

ORIGINAL

Predictors of life skills in people with schizophrenia

Takeo Tominaga¹, Masahito Tomotake², Tomoya Takeda³, Yoshinori Ueoka⁴, Tsunehiko Tanaka⁵, Shin-ya Watanabe¹, Naomi Kameoka⁶, Masahito Nakataki⁶, Shusuke Numata¹, Yumiko Izaki⁷, Satsuki Sumitani⁸, Hiroko Kubo⁹, Yasuhiro Kaneda¹⁰, and Tetsuro Ohmori¹

¹Department of Psychiatry, Graduate School of Biomedical Sciences, Tokushima University, Tokushima, Japan, ²Department of Mental Health, Graduate School of Biomedical Sciences, Tokushima University, Tokushima, Japan, ³Department of Psychology, Fukuyama University, Fukuyama, Japan, ⁴Department of Early Childhood Care and Education, Shikoku University, Junior College, Tokushima, Japan, ⁵Faculty of Education Specialized courses educational psychology, Niigata University, Niigata, Japan, ⁶Department of Psychiatry, Tokushima University Hospital, Tokushima, Japan, ⁷Health service, counseling and accessibility center, Tokushima University, Tokushima, Japan, ⁸Academic support office for students with special needs, Tokushima University, Tokushima, Japan, ⁹Department of Psychiatry, Aizato Hospital, Itano-gun, Japan, ¹⁰Department of Psychiatry, Iwaki Clinic, Anan, Japan

Abstract : Objective : The purpose of the present study is to examine clinical factors related to life skills in people with schizophrenia. **Method :** The participants were 51 stabilized outpatients with schizophrenia. Their mean age was 38.91 (SD = 10.73) years. Life skills were assessed using the Life skills profile (LSP). Cognitive function was evaluated with the Measurement and Treatment Research to Improve Cognition in Schizophrenia Consensus Cognitive Battery (MCCB). Clinical symptoms were assessed using the Positive and Negative Syndrome scale (PANSS), the Calgary Depression Scale for Schizophrenia (CDSS) and the Drug-Induced Extrapyrimal Symptoms Scale (DIEPSS). **Results :** Cognitive function was not correlated with the LSP scores at all. Among clinical symptoms, scores of the PANSS positive and negative syndrome scales, the CDSS, and the DIEPSS had negative correlations with the LSP total score and the subscales. Stepwise regression analyses showed that the CDSS and PANSS negative syndrome scale scores were independent predictors of the LSP total score and two of the subscales. **Conclusions :** These results indicate that cognitive function is not associated with life skills but clinical symptoms such as depressive and negative symptoms have considerable impacts on life skills in people with schizophrenia. *J. Med. Invest.* 67: 75-82, February, 2020

Keywords : schizophrenia, life skill, depressive symptom, negative symptom, cognitive function

INTRODUCTION

Functional outcome is defined as wide-ranging real-world functions including independent living, financial management, employment and leisure/social activities (1,2), and it is known that poor functional outcome is common in patients with schizophrenia (3-7). Therefore, finding contributors to functional outcome is an important issue in schizophrenia research. Previous studies have shown that several clinical factors such as positive, negative, depressive and extrapyramidal symptoms are associated with functional impairments (8-21).

Recently, much more attention has been paid to cognitive impairment of schizophrenia patients because it is considered to be a core feature of schizophrenia (22,23). Previous researchers have found that cognitive impairment persists throughout the illness and exists even in premorbid period (24,25). According to the previous reports, patients with schizophrenia have about 1-1.5 standard deviations deficits compared to healthy controls in several cognitive domains, particularly memory, attention, executive function and speed of processing (26-28). Previous studies also have indicated that neurocognition such as verbal memory, working memory, executive function and vigilance are related to functional outcome in people with schizophrenia (29-31), and that neurocognition may be a stronger predictor of

functional outcome than symptomatology, explaining 20-60% of variance of it (30,32,33). More recently, social cognition, referred to as an array of abilities that involve cognitive capability applied to social situations (34), has attracted attention as a predictor of functional outcome (35). However, some previous studies have demonstrated that symptomatology is more influential in functional outcome than cognitive function (20,36-38). The inconsistency among the previous findings can be explained mainly by difference of study design, sample population, sample size, cognitive tests and functional outcome scales. Especially, as for assessing cognitive function and functional outcome, researchers have used different neuropsychological tests and functional outcome scales. Therefore, comparisons across studies seem to be difficult.

In this situation, the National Institute of Mental Health Measurement and Treatment Research to Improve Cognition in Schizophrenia (NIMH-MATRICES) Initiative developed a consensus cognitive battery for schizophrenia research that is the MATRICES Consensus Cognitive Battery (MCCB) (39). The MCCB is a comprehensive cognitive battery that contains not only neurocognitive domain but also social cognitive domain. On the other hand, as for functional outcome, there are no standardized scales at present. However, the six scales selected by the Validation of Everyday Real-word Outcomes (VALERO) study are often used (40). The six scales are as follows: the Quality of Life Scale (QLS), the Specific Level of Functioning, the Social Behavior Schedule, the Social Functioning Scale, the Independent Living Skills Schedule and the Life Skills Profile (LSP).

Regarding the direction of research in this area, it seems that interest has shifted from whether cognitive function is connected to functional outcome to how cognitive function is related to it.

Received for publication September 17, 2019; accepted December 2, 2019.

Address correspondence and reprint requests to Takeo Tominaga, Department of Psychiatry, Graduate School of Biomedical Sciences, Tokushima University, 3-18-15, Kuramoto-cho, Tokushima 770-8503, Japan and Fax: +81-88-633-7131.

