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ORIGINAL RESEARCH

Survey of Health Literacy Among Japanese Outpatients with Mental Illness

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Purpose: Low health literacy has been associated with adverse outcomes in health maintenance and the course of chronic physical illness. In particular, anxiety disorders can also affect one's physical health, causing issues including cardiovascular, respiratory, gastrointestinal and immune system disorders. However, there are no reports on physical health literacy among Japanese patients with mental illness.

Patients and Methods: A patient background questionnaire, the Japanese version of the Ten-Item Personality Inventory, and the Japanese version of the Health Literacy Scale (HLS-EU-Q47; European Health Literacy Survey Questionnaire) were distributed face to face to 1000 psychiatric outpatients. A total of 785 valid responses including 211 patients with schizophrenia, 261 patients with mood disorders, and 234 patients with anxiety disorders were obtained by mail.

Results: Health literacy was "limited" in 52% of patients with schizophrenia, 51% of those with mood disorders, and 38% of those with anxiety disorders. Among patients with mood disorders, there were no differences between those with major depressive disorder and those with bipolar disorder. Anxiety disorders were associated with higher health literacy than schizophrenia and mood disorders (odds ratio (OR) 1.85, 95% confidence interval (95% CI) 1.07, 3.34), and in terms of personality, neuroticism (OR 0.85, 95% CI 0.75, 0.97) and openness (OR 0.85, 95% CI 0.74, 0.98) were associated with limited health literacy, while agreeableness (OR 1.36, 95% CI 1.18, 1.57) and extraversion OR 1.34, 95% CI 1.17, 1.52) were associated with higher health literacy.

Conclusion: The results of this study indicate limited health literacy in patients with mental illness, in particular, limited health literacy in outpatients with schizophrenia and mood disorders. In addition, gender and some personality traits were associated with physical health literacy. Based on these results, physical health education should be individualized.

Keywords: health literacy, mental illness, anxiety disorders, personality traits

Introduction

It is known that people experiencing severe mental illness have a life expectancy that is 10 to 15 years shorter than that of the general population.[1] This is due to the high prevalence of abnormalities in glycolipid metabolism, so-called metabolic syndrome,[2,3] among patients with psychiatric disorders. Difficulties in self-care in these patients are considered to promote this condition.[4] In particular, anxiety disorders can also affect physical health, leading to issues including cardiovascular,[5] respiratory,[6] gastrointestinal[7] and immune system disorders.[8] Chronic stress and anxiety can contribute to high blood pressure, atherosclerosis, and other health problems affecting the heart and blood vessels.[5] People with anxiety may experience shortness of breath or hyperventilation, which can worsen respiratory conditions, such as asthma or chronic obstructive pulmonary disease (COPD).[6] Anxiety can cause or exacerbate digestive issues by affecting the way the digestive system functions.[7] Chronic stress and anxiety can weaken the immune system, making individuals more susceptible to infections and illnesses, including cancer.[8]

Health literacy is the degree of an individual's ability to research, obtain, understand, and effectively use basic health information and services needed to make appropriate health decisions.[9] Health literacy is influenced by the ability to read and write medical information as well as by the ability to take action.[10] In recent years, health literacy has become

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a significant factor influencing health decision making in an environment inundated with a large amount of information due to the introduction of information and communication technology (ICT), and the association of health literacy with health behaviors has been reported. Increased physical health literacy may promote engagement in self-management behaviors and have long-term effects on health status.[11] Factors that enhance these health behaviors are related to self-efficacy, coping with stress, and effort, which are deeply influenced by personality.[12]

Two studies have examined the relationship between personality and physical health literacy: Iwasa & Yoshida[13] reported that some personality traits (eg, extraversion, openness, and conscientiousness) may influence physical health literacy among healthy older adults living in Japan. In addition, a study by Mai et al[14] found that in two-parent families, education, extraversion, agreeableness, conscientiousness, neuroticism, and openness were significantly associated with physical health literacy in Chinese subjects. In contrast, monthly income, agreeableness, and openness were factors influencing health literacy in single-parent families. However, to date, no studies have examined the relationship between personality and health literacy in people living with mental illness.

There are reports on physical health literacy in patients with physical illness[11,15] and mental health literacy in the general population.[16] However, there are very few reports on health literacy among patients with mental illnesses worldwide, and only one report[17] showed that schizophrenia patients had better health literacy than healthy individuals. Therefore, we conducted a survey to quantitatively clarify physical health literacy among Japanese patients with major mental illnesses, such as schizophrenia, mood disorders, and anxiety disorders. To the best of our knowledge, no study has examined the relationship between personality and health literacy in mental illness subjects. We also identified factors such as personality traits that are associated with physical health literacy.

Method

Subjects

This study was a multicenter cross-sectional study. Data were collected at 5 sites: three were general hospitals, including a university hospital; two were psychiatric hospitals; and one was a mental health clinic. Four sites were in Aomori Prefecture and one was in Akita Prefecture; these are in the rural north-eastern region. The study was approved by the Ethics Committee of Hirosaki University Hospital and the affiliated hospitals where it was conducted. Outpatients at each hospital were given a written and oral explanation of the purpose and content of the study. A total of 1000 patients attending outpatient clinics for psychiatric disorders who were at least 20 years old at the time consent was obtained were included in the study.

Patients who agreed to participate were given a patient background questionnaire, the Japanese version[18] of the Ten Item Personality Inventory[19] (TIPI-J), and a health literacy scale (HLS-EU-Q47; European Health Literacy Survey Questionnaire).[20]

Personality Inventory

The TIPI-J, which consisted of ten items and which was developed by Gosling et al[19] measures five important personality traits including openness, conscientiousness, extraversion, agreeableness, and emotional stability. Each sub-item in this seven-point Likert scale was rated from 1 (Strongly disagree) to 7 (Strongly agree) and consisted of two items.

