	-0.66****	-0.31	-0.54***
	Self-Esteem	-0.49**	-0.27	-0.48***
	Sexual Life	-0.18	-0.35*	-0.32
	Public Distress	-0.47**	-0.41*	-0.43**
	Work	-0.48**	-0.39*	-0.46**
	Grand Total	-0.65****	-0.41*	-0.57***

*p < .05, **p < .01, ***p < .001, and ****p < .0001 by Spearman rank correlations.

Table 4. Correlations between IWQOL-Lite Subscales and Variables

		BMI	BPRS						Dosage
			AC	AN	AD	HS	TD	Total	
IWQOL-Lite	Physical Function	-.03	-.24	-.21	-.40*	-.05	.07	-.20	.15
		(-.33)	(-.25)	(-.33)	(-.57*)	(.13)	(-.18)	(-.36)	(.07)
	Self-Esteem	-.07	-.16	-.24	-.32	.04	.28	-.04	.07
		(-.14)	(-.11)	(-.41)	(-.18)	(-.06)	(.10)	(-.14)	(-.23)
	Sexual Life	-.01	-.07	-.21	-.02	.11	.28	.12	.16
		(.25)	(-.16)	(-.54*)	(-.26)	(-0.9)	(-.03)	(-.27)	(-.15)
	Public Distress	-.18	-.08	-.13	-.37*	.16	.02	-.09	.10
		(-.64**)	(-.39)	(-.23)	(-.50)	(.03)	(-.45)	(-.49)	(-.22)
	Work	.10	-.10	-.25	-.28	.12	.12	-.04	.06
		(-.30)	(-.25)	(-.43)	(-.27)	(-.11)	(-.12)	(-.33)	(-.42)
	Grand Total	-.06	-.20	-.24	-.34*	.13	.17	-.06	.19
		(-.26)	(-.32)	(-.36)	(-.46)	(.08)	(-.10)	(-.34)	(-.06)

BMI = body mass index; AC = activation; AD = anxiety/depression; AN = anergia; HS = hostitle/suspiciousness; TD = thought disturbance. *p < .05 by Spearman rank correlations.

Results obtained from a sample with only overweight subjects (BMI > 25) in parentheses (n = 16).

Correlations with body mass index (BMI) and psychopathology

We found no significant correlations between BMI and scores of the IWQOL-Lite subscales and 'Grand Total' (Table 4). The scores of the IWQOL-Lite 'physical function', 'public distress', and 'Grand Total' were significantly correlated with the score of BPRS AD factor. When we use only overweight subjects (BMI > 25), the score of the IWQOL-Lite 'public distress' was significantly correlated with BMI. Also, the scores of the IWQOL-Lite 'physical function' and 'sexual life' were significantly correlated with the scores of BPRS AD and AN factors, respectively.

DISCUSSION

Overall, the results of this study show that the IWQOL-Lite is useful to evaluate QOL in persons with schizophrenia, but provide little support for the utility of the IWQOL-Lite across the BMI spectrum, or give any data on its sensitivity to change.

For internal consistency, Cronbach's alpha was as high as those in the general population (Physical Function: alpha = 0.94, N = 1987; Self-Esteem, 0.93; Sexual Life, 0.91; Public Distress, 0.90; Work, 0.90; and Total, 0.96) and in patients with schizophrenia (Physical Function: alpha = 0.94, N = 111; Self-Esteem, 0.93; Sexual Life, 0.93; Public Distress, 0.90; Work, 0.87; and Total, 0.97), as shown by Kolotkin *et al.* (2006; 2001). Also, the correlations of items with their scale total revealed that almost all items were significantly correlated with their own scale score. As described elsewhere (Wilkinson *et al.*, 2000), we considered that test-retest was not necessary, as the alpha statistic indicates that responses were non-random and consequently reflective of an underlying phenomenon.