Not all types of cognitive function are equally important when it comes to navigating the real world (22), and as far as we know, it seems unclear which cognitive domain is related to which aspect of functional outcome. Our research group has reported that particularly Symbol Coding test to evaluate speed of processing was correlated with the QLS scores (18,20). Besides our study, since the MCCB was developed, several studies have also reported the relationship between cognitive function measured by it and functional outcome (41-51). However, to our knowledge, among those studies, few studies evaluated functional outcome using the LSP (48).

Although one of the ultimate treatment goals of schizophrenia is thought to be an improvement in functional outcome such as employment and social activities, many of schizophrenia patients have not accomplished it. For example, the employment rate is as low as about 10-20% (52-54). Therefore, becoming able to live well in a community is a crucial first step to lead to good functional outcome. To assess the ability to complete the first step, the LSP is considered suitable because it was selected as one of the everyday living skills scales in the VALERO study (40).

The purpose of the present study was to clarify the relationship between life skills measured by the LSP and other clinical factors including cognitive function measured by the MCCB in people with schizophrenia.

METHODS

Participants

Fifty-one stabilized outpatients with a DSM-IV (55) diagnosis of schizophrenia were recruited from the Department of Psychiatry, Tokushima University Hospital. Patients with any organic central nervous system disorders, substance-related disorders, mental retardation or severe somatic disorders were excluded. After receiving explanations on the content and possible disadvantages of the study as well as confidentiality protection, participants gave written informed consent to participate in the current study. They had been receiving regular outpatient treatment and had not been hospitalized in the previous 6 months due to exacerbation of psychiatric symptoms.

This study was approved by the Ethics Committee of Tokushima University.

Instruments

To assess life skills, we used the LSP that was developed by Rosen et al. (56) as a measure of functioning in chronic mental patients. The reliability and validity of the scale have been already confirmed (56,57). Family members, psychiatric professionals, or case workers can be used as the informant in the interview (40). This instrument consists of five subscales measured by a total 39 items. Each item is rated from 1 to 4. The five subscales are self-care, non-turbulence, socialization, communication, responsibility. Higher scores indicate a better functional outcome. In the present study, 50 of 51 cases were evaluated by family members living together, and one case by a home helper.

Regarding evaluation of cognitive function, we used the MCCB which has been developed as a comprehensive measure of cognitive domains significantly impaired in schizophrenia patients. The MCCB consists of ten tests that measure seven cognitive domains. They are as follows: speed of processing (Brief Assessment of Cognition in Schizophrenia-Symbol Coding [BACS-SC], Category Fluency Animal Naming [Fluency] and Trail Making Test Part A [TMT-A]), attention/vigilance (Continuous Performance Test-Identical Pairs [CPT-IP]), working memory (Wechsler Memory Scale III Spatial Span [WMS-III

SS) and Letter Number Span [LNS]), verbal learning (Hopkins Verbal Learning Test-Revised [HVLTR]), visual learning (Brief Visuospatial Memory Test-Revised [BVMTR]), reasoning and problem solving (Neuropsychological Assessment Battery [NAB] Maze), and social cognition (Mayer-Salovey-Caruso-Emotional Intelligence Test [MSCEIT] Managing Emotions [ME]) (39). Each raw score for the ten subtests was standardized to the T-score (mean = 50, SD = 10). For the cognitive domain consisting of more than one test (speed of processing and working memory), the domain T-score was derived from a composite of the test scores within each domain, and for the other cognitive domains, T-score represents the domain score. The MCCB composite score gives equal weighting to each of the seven cognitive domains. The MCCB has good test-retest reliability, practicability and tolerability (39), and it is reported that the Japanese version of the MCCB (MCCB-J) has good psychometric properties and validity (58). In the present study, data were collected using the Japanese version by clinical psychologists who were well trained for the use of it.

Clinical symptoms were evaluated with the Positive and Negative Syndrome Scale (PANSS) and the Calgary Depression Scale for Schizophrenia (CDSS). The PANSS is composed of 30 items and higher scores represent a greater level of symptom severity (59). Experienced psychiatrists conducted the interviews according to the Evaluation Manual for the PANSS (60). Particularly, depressive symptom was strictly evaluated with the CDSS that was specifically developed to distinguish depressive symptom from positive and negative symptom or antipsychotic-induced adverse effects. The scale is a 9-item questionnaire (depression, hopelessness, self-depreciation, guilty ideas of reference, pathological guilt, morning depression, early wakening, suicide and observed depression) and higher scores represent a greater level of depression. The reliability and validity of the scale have been already confirmed (61,62).

Drug-induced extrapyramidal adverse effects were evaluated using the Drug-Induced Extrapyramidal Symptoms Scale (DIEPSS). The scale consists of eight individual parameters (gait, bradykinesia, sialorrhea, muscle rigidity, tremor, akathisia, dystonia, and dyskinesia) and one global assessment. Higher scores represent a greater level of extrapyramidal adverse effects. In this study, we evaluated the extrapyramidal symptom score by summing eight individual parameters. Experienced psychiatrists conducted the interviews according to the Rater's Manual for the DIEPSS (63).

Statistical analysis

First, to clarify significant associations between the LSP scores and other clinical variables, Spearman's rank correlation coefficients were calculated. We used the false discovery rate correction to adjust for multiple testing. Then the LSP total score and the subscale scores were chosen as dependent variables. Using the clinical variables that showed significant correlations with each dependent variable, stepwise regression analyses were performed to specify which clinical variables would be the best predictors of each dependent variable. Statistical analyses were carried out with IBM SPSS Statistics Version 22 for Windows (Japan IBM, Tokyo, Japan) and RStudio (RStudio Team, 2015. RStudio: Integrated Development for R. RStudio, Inc., Boston, MA. URL <http://www.rstudio.com/>).

RESULTS

roughly Table 1 presents the demographic characteristics and clinical variables of the participants. All participants were Japanese, and 26 were men and 25 women. Their mean age was

38.91 years (SD = 10.73). Doses of antipsychotics were converted to chlorpromazine equivalents according to the conversion chart (64).

Spearman rank correlation coefficients were calculated to study the relationship between the LSP and clinical variables because most of the data were non-normal distribution. Table 2 shows the results of the correlation analyses between the LSP scores and the MCCB cognitive domain scores. Neither the MCCB cognitive domain score nor composite score was signifi-

cantly correlated with the LSP scores. In addition to that, each subtest score of the MCCB also have no significant correlation with the LSP scores.

The results of the correlation analyses between the LSP scores and other clinical variables are shown in Table 3. The PANSS positive syndrome scale score was significantly correlated with the LSP total score ($r = -0.38, p < 0.05$) and communication subscale score ($r = -0.47, p < 0.01$). The PANSS negative syndrome scale score had significant correlations with the LSP total score

Table 1. Demographic characteristics of participants

<i>n</i> (men/women)		51 (26/25)
Age (years)		38.91 ± 10.73
Duration of illness (years)		15.05 ± 9.10
Number of hospitalization		1.55 ± 1.49
Dose of antipsychotics (mg/day)*		545.14 ± 399.03
Type of schizophrenia (<i>n</i>)	Paranoid	40
	Residual	8
	Disorganized	2
	Catatonic	0
	Undifferentiated	1
Marital state (<i>n</i>)	Married	8
	Never married	40
	Divorced	2
	Widowed	1
Social state (<i>n</i>)	Full time	11
	Part time	24
	No employment	16
PANSS	Total	75.39 ± 14.64
	Positive syndrome	16.82 ± 4.53
	Negative syndrome	20.39 ± 5.50
CDSS (Total)		3.51 ± 2.96
DIEPSS (Total)		1.12 ± 1.07
MCCB (T-score)	Speed of processing	17.51 ± 24.98
	BACS-SC	25.37 ± 21.54
	Fluency	41.82 ± 11.35
	TMT-A	31.08 ± 16.16
	Attention/vigilance (CPT-IP)	36.29 ± 10.52
	Working memory	36.29 ± 14.34
	WMS-III SS	37.84 ± 13.17
	LNS	40.04 ± 12.76
	Verbal learning (HVLTR)	39.75 ± 13.25
	Visual learning (BVMT-R)	42.92 ± 10.44
	Reasoning and problem solving (NAB Maze)	38.25 ± 9.82
	Social cognition (MSCEIT ME)	26.61 ± 7.78
	Composite score	19.10 ± 18.68
LSP	Total	135.27 ± 11.97
	Self-care	33.61 ± 4.18
	Non-turbulence	44.90 ± 3.86
	Socialization	16.49 ± 3.67
	Communication	21.59 ± 2.44
	Responsibility	18.69 ± 1.67

Note : Data are expressed as mean ± SD unless otherwise specified. *Chlorpromazine equivalent. PANSS ; Positive and Negative Syndrome Scale ; CDSS : Calgary Depression Scale for Schizophrenia, DIEPSS ; Drug-Induced Extrapyramidal Symptoms Scale, MCCB Measurement and Treatment Research to Improve Cognition in Schizophrenia Consensus Cognitive Battery, BACS-SC ; Brief Assessment of Cognition in Schizophrenia-Symbol Coding, Fluency ; Category Fluency Animal Naming, TMT-A ; Trail Making Test Part A, CPT-IP ; Continuous Performance Test-Identical Pairs, WMS-III SS ; Wechsler Memory Scale III Spatial Span, LNS ; Letter Number Span, HVLTR ; Hopkins Verbal Learning Test-Revised, BVMT-R ; Brief Visuospatial Memory Test-Revised, NAB ; Neuropsychological Assessment Battery, MSCEIT ME ; Mayer-Salovey-Caruso-Emotional Intelligence Test Managing Emotions, LSP ; Life Skills Profile

Table 2. Correlation between LSP scores and MCCB cognitive domain scores

	LSP					
	Total	Self-care	Non-turbulence	Socialization	Communication	SResponsibility
Speed of Processing	0.24 (0.447)	0.24 (0.447)	-0.09 (0.725)	0.26 (0.427)	0.20 (0.513)	0.16 (0.563)
Attention/Vigilance	0.20 (0.513)	0.28 (0.406)	-0.09 (0.725)	0.11 (0.671)	0.09 (0.725)	0.29 (0.406)
Working Memory	0.32 (0.406)	0.30 (0.406)	0.15 (0.563)	0.15 (0.563)	0.33 (0.406)	0.19 (0.513)
Verbal Learning	0.12 (0.671)	0.10 (0.682)	0.12 (0.671)	0.07 (0.823)	0.11 (0.671)	0.11 (0.682)
Visual Learning	0.17 (0.563)	0.16 (0.563)	0.04 (0.873)	0.18 (0.563)	0.17 (0.563)	0.06 (0.863)
Reasoning and Problem Solving	-0.04 (0.873)	-0.03 (0.909)	0.02 (0.937)	-0.04 (0.873)	-0.01 (0.939)	-0.05 (0.863)
Social Cognition	0.15 (0.563)	0.20 (0.513)	0.08 (0.773)	-0.02 (0.921)	0.12 (0.671)	0.11 (0.671)
Composite Score	0.26 (0.427)	0.28 (0.406)	0.04 (0.873)	0.20 (0.513)	0.19 (0.513)	0.19 (0.513)

Note : Spearman rank correlations (false discovery rate correction). * $p < 0.05$; ** $p < 0.01$. Figures in the parentheses show p values.