Correlations between the IWQOL-Lite and SQLS supported, in part, the construct validity of the IWQOL-Lite as a subjective QOL scale, and suggested that the IWQOL-Lite did not evaluate the same fields, but the fields related to those assessed by the conventional assessment scales. Meanwhile, the results of this study provided little support for the utility of the IWQOL-Lite across the BMI spectrum, and were inconsistent with those in the previous report (Kolotkin *et al.*, 2006). It is possible that the differences in cultural background account for the different results between the studies. Also, the size and/or characteristics of the sample might explain them: we have only 16 overweight subjects. To test these hypotheses, further cross-national evaluation with a larger sample is required. Psychopathology, particularly anxiety/depression, rather than BMI was more importantly associated with the IWQOL-Lite. This finding was not surprising, since the QOL, particularly subjective one, has been suggested to be strongly affected by anxiety/depression psychopathology

(Kaneda *et al.*, 2004; Kaneda, 2003; Voruganti *et al.*, 1997). Therefore, when assessing weight-related QOL in persons with schizophrenia, psychopathology, particularly anxiety/depression, should be carefully considered.

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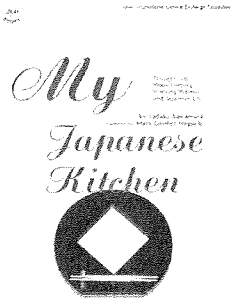

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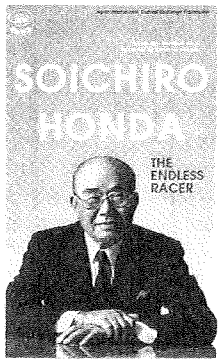

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Brief report

Determinants of work outcome in schizophrenia and schizoaffective disorder: Role of cognitive function

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ABSTRACT

Cognitive impairment has been reported to be more important than clinical symptomatology as a determinant of work and social function in schizophrenia. In a retrospective analysis of a group of 152 patients with chronic schizophrenia or schizoaffective disorder, performance on a battery of neuropsychological tests was contrasted in employed (32, 21.1%) versus unemployed subgroups. As predicted, neurocognitive performance was more important than clinical symptoms in predicting employment status. Among neurocognitive functions, verbal working memory (as reflected by the Consonant Trigram Test) was the strongest predictor of employment status.

1. Introduction

There has been considerable research into why people with schizophrenia are unable to obtain and keep competitive employment. Cognitive impairment, a core feature of schizophrenia, has been reported to be the most important determinant of work and social function in schizophrenia (Meltzer et al., 1996; Green et al., 2000; McGurk and Meltzer, 2000). Among several domains of cognitive function, verbal memory and executive function appear to be the cognitive functions that most affect work and social function (Meltzer et al., 1996; Green et al., 2000; McGurk and Meltzer, 2000). By contrast, most studies find that psychotic symptoms are not significantly associated with functional outcome (Green et al., 2000). However, several recent studies have suggested that psychopathology, and in particular positive symptoms, may be as important as, or more important than, cognitive dysfunction with regard to functional outcome (Ertugrul and Ulug, 2002). The purpose of this cross-sectional study was to test the hypotheses that specific types of cognitive impairment in patients with schizophrenia, but not psychotic symptoms, would predict work status.

2. Methods

Data from a previous study were used, and the subjects consisted of 152 patients with a DSM-III-R (American Psychiatric Association, 1987) diagnosis of chronic schizophrenia or schizoaffective disorder. Among the patients, 28 (18%) were women; the patients had a mean age of 42.7 (SD = 11.2), and a mean age at onset of 23.0 years (SD = 7.8). The assessments were performed using the Brief Psychiatric Rating Scale (BPRS; Overall and Gorham, 1962) for psychotic symptoms. Work status was defined as follows: (1) employed = full-time (minimum of 30 h/week or full-time student status) or part-time (1–29 h/week or part-time student status); and (2) unemployed = unemployed and not in school. The cognitive test battery consisted of measures addressing the following functions: (1) psychomotor speed and attention [Continuous Performance Test (CPT; Loong, 1991)]; (2) verbal [Consonant Trigram Test (CTT; Peterson and Peterson, 1959)] and spatial working memory [Spatial Working Memory Test (SWMT; McGurk et al., 1996)]; (3) verbal fluency [Controlled Word Association Test (CWAT; Benton et al., 1983)]; (4) verbal learning and memory [California Verbal Learning Test (CVLT; Delis et al., 1987) total words recalled for list A1–5, and long delay free recall (LDFR)]; and (5) executive function [Wisconsin Card Sorting Test (WCST; Berg, 1948) category (CAT) and percent perseveration (PP)].