MCCB ; Measurement and Treatment Research to Improve Cognition in Schizophrenia, LSP ; Life Skills Profile

Table 3. Correlation between LSP scores and other clinical variables

	LSP					
	Total	Self-care	Non-turbulence	Socialization	Communication	Responsibility
Duration of illness	0.09 (0.683)	0.05 (0.754)	-0.07 (0.694)	0.16 (0.444)	-0.08 (0.690)	0.15 (0.471)
Number of hospitalization	0.08 (0.683)	0.07 (0.694)	-0.20 (0.292)	0.17 (0.391)	0.05 (0.754)	0.02 (0.901)
Dose of antipsychotics	-0.15 (0.458)	-0.22 (0.250)	-0.13 (0.487)	-0.08 (0.683)	-0.14 (0.487)	-0.08 (0.683)
PANSS						
Positive syndrome	-0.38* (0.021)	-0.21 (0.283)	-0.20 (0.310)	-0.31 (0.084)	-0.47** (0.005)	-0.29 (0.114)
Negative syndrome	-0.45** (0.007)	-0.48** (0.005)	0.01 (0.950)	-0.45** (0.007)	-0.39* (0.018)	-0.25 (0.190)
CDSS	-0.44** (0.007)	-0.48** (0.005)	-0.12 (0.567)	-0.41* (0.011)	-0.23 (0.223)	-0.24 (0.212)
DIEPSS	-0.47** (0.005)	-0.43** (0.008)	-0.14 (0.487)	-0.44** (0.007)	-0.38* (0.022)	-0.25 (0.197)

Notes : Spearman rank correlations (false discovery rate correction). * $p < 0.05$; ** $p < 0.01$. Figures in the parentheses show p values.

MCCB ; Measurement and Treatment Research to Improve Cognition in Schizophrenia, LSP ; Life Skills Profile, PANSS ; Positive and Negative Syndrome Scale, CDSS ; Calgary Depression Scale for Schizophrenia, DIEPSS ; Drug Induced Extrapyrimal Symptoms Scale

($r = -0.45, p < 0.01$), self-care subscale score ($r = -0.48, p < 0.01$), socialization subscale score ($r = -0.45, p < 0.01$), and communication subscale score ($r = -0.39, p < 0.05$). The CDSS total score was significantly correlated with the LSP total score ($r = -0.44, p < 0.01$), self-care subscale score ($r = -0.48, p < 0.01$), and socialization subscale score ($r = -0.41, p < 0.05$). The DIEPSS score showed significant correlations with the LSP total score ($r = -0.47, p < 0.01$), self-care subscale score ($r = -0.43, p < 0.01$), socialization subscale score ($r = -0.44, p < 0.01$), and communication subscale score ($r = -0.38, p < 0.05$). However, no significant correlation was found between the LSP scores and duration of illness, number of hospitalization, and dose of antipsychotics.

Table 4 shows the results of stepwise regression analyses on the LSP scores. The PANSS negative syndrome scale score significantly predicted the LSP total score, self-care subscale score, and socialization subscale score. The CDSS score significantly predicted the LSP total score, self-care subscale score, and socialization subscale score. The PANSS positive syndrome scale score significantly predicted the LSP communication subscale score. The CDSS score was stronger predictor of the LSP total score ($\beta = -0.44, p = 0.0004$) than the PANSS negative syndrome scale score ($\beta = -0.37, p = 0.0020$).

DISCUSSION

As for the relationship between cognitive function and functional outcome, it is reported that verbal memory, working memory, executive function and vigilance were significantly associated with functional outcome (29-31). Moreover, in a recent meta-analysis study, Fett et al. (35) revealed that a variety of neurocognitive domains such as reasoning and problem solving, processing speed, attention and vigilance, working memory, verbal learning and memory, visual learning and memory, verbal fluency, and overall neurocognition are significantly associated with functional outcome. Concerning social cognition, their meta-analysis study also showed that social cognition, particularly

theory of mind was more strongly associated with functional outcome than neurocognition (35).

There are some existing literatures investigating the relation between cognitive function and life skills assessed with the LSP. Norman et al. (38) reported that neurocognitive functions evaluated by several cognitive measures were not correlated with the LSP scores at all. Using the database of VALERO study Phase I, Sabbag et al. (48) showed that the LSP summary scores were not related to neurocognition evaluated by the modified MCCB which did not include the MSCEIT. Farreny et al. (65) reported that executive function evaluated by the Behavioral Assessment of the Dysexecutive Syndrome was not correlated with the LSP scores at baseline in the cognitive remediation study. On the other hand, Stratta et al. (66) showed that executive function evaluated by Wisconsin Card Sorting Test was related to the LSP scores. Considering those previous findings, the relation between cognitive function and life skills assessed with the LSP still seems unclear.

As for the studies using the QLS as a measure of functional outcome, our research group has reported that Symbol Coding subtest of the Brief Assessment of Cognition in Schizophrenia (BACS) and the MCCB to evaluate speed of processing was correlated with the QLS scores and this subtest was an independent predictor of the QLS scores (18,20). Other studies also suggest that speed of processing is closely related to QLS scores (45,67). Moreover, several previous studies showed that other cognitive domains such as executive function, verbal memory, working memory and social cognition were associated with the QLS (16,68-76). From these findings, it seems certain that the QLS is related to cognitive function to some extent. The QLS is composed of many items to evaluate high social functions such as work and social activities (77). On the other hand, the LSP evaluates life skills, especially rather basic ones that people need to have in daily life. Therefore, although cognitive function is related to functional outcome (29-31,35), the results of the present study indicate that cognitive function may not play a function in basic life skills in people with schizophrenia.

Table 4. Results of stepwise regression analyses on LSP

Dependent variable	Independent variable	Adjusted R ²	β	α	B
Total	CDSS	0.39*** (0.0000)	-0.44*** (0.0004)	158.10	-1.78
	PANSS-negative syndrome		-0.37** (0.0020)		-0.81
Self-care	CDSS	0.41*** (0.0000)	-0.42*** (0.0004)	42.12	-0.60
	PANSS-negative syndrome		-0.41*** (0.0005)		-0.32
Non-turbulence					
Socialization	PANSS-negative syndrome	0.36*** (0.0000)	-0.43*** (0.0007)	23.84	-0.28
	CDSS		-0.36** (0.0035)		-0.45
Communication	PANSS-positive syndrome	0.18** (0.0012)	-0.44** (0.0012)	25.60	-0.24
Responsibility					

Note : * $p < 0.05$; ** $p < 0.01$, *** $p < 0.001$. Figures in the parentheses show p values. LSP ; Life Skills Profile, CDSS ; Calgary Depression Scale for Schizophrenia, PANSS ; Positive and Negative Syndrome Scale

Next, in regard to the clinical variables other than cognitive function, the results of the present study indicate that positive and negative symptoms, extrapyramidal symptom and depressive symptom are significantly related to low life skills. Particularly, negative and depressive symptoms are considered key factors influencing wide range of life skills. These results are largely consistent with our research group's previous study (8). Recently, Puig et al. (78) also reported that negative symptom is related to the LSP communication-social contact subscale score. Matsuda et al. (79) found that improvement on negative symptom was significantly related to improvement on the LSP socialization score in the follow-up study of first-episode schizophrenia patients. On the other hand, Norman et al. (38) showed that positive symptom is more tied to the LSP scores than negative symptom.

The results of the present study clearly showed that cognitive function does not influence life skills and depressive symptom is a stronger predictor of low life skills than negative symptom. This is a novel finding in the present study. Considering these results, interventions to treat depressive symptom may be particularly important to improve life skills in people with schizophrenia.

The present study has some limitations. First, since it was a cross-sectional study, the causal relationship between clinical variables and life skills could not be identified. Second, the sample size is small. So, further research with larger sample size may be needed to confirm the results. Third, as the sample consisted entirely of stabilized outpatients, the results may not be able to apply to the whole schizophrenia patients.

In conclusion, the results of the present study indicate that cognitive function is not associated with life skills evaluated by the LSP, but clinical symptoms such as negative and depressive symptoms have significant impacts on the skills in people with schizophrenia.

CONFLICT OF INTERESTS

The authors declare that there is no conflict of interest.

ACKNOWLEDGEMENTS

We are grateful to Ms. Mai Doi, Ms. Atsuko Watanabe, Ms. Ayako Kamitani and Ms. Ayano Arai for their help with cognitive assessment.

REFERENCES

- Harvey PD, Bellack AS : Toward a terminology for functional recovery in schizophrenia : is functional remission a viable concept? *Schizophr Bull* 35 : 300-306, 2009
- Sumiyoshi T, Sumiyoshi C : Functional outcome in patients with schizophrenia : the concept and the measurement. *Act Nerv Super* 57 : 1-11, 2015
- Bellack AS, Morrison RL, Wixted JT, Mueser KT : An analysis of social competence in schizophrenia. *Br J Psychiatry* 156 : 809-818, 1990
- Gupta S, Andreasen NC, Arndt S, Flaum M, Hubbard WC, Ziebell S : The Iowa Longitudinal Study of Recent Onset Psychosis : one-year follow-up of first episode patients. *Schizophr Res* 23 : 1-13, 1997
- Hegarty JD, Baldessarini RJ, Tohen, M, Waternaux C, Oepen, G : One hundred years of schizophrenia : a meta-analysis of the outcome literature. *Am J Psychiatry* 151 : 1409-1416, 1994
- Robinson DG, Woerner MG, McMeniman M, Mendelowitz A, Bilder RM : Symptomatic and functional recovery from a first episode of schizophrenia or schizoaffective disorder. *Am J Psychiatry* 161 : 473-479, 2004
- Wiersma D, Wanderling J, Dragomirecka E, Ganey K, Harrison G, An Der Heiden W, Nienhuis FJ, Walsh D : Social disability in schizophrenia : its development and prediction over 15 years in incidence cohorts in six European centres. *Psychol Med* 30 : 1155-1167, 2000
- Aki H, Tomotake M, Kaneda Y, Iga J, Kinouchi S, Shibuya-Tayoshi S, Tayoshi SY, Motoki I, Moriguchi K, Sumitani S, Yamauchi K, Taniguchi T, Ishimoto Y, Ueno S, Ohmori T : Subjective and objective quality of life, levels of life skills, and their clinical determinants in outpatients with schizophrenia. *Psychiatry Res* 158 : 19-25, 2008
- Browne S, Roe M, Lane A, Gervin M, Morris M, Kinsella A, Larkin C, Callaghan EO : Quality of life in schizophrenia: relationship to sociodemographic factors, symptomatology and tardive dyskinesia. *Acta Psychiatr Scand* 94 : 118-124, 1996
- Eack SM, Newhill CE : Psychiatric symptoms and quality of life in schizophrenia : a meta-analysis. *Schizophr Bull* 33 : 1225-1237, 2007
- Fervaha G, Foussias G, Agid O, Remington G : Impact of primary negative symptoms on functional outcomes in schizophrenia. *Eur Psychiatry* 29 : 449-455, 2014
- Hofer A, Rettenbacher MA, Widschwendter CG, Kemmler G, Hummer M, Fleischhacker WW : Correlates of subjective and functional outcomes in outpatient clinic attendees with schizophrenia and schizoaffective disorder. *Eur Arch Psychiatry Clin Neurosci* 256 : 246-255, 2006
- Jin H, Zisook S, Palmer BW, Patterson TL, Heaton RK, Jeste DV : Association of depressive symptoms with worse functioning in schizophrenia : a study in older outpatients. *J Clin Psychiatry* 62 : 797-803, 2001
- Rabinowitz J, Levine SZ, Garibaldi G, Bugarski-Kirola D, Berardo CG, Kapur S : Negative symptoms have greater impact on functioning than positive symptoms in schizophrenia : analysis of CATIE data. *Schizophr Res* 137 : 147-150, 2012
- Rocca P, Bellino S, Calvarese P, Marchiaro L, Patria L, Rasetti R, Bogetto F : Depressive and negative symptoms in schizophrenia : different effects on clinical features. *Compr Psychiatry* 46 : 304-310, 2005
- Savilla K, Kettler L, Galletly C : Relationships between cognitive deficits, symptoms and quality of life in schizophrenia. *Aust N Z J Psychiatry* 42 : 496-504, 2008
- Strejilevich SA, Palatnik A, Avila R, Bustin J, Cassone J, Figueroa S, Gimenez M, de Erausquin GA : Lack of extrapyramidal side effects predicts quality of life in outpatients treated with clozapine or with typical antipsychotics. *Psychiatry Res* 133 : 277-280, 2005
- Tominaga T, Tomotake M, Takeda T, Ueoka Y, Tanaka T, Watanabe SY, Kameoka N, Nakataki M, Numata S, Izaki Y, Sumitani S, Kubo H, Kaneda Y, Ohmori T : Relationship between social and cognitive functions in people with schizophrenia. *Neuropsychiatr Dis Treat* 14 : 2215-2224, 2018
- Tomotake M, Kaneda Y, Iga J, Kinouchi S, Tayoshi S, Motoki I, Sumitani S, Yamauchi K, Taniguchi T, Ishimoto Y, Ueno S, Ohmori T : Subjective and objective measures of quality of life have different predictors for people with schizophrenia. *Psychol Rep* 99 : 477-487, 2006
- Ueoka Y, Tomotake M, Tanaka T, Kaneda Y, Taniguchi K,