3. Results and discussion

Of the 152 patients, 32 (21.1%) were employed. The age ($t = 2.75$, $df = 147$, $P < 0.01$) and duration of the illness ($t = 3.15$, $df = 71$, $P < 0.01$) were significantly lower in employed patients. Comparison of employed and unemployed groups showed significantly better CPT [$F(1,63) = 5.9$, $P = 0.01$], CTT [$F(1,122) = 9.2$, $P < 0.01$], SWMT [$F(1,95) = 8.2$, $P < 0.01$], BPRS Total [$F(1,119) = 4.9$, $P = 0.02$], and BPRS Positive [$F(1,119) = 6.1$, $P = 0.01$] scores in the employed group. When the analysis was repeated after covarying the duration of the illness, the results were virtually identical. A logistic regression analysis with a forward stepwise procedure indicated that the CTT score ($\chi^2 = 7.64$, $df = 1$, $P < 0.01$) was the strongest predictor of employment status.

As predicted, neurocognitive performance was more important than clinical symptoms in predicting employment status. Among neurocognitive functions, verbal working memory was more

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important than other types of cognitive function for employment outcome. Treatment that enhances cognitive function, especially verbal working memory, may lead to better employment outcome in patients with schizophrenia or schizoaffective disorder. A further longitudinal study should be carried out to confirm the results of the present study.

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Verbal Working Memory Impairment in Patients With Current Episode of Unipolar Major Depressive Disorder and in Remission

Yasuhiro Kaneda, MD, PhD

Abstract: In this naturalistic cross-sectional study, the author tested the hypothesis that verbal working memory (WM) in major depressive disorder (MDD) persists even after remission. The subjects consisted of 54 adult clinic outpatients and 54 age- and sex-equated healthy comparison subjects. The author found that the digit sequencing task scores for verbal WM were significantly less in both patients with a current episode of MDD and patients in remission than in the controls. Also, there were no significant correlations between the digit sequencing task scores and the dose of antidepressants or benzodiazepines in patients experiencing remission. It is suggested that WM/central executive function in MDD might be impaired, and thus verbal WM might be, at least to a degree, trait related.

Key Words: cross-sectional study, major depressive disorder, verbal working memory

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Patients with major depressive disorder (MDD) have been reported to perform less well in neurocognitive tests than healthy controls, even after their depression is successfully treated with modern antidepressants.[1,2] In a recent report, Gualtieri and Morgan[3] reported that substantial numbers of patients with depression are cognitively impaired. Despite evidence indicative of an MDD-associated deficit in verbal working memory (WM) function,[4] there have been comparatively few investigations of verbal WM in MDD after remission. The purpose of this study was to assess the hypothesis that verbal WM in MDD persists even after remission.

EXPERIMENTAL PROCEDURES

Sample

The subjects for this naturalistic cross-sectional study consisted of 54 adult clinic outpatients (aged 21–59 years): 22 patients who met the *Diagnostic and Statistical Manual of Mental Disorders-IV*[5] criteria for a current episode of unipolar MDD (nonpsychotic) and 32 patients who were in remission (full/partial), and 54 age- and sex-equated healthy comparison subjects. The patients had no comorbid psychiatric disorders and no medical, neurological, or developmental conditions that might affect cognition (eg, attention-deficit/hyperactivity disorder, brain injury, mild cognitive impairment, and chronic pain). The investigation was carried out in accordance with the Declaration of Helsinki, and the informed consent was obtained from all subjects. In both the patients and the controls, 35 (65%) were women; the patients and the controls had a mean (SD) age of 41.0 (10.6), and the patients had a mean age at onset of 37.7 (11.7) years. Seven (32%) of the 22 patients with a current episode of MDD were given antidepressants, and 6 (27%) of them were given benzodiazepines. Twenty-eight (88%) of the 32 patients who were in remission were given antidepressants, and 16 (50%) of them were given benzodiazepines (Table 1).

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Clinical Assessments

The assessments were performed using the HAM-D7[6] for severity of depression and remission; full remission was defined as an HAM-D7 score of 3 or less and partial remission as a score of 10 or less. The BACS[7] digit sequencing task (patients are presented with clusters of numbers in random order of increasing length, and they are asked to tell the experimenter the numbers in order, from lowest to highest) was used for verbal WM. The BACS digit sequencing task has been validated in the healthy controls.[7]

Data Analysis

The JMP (Version 8.0.1, Tokyo, Japan) for Macintosh was used to perform the analysis. For numerical variables, the *t* test procedures for independent group comparison were used to compare the differences in variables between 2 groups, and the differences between 3 groups were compared using the analysis of variance (ANOVA), followed by post hoc comparisons. The Pearson product moment correlation was used to examine the relationships between 2 numerical variables.

RESULTS

First, a comparison of the digit sequencing task scores between all patients (mean [SD], 17.1 [4.4]) and the controls (mean [SD], 20.6 [4.5]) revealed that the scores in the patients were significantly lower than those in the controls ($P < 0.0001$). When the analysis was repeated after covarying the education level, the results were virtually identical. Second, when we further compared the differences in the digit sequencing task scores between the 3 groups—the patients with a current episode of MDD (mean [SD], 17.2 [4.3]), the patients in remission (mean [SD], 17.0 [4.5]), and the controls, significant differences were found ($F_{2,105} = 8.39$, $P < 0.001$); the digit sequencing task scores were significantly less in both patient groups than in the controls. Controlling for age and education level indicated that the results were virtually identical. Third, an examination of the relationship between depression and digit sequencing task scores revealed that there were no significant correlations between them in either patients with a current episode of MDD or patients in remission. In addition, there were no significant correlations between the digit sequencing task scores and the dose of antidepressants ($r = -0.03$, $df = 31$, $P = 0.86$) or benzodiazepines ($r = -0.33$, $df = 31$, $P = 0.07$) in patients experiencing remission.

TABLE 1. Demographic Data

	n (F/M)	Age, yr	Education, yr	Age at Onset, yr	Duration of the Illness, yr	Dose of Antidepressants, mg/d*	Dose of Benzodiazepines, mg/d†	HAM-D7 (Total)	BACS Digit Sequencing Task Score
Healthy	54 (35/19)	41.0 (10.6)	13.6 (1.9)	—	—	—	—		20.6 (4.5)
Patients in acute depression	22 (13/9)	37.1 (9.0)	11.9 (2.0)	32.2 (11.2)	4.4 (5.3)	13.2 (22.8)	9.8 (16.0)	15.2 (1.9)	17.2 (4.3)
Patients in remission	32 (22/10)	43.7 (10.9)	12.2 (2.3)	41.1 (10.8)	2.1 (2.2)	22.5 (21.7)	8.7 (12.7)	6.9 (2.9)	17.0 (4.5)
Total No. Patients	54 (35/19)	41.0 (10.6)	12.0 (2.2)	37.7 (11.7)	3.0 (3.9)	18.7 (22.4)	9.1 (14.0)	10.4 (4.8)	17.1 (4.4)

Data are given as mean (SD).
*Paroxetine equivalent.
†Diazepam equivalent.
BACS indicates Brief Assessment of Cognition in Schizophrenia; F/M, female/male; HAM-D7, 7-item Hamilton Rating Scale for Depression.

DISCUSSION

These findings therefore suggested that an MDD-associated deficit in verbal WM indeed existed in acute depression and even after remission. These findings are consistent with those of Nebes et al[8] who found that verbal VM dysfunction persisted in older patients with depression even after their mood disorder had responded to antidepressant medications. The observations in this study may be explained by an impairment of WM/central executive function in MDD supported by Rose and Ebmeier[4] because executive function impairment is considered to be, at least to a degree, trait related.[9] However, still the possibility of influence of antidepressants/benzodiazepines[10,11] on the results cannot be ruled out. Another limitation in this study was that patients with full and partial remissions were combined for statistical analyses mainly because there were few patients with full remission. Therefore, a further longitudinal study using patients in remission without medication might be necessary to confirm the results of the present study.

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BRIEF REPORT

Verbal working memory and functional outcome in patients with unipolar major depressive disorder

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Abstract

In this naturalistic cross-sectional study, the author tested the hypothesis that verbal working memory (WM) in major depressive disorder (MDD) would predict functional outcome. The subjects consisted of 54 clinic adult out-patients. The author found that, in the patients with current episode of MDD, functional outcome was significantly correlated with depressive scores, but not with Digit Sequencing Task scores. Meanwhile, in a sample of full remitted or partial remitted (mildly depressed) patients, functional outcome was significantly correlated with both Digit Sequencing Task scores and depressive scores. Moreover, in a sample of full remitted or partial remitted (mildly depressed) patients, the Digit Sequencing Task score significantly contributed to the prediction of the functional outcome, but the depressive score did not. The findings in this study suggested that enhancement of verbal WM function may be useful to achieve normalization of functioning as an important component of remission in addition to symptomatic remission.