- Nakataki M, Numata S, Tayoshi S, Yamauchi K, Sumitani S, Ohmori T, Ueno S, Ohmori T : Quality of life and cognitive dysfunction in people with schizophrenia. *Prog Neuropsychopharmacol Biol Psychiatry* 35 : 53-59, 2011
21. Yamauchi K, Aki H, Tomotake M, Iga J, Numata S, Motoki I, Izaki Y, Tayoshi S, Kinouchi S, Sumitani S, Tayoshi S, Takikawa Y, Kaneda Y, Taniguchi T, Ishimoto Y, Ueno S, Ohmori T : Predictors of subjective and objective quality of life in outpatients with schizophrenia. *Psychiatry Clin Neurosci* 62 : 404-411, 2008
 22. Green MF, Harvey PD : Cognition in schizophrenia : Past, present, and future. *Schizophr Res Cogn* 1 : e1-9, 2014
 23. Kraus MS, Keefe RS : Cognition as an outcome measure in schizophrenia. *Br J Psychiatry* 191 (Suppl. 50) : s46-51, 2007
 24. Kahn RS, Keefe RS : Schizophrenia is a cognitive illness : time for a change in focus. *JAMA Psychiatry* 70 : 1107-1112, 2013
 25. Palmer BW, Dawes SE, Heaton RK : What do we know about neuropsychological aspects of schizophrenia? *Neuropsychol Rev* 19 : 365-384, 2009
 26. Dickinson D, Ramsey ME, Gold JM : Overlooking the obvious : a meta-analytic comparison of digit symbol coding tasks and other cognitive measures in schizophrenia. *Arch Gen Psychiatry* 64 : 532-542, 2007
 27. Reichenberg A : The assessment of neuropsychological functioning in schizophrenia. *Dialogues Clin Neurosci* 12 : 383-392, 2010
 28. Reichenberg A, Harvey PD : Neuropsychological impairments in schizophrenia : Integration of performance-based and brain imaging findings. *Psychol Bull* 133 : 833-858, 2007
 29. Green MF : What are the functional consequences of neurocognitive deficits in schizophrenia? *Am J Psychiatry* 153 : 321-330, 1996
 30. Green MF, Kern RS, Braff DL, Mintz J : Neurocognitive deficits and functional outcome in schizophrenia : are we measuring the "right stuff"? *Schizophr Bull* 26 : 119-136, 2000
 31. Green MF, Kern RS, Heaton RK : Longitudinal studies of cognition and functional outcome in schizophrenia: implications for MATRICS. *Schizophr Res* 72 : 41-51, 2004
 32. Christensen TØ : The influence of neurocognitive dysfunctions on work capacity in schizophrenia patients : a systematic review of the literature. *Int J Psychiatry Clin Pract* 11 : 89-101, 2007
 33. Velligan DI, Mahurin RK, Diamond PL, Hazleton BC, Eckert SL, Miller AL : The functional significance of symptomatology and cognitive function in schizophrenia. *Schizophr Res* 25 : 21-31, 1997
 34. Harvey PD, Penn D : Social cognition : the key factor predicting social outcome in people with schizophrenia? *Psychiatry (Edgmont)* 7 : 41-44, 2010
 35. Fett AK, Viechtbauer W, Dominguez MD, Penn DL, van Os J, Krabbendam L : The relationship between neurocognition and social cognition with functional outcomes in schizophrenia : a meta-analysis. *Neurosci Biobehav Rev* 35 : 573-588, 2011
 36. Ertuğrul A, Uluğ B : The influence of neurocognitive deficits and symptoms on disability in schizophrenia. *Acta Psychiatr Scand* 105 : 196-201, 2002
 37. Mohamed S, Rosenheck R, Swartz M, Stroup S, Lieberman JA, Keefe RS : Relationship of cognition and psychopathology to functional impairment in schizophrenia. *Am J Psychiatry* 165 : 978-987, 2008
 38. Norman RM, Malla AK, Cortese L, Cheng S, Diaz K, McIntosh E, McLean TS, Rickwood A, Voruganti LP : Symptoms and cognition as predictors of community functioning : a prospective analysis. *Am J Psychiatry* 156 : 400-405, 1999