Key words: *Cross-sectional study, functional outcome, major depressive disorder, verbal working memory*

Introduction

Major depressive disorder (MDD) is a significant health problem with economic implications, and estimates of the economic burden of depression range from $52 billion in 1990 to $83 billion in 2000 (Malone 2007). Among several factors, employment is considered to have a great impact on the societal costs of depression, due to lost income, lost productivity, and disability income payments.

In a previous report (Kaneda et al. in press), the author demonstrated that neurocognitive performance, particularly verbal working memory (WM), was more important than clinical symptoms to predict employment status in patients with schizophrenia. Patients with major depressive disorder also have been reported to perform less well in neurocognitive tests than normal controls, even after their depression is successfully treated with modern antidepressants (Gualtieri et al. 2006; Reppermund et al. 2008). In a recent report, Gualtieri and Morgan (2008) reported that substantial numbers of patients with depression are cognitively impaired, and the author also demonstrated that a depression-associated deficit in verbal WM existed even after remission (Kaneda in press). However, little emphasis has been placed on relation between neurocognitive function and psychosocial or functional outcome in studies of depression to date. The purpose of this study was to test the hypothesis that a specific type of cognitive impairment, namely verbal WM, in patients with MDD would predict functional outcome.

Experimental procedures

Sample

The subjects for this naturalistic cross-sectional study consisted of 54 clinic adult out-patients (aged 21–59 years): 22 patients who met DSM-IV (American Psychiatric Association 1994) criteria for current episode of unipolar MDD (nonpsychotic) and 32 patients who were in full remission or partial remission (mild depression). Patients had no comorbid psychiatric disorders and no medical, neurological or developmental conditions that might affect cognition. The investigation was carried out in accordance with the Declaration of Helsinki and the informed consent was obtained from all subjects.

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Thirty-five (65%) were women; the patients had a mean age of 41.0 (SD = 10.6), and a mean age at onset of 37.7 (11.7) years. Seven out of 22 (32%) patients with current episode of MDD were on antidepressants, and six (27%) of them were on benzodiazepines. Twenty-eight out of 32 (88%) remitted patients were on the antidepressants, and 16 (50%) of them were on benzodiazepines.

Clinical assessments

The assessments were performed using the seven-item Hamilton Rating Scale for Depression (HAM-D7; McIntyre et al. 2002) for severity of depression and remission: full remission defined as an HAM-D7 of 3 or less, and partial remission (mild depression) as a score of 10 or less, and Brief Assessment of Cognition in Schizophrenia (BACS; Keefe et al. 2004) Digit Sequencing Task (patients are presented with clusters of numbers in random order of increasing length, and they are asked to tell the experimenter the numbers in order, from lowest to highest) for verbal WM. The BACS Digit Sequencing Task has been validated in normal controls (Keefe et al. 2004). Digit Sequencing Task scores for each depression group were normalized against their respective age-matched control group (data available upon request). Functional outcome (productivity), such as working, doing household chores, or going to school was assessed by the author based on the interviews with patients and their partners/parents/children, and was defined as follows: 0=non-impaired, 1=mildly impaired, 2=moderately impaired, 3=severely impaired). Demographic data are presented in Table I.

Data analysis

JMI (Version 5.1.2) for Macintosh was used to perform the analysis. For numerical variables, the *t*-tests procedures for independent group comparison were used to compare the differences in variables between two groups, and the differences between three groups were compared by the analysis of variance (ANOVA), followed by *post hoc* comparisons. Pearson's correlation was used to examine the relationships between two numerical variables. A logistic regression model with forward selection criteria was used to predict the functional outcome using the demographic variables, depressive and verbal WM scores.

Results

First, as reported elsewhere (Kaneda in press), Digit Sequencing Task scores were not significantly different between the two groups of patients with

Table I. Demographic data.