 39. Nuechterlein KH, Green MF, Kern RS, Baade LE, Barch DM, Cohen JD, Essock S, Fenton WS, Frese FJ 3rd, Gold JM, Goldberg T, Heaton RK, Keefe RS, Kraemer H, Mesholam-Gately R, Seidman LJ, Stover E, Weinberger DR, Young AS, Zalcman S, Marder SR : The MATRICS Consensus Cognitive Battery, part 1 : test selection, reliability, and validity. *Am J Psychiatry* 165 : 203-213, 2008
 40. Leifker FR, Patterson TL, Heaton RK, Harvey PD : Validating measures of real-world outcome : the results of the VALERO expert survey and RAND panel. *Schizophr Bull* 37 : 334-343, 2011
 41. August SM, Kiwanuka JN, McMahon RP, Gold JM : The MATRICS Consensus Cognitive Battery (MCCB) : clinical and cognitive correlates. *Schizophr Res* 134 : 76-82, 2012
 42. Durand D, Strassnig M, Sabbag S, Gould F, Twamley EW, Patterson TL, Harvey PD : Factors influencing self-assessment of cognition and functioning in schizophrenia : implications for treatment studies. *Eur Neuropsychopharmacol* 25 : 185-191, 2015
 43. Gould F, McGuire LS, Durand D, Sabbag S, Larrauri C, Patterson TL, Twamley EW, Harvey PD : Self-assessment in schizophrenia : Accuracy of evaluation of cognition and everyday functioning. *Neuropsychology* 29 : 675-682, 2015
 44. Kern RS, Gold JM, Dickinson D, Green MF, Nuechterlein KH, Baade LE, Keefe RS, Mesholam-Gately RI, Seidman LJ, Lee C, Sugar CA, Marder SR : The MCCB impairment profile for schizophrenia outpatients : results from the MATRICS psychometric and standardization study. *Schizophr Res* 126 : 124-131, 2011
 45. Lin CH, Huang CL, Chang YC, Chen PW, Lin CY, Tsai GE, Lane HY : Clinical symptoms, mainly negative symptoms, mediate the influence of neurocognition and social cognition on functional outcome of schizophrenia. *Schizophr Res* 146 : 231-237, 2013
 46. Lystad JU, Falkum E, Haaland VØ, Bull H, Evensen S, Bell MD, Ueland T : Neurocognition and occupational functioning in schizophrenia spectrum disorders : The MATRICS Consensus Cognitive Battery (MCCB) and workplace assessments. *Schizophr Res* 170 : 143-149, 2016
 47. Lystad JU, Falkum E, Mohn C, Haaland VØ, Bull H, Evensen S, Rund BR, Ueland T : The MATRICS Consensus Cognitive Battery (MCCB) : performance and functional correlates. *Psychiatry Res* 220 : 1094-1101, 2014
 48. Sabbag S, Twamley EM, Vella L, Heaton RK, Patterson TL, Harvey PD : Assessing everyday functioning in schizophrenia : not all informants seem equally informative. *Schizophr Res* 131 : 250-255, 2011
 49. Shamsi S, Lau A, Lencz T, Burdick KE, DeRosse P, Brenner R, Lindenmayer JP, Malhotra AK : Cognitive and symptomatic predictors of functional disability in schizophrenia. *Schizophr Res* 126 : 257-264, 2011
 50. Sumiyoshi C, Harvey PD, Takaki M, Okahisa Y, Sato T, Sora I, Nuechterlein KH, Subotnik KL, Sumiyoshi T : Factors predicting work outcome in Japanese patients with schizophrenia : role of multiple functioning levels. *Schizophr Res Cogn* 2 : 105-112, 2015
 51. Torgalsbøen AK, Mohn C, Czajkowski N, Rund BR : Relationship between neurocognition and functional recovery in first-episode schizophrenia : Results from the second year of the Oslo multi-follow-up study. *Psychiatry Res* 227 : 185-191, 2015
 52. Evensen S, Wisløff T, Lystad JU, Bull H, Ueland T, Falkum

- E : Prevalence, Employment Rate, and Cost of Schizophrenia in a High-Income Welfare Society : A Population-Based Study Using Comprehensive Health and Welfare Registers. *Schizophr Bull* 42 : 476-483, 2016
53. Mangalore R, Knapp M : Cost of schizophrenia in England. *J Ment Health Policy Econ* 10 : 23-41, 2007
 54. Marwaha S, Johnson S : Schizophrenia and employment - a review. *Soc Psychiatry Psychiatr Epidemiol* 39 : 337-49, 2004
 55. American Psychiatric Association : Diagnostic and Statistical Manual of Mental Disorders. 4th Edition. American Psychiatric Association, Washington DC, 1994
 56. Rosen A, Hadzi-Pavlovic D, Parker G : The life skills profile : a measure assessing function and disability in schizophrenia. *Schizophr Bull* 15 : 325-337, 1989
 57. Hasegawa K, Ogawa K, Kondoh C, Iseda T, Ikebuchi E, Miyake Y : The reliability and validity of the Japanese version of the Life Skills Profile. *Seishin Igaku* 39 : 547-555, 1997 (in Japanese)
 58. Kaneda Y, Ohmori T, Okahisa Y, Sumiyoshi T, Pu S, Ueoka Y, Takaki M, Nakagome K, Sora I : Measurement and Treatment Research to Improve Cognition in Schizophrenia Consensus Cognitive Battery : validation of the Japanese version. *Psychiatry Clin Neurosci* 67 : 182-188, 2013
 59. Kay SR, Fiszbein A, Opler LA : The positive and negative syndrome scale (PANSS) for schizophrenia. *Schizophr Bull* 13 : 261-276, 1987
 60. Kay SR, Opler LA, Fiszbein A : Positive and negative syndrome scale (PANSS) rating manual. Seiwa Pub, Tokyo, 1991 (in Japanese)
 61. Addington D, Addington J, Maticka-Tyndale E : Assessing depression in schizophrenia : the Calgary Depression Scale. *Br J Psychiatry* 163 (Suppl. 22) : 39-44, 1993
 62. Kaneda Y, Fujii A, Ohmori T : Psychometric properties of the Japanese version of the Calgary Depression Scale for Schizophrenics. *J Nerv Ment Dis* 188 : 237-239, 2000
 63. Inada T : Evaluation and diagnosis of drug-induced extrapyramidal symptoms : commentary on the DIEPSS and guide to its usage. Seiwa Pub, Tokyo, 1996 (In Japanese)
 64. Inada T, Inagaki A : Psychotropic dose equivalence in Japan. *Psychiatry Clin Neurosci* 69 : 440-447, 2015
 65. Farreny A, Aguado J, Ochoa S, Haro JM, Usall J : The role of negative symptoms in the context of cognitive remediation for schizophrenia. *Schizophr Res* 150 : 58-63, 2013
 66. Stratta P, Daneluzzo E, Riccardi I, Bustini M, Rossi A : Metacognitive ability and social functioning are related in persons with schizophrenic disorder. *Schizophr Res* 108 : 301-302, 2009
 67. Ojeda N, Sánchez P, Peña J, Elizagárate E, Yoller AB, Gutiérrez-Fraile M, Ezcurra J, Napal O : An explanatory model of quality of life in schizophrenia : the role of processing speed and negative symptoms. *Actas Esp Psiquiatr* 40 : 10-18, 2012
 68. Addington J, Addington D : Neurocognitive and social functioning in schizophrenia. *Schizophr Bull* 25 : 173-182, 1999
 69. Addington J, Saeedi H, Addington D : Facial affect recognition : a mediator between cognitive and social functioning in psychosis? *Schizophr Res* 85 : 142-150, 2006
 70. Addington J, Saeedi H, Addington D : Influence of social perception and social knowledge on cognitive and social functioning in early psychosis. *Br J Psychiatry* 189 : 373-378, 2006
 71. Bozikas VP, Kosmidis MH, Kafantari A, Gamvrula K, Vasiliadou E, Petrikis P, Fokas K, Karavatos A : Community dysfunction in schizophrenia : rate-limiting factors. *Prog Neuropsychopharmacol Biol Psychiatry* 30 : 463-470, 2006
 72. Fiszdon JM, Choi J, Goulet J, Bell MD : Temporal relationship between change in cognition and change in functioning in schizophrenia. *Schizophr Res* 105 : 105-113, 2008
 73. Lipkovich IA, Deberdt W, Csernansky JG, Sabbe B, Keefe RS, Kollack-Walker S : Relationships among neurocognition, symptoms and functioning in patients with schizophrenia : a path-analytic approach for associations at baseline and following 24 weeks of antipsychotic drug therapy. *BMC Psychiatry* 9 : 44, 2009
 74. Lysaker PH, Davis LW : Social function in schizophrenia and schizoaffective disorder : associations with personality, symptoms and neurocognition. *Health Qual Life Outcomes* 2 : 15, 2004
 75. Poole JH, Ober BA, Shenaut GK, Vinogradov S : Independent frontal-system deficits in schizophrenia : cognitive, clinical, and adaptive implications. *Psychiatry Res* 85 : 161-176, 1999
 76. Poole JH, Tobias FC, Vinogradov S : The functional relevance of affect recognition errors in schizophrenia. *J Int Neuropsychol Soc* 6 : 649-658, 2000
 77. Heinrichs DW, Hanlon TE and Carpenter WT Jr. : The Quality of Life Scale : an instrument for rating the schizophrenic deficit syndrome. *Schizophr Bull* 10 : 388-398, 1984
 78. Puig O, Penadés R, Baeza I, De la Serna E, Sánchez-Gistau V, Lázaro L, Bernardo M, Castro-Fornieles J : Assessment of real-world daily-living skills in early-onset schizophrenia through the Life Skills Profile scale. *Schizophr Res* : 145 : 95-100, 2013
 79. Matsuda Y, Sato S, Hatsuse N, Watanabe Y, Kishimoto T, Ikebuchi E : Neurocognitive functioning in patients with first-episode schizophrenia 1 year from onset in comparison with patients 5 years from onset. *Int J Psychiatry Clin Pract* : 18 : 63-69, 2014