	N (F/M)	Age (years)	Education (years)	Age at onset (years)	Duration of the illness (years)	Dose of antidepressants (mg/day)[1]	Dose of benzodiazepines (mg/day)[2]	HAM-D7 (Total)	BACS Digit Sequencing Task score (raw)	BACS Digit Sequencing Task score (z score[3])
Total patients	54 (35/19)	41.0 (10.6)	12.0 (2.2)	37.7 (11.7)	3.0 (3.9)	18.7 (22.4)	9.1 (14.0)	10.4 (4.8)	17.1 (4.4)	−0.75 (1.3)
Patients in acute depression	22 (13/9)	37.1 (9.0)	11.9 (2.0)	32.2 (11.2)	4.4 (5.3)	13.2 (22.8)	9.8 (16.0)	15.2 (1.9)	17.2 (4.3)	−0.97 (1.5)
Patients in remission	32 (22/10)	43.7 (10.9)	12.2 (2.3)	41.1 (10.8)	2.1 (2.2)	22.5 (21.7)	8.7 (12.7)	6.9 (2.9)	17.0 (4.5)	−0.59 (1.2)

[1]Paroxetine equivalent data are given as mean (SD).
[2]Diazepam equivalent data are given as mean (SD).
[3]z scores were calculated using the age-matched control group means and standard deviations.
BACS, Brief Assessment of Cognition in Schizophrenia; HAM-D7, seven-item Hamilton Rating Scale for Depression.

current episode of MDD and in full remission or partial remission (mild depression), even after controlling for the education level.

Second, examination of the relationships between functional outcome and Digit Sequencing Task and depressive scores in the two groups, patients with current episode of MDD and in full remission or partial remission (mild depression), the results were different between the two: in the patients with current episode of MDD, functional outcome was significantly correlated with depressive scores ($r=0.45$, $df=21$, $P<0.05$), but not with Digit Sequencing Task scores ($r=-0.14$, $df=21$, $P=0.54$). Meanwhile, in a sample of full remitted or partial remitted (mildly depressed) patients, functional outcome was significantly correlated with both Digit Sequencing Task scores ($r=-0.43$, $df=31$, $P<0.05$) and depressive scores ($r=0.38$, $df=31$, $P<0.05$).

Third, in a multiple regression analysis with a forward stepwise procedure, the depressive score in the group of patients with current episode of MDD ($F=5.1$, $df=1$, $P<0.05$) significantly contributed to the prediction of the functional outcome, but the Digit Sequencing Task score did not. Meanwhile in a sample of full remitted or partial remitted (mildly depressed) patients, the Digit Sequencing Task score ($F=4.5$, $df=1$, $P<0.05$) significantly contributed to the prediction of the functional outcome, but the depressive score did not.

Fourth, examination of the relationships between Digit Sequencing Task and depressive scores revealed that Digit Sequencing Task scores were not significantly correlated with depressive scores in either patients with current episode of MDD ($r=-0.03$, $df=21$, $P=0.89$) or in full remission or partial remission (mild depression) ($r=-0.32$, $df=31$, $P=0.08$). In addition, there were no significant correlations between Digit Sequencing Task scores and the dose of antidepressants ($r=-0.13$, $df=31$, $P=0.49$) or benzodiazepines ($r=-0.30$, $df=31$, $P=0.09$) in a sample of full remitted or partial remitted (mildly depressed) patients.

Discussion

These findings in this study suggested relations between MDD-associated deficit in verbal WM and functional outcome in a sample of full remitted or partial remitted (mildly depressed) patients. The findings seems to be inconsistent with those of Kennedy et al. (2007), who reported, in their review, that residual symptomatology after remission from depression may lead to enduring psychosocial impairment, as may subtle neurocognitive deficits. Nonetheless, the findings in this study do not underscore the importance of clinical remission from depression, which is defined objective outcome indicated by a quantifiable score with a depressive symptom measurement tool. On the contrary, symptomatic full remission should be always achieved as the primary goal of treatment, since it is the optimal outcome in depression (McIntyre et al. 2005; Möller 2008). Meanwhile, the findings in this study suggested that enhancement of verbal WM function by, e.g., cognitive rehabilitation may be useful to achieve normalization of functioning as an important component of remission (Zimmerman et al. 2006) when symptomatic full remission is failed to achieve. Besides, the possibility of influence of medications, particularly benzodiazepines (Stewart 2005), on the verbal WM dysfunction cannot completely be ruled out. Another limitation in this study was that patients in full remission and partial remission (mild depression) were combined for statistical analyses, mainly because there were few patients in full remission. Therefore, a further longitudinal study using patients without benzodiazepines might be necessary to confirm the results of the present study.

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Statement of interest

None.

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