Health Literacy Inventory

The Japanese version of the HLS-EU-Q47[20] was distributed according to the method of Nakayama et al.[21] The HLS-EU-Q47 consists of 47 items measuring health literacy. The difficulty of each item is rated on a 4-point Likert scale (1 = very difficult, 2 = difficult, 3 = easy, 4 = very easy), with the lowest mean score being 1 and the highest score being 4. Thus, the mean score varies from 1 to 4, with a range of 4–1=3. The HLS-EU-Q47 is based on a conceptual model of health literacy and measures four abilities for handling health-related information (access/obtain, understand, evaluate/judge/assess, and apply/use) in three domains listed below, including health care. The Health Literacy Index was constructed as the General Health Literacy Index (GEN-HL) consisting of all items. This system provides an overall index and three domains: the Health Care Health Literacy Index (HC-HL), the Disease Prevention Health Literacy Index (DP-HL), and

the Health Promotion Health Literacy Index (HP-HL). The health literacy index is standardized as a unified index ranging from 0 to 50 with the following formula.

$$\text{Index} = (\text{mean} - 1) * (50/3).$$

Here, Index is the specific index calculated, and the mean is the average of all items answered by each individual; 1 is the minimum value of the mean, 3 is the range of the mean, and 50 is the maximum value chosen for the new index. This is the maximum value of the new indicator. Thus, the following indicator values were obtained, where 0 represents the lowest health literacy and 50 represents the highest health literacy. Less than 33 points was classified as "limited" based on previous literature.[21]

Statistical Analyses

This study dealt only with data on schizophrenia, mood disorders, and anxiety disorders for which sufficient sample sizes were available. ANOVA, the χ-square test, and logistic regression analysis were used for statistical analysis, with $P < 0.05$ indicating statistical significance. In logistic regression analyses, the dependent variable was literacy status (Sufficient or above=1, limited=0), with personality, age, sex, marital status, alcohol and smoking status assigned as independent variables. Dummy variables were used for sex (male = 1, female = 0), alcohol (yes = 1, no = 0) and smoking (yes = 1, no = 0) respectively. Dummy variables were used for each marital status and each diagnosis name without categorical data. For example, a combination of dummy variables was assigned to married people (1, 0, 0, 0) and to unmarried people (0, 1, 0, 0). A combination of dummy variables was assigned to patients with schizophrenia (1, 0, 0) and mood disorders (0, 1, 0). Real numbers and TIPI scores were used for age, education and personality, respectively. This statistical method does not determine the relationship between independent variables. IBM SPSS Statistics Ver 28 was used for data analysis.

Results

Table 1 shows the characteristics of the participants. After face-to-face distribution of the questionnaires, a total of 785 valid responses were received by mail. Five-hundred seventy responses were received from general hospitals, 100 from psychiatric hospitals and 115 from mental clinics. The median age was 46.3 years for 211 patients with schizophrenia, 54.0 years for patients with 261 mood disorders, 48.1 years for 234 patients with anxiety disorders, 37.6 years for 79 patients with other disorders, including F5 psychosomatic disorders (n=10), F6 personality disorders (n=25), F7 intellectual disorder (n=11), F8 autism spectrum disorder (ASD) (n=24), and F9 attention-deficit/hyperactivity disorder (ADHD) (n=5). The proportion of women was 59% for patients with schizophrenia, 66% for patients with mood disorders, and 72% for patients with anxiety disorders.

Table 1 Characteristics of Subjects with Mental Illness

Characteristics	Schizophrenia n=211		Mood Disorders n=261		Anxiety Disorders n=234		Others n=79	
Age	46.3	(12.9)	54.0	(15.1)	48.1	(17.0)	37.4	(13.4)
Gender, Female (n,%)	124	59%	173	66%	169	72%	45	57%
Marriage state (n,%)								
Married	49	23%	150	57%	115	49%	16	20%
Unmarried	132	63%	57	22%	70	30%	42	53%
Divorced	25	12%	33	13%	33	14%	14	18%
Bereaved	5	2%	19	7%	10	4%	1	1%
Missing	0	0%	2	1%	6	3%	6	8%

(*Continued*)

Table 1 (Continued).

Characteristics	Schizophrenia n=211		Mood Disorders n=261		Anxiety Disorders n=234		Others n=79	
Academic career (n,%)								
Junior high school	34	16%	37	14%	38	16%	14	18%
High school	107	51%	119	46%	121	52%	32	41%
University	33	16%	44	17%	28	12%	13	16%
Vocational school	33	16%	57	22%	44	19%	11	14%
Missing	0	0%	4	2%	3	1%	9	11%
Smoking (n,%)								
No	155	73%	208	80%	191	82%	56	71%
Yes	56	27%	53	20%	41	18%	20	25%
Missing	0	0%	0	0%	2	1%	3	4%
Drinking habits (n,%)								
No	166	79%	185	71%	176	75%	49	62%
Yes	42	20%	74	28%	53	23%	23	29%
Missing	3	1%	2	1%	5	2%	7	9%
Length of hospital visit	15.1	(9.6)	8.9	(8.1)	6.2	(7.4)	8.3	(9.1)
Personality Trait								
Extraversion	3.1	(1.3)	3.6	(1.3)	3.5	(1.3)	3.4	(1.3)
Agreeableness	4.7	(1.2)	4.9	(1.1)	4.9	(1.2)	4.1	(1.3)
Conscientiousness	3.7	(1.4)	3.8	(1.3)	3.9	(1.4)	3.4	(1.5)
Neuroticism	4.5	(1.4)	4.9	(1.2)	5.0	(1.2)	5.5	(1.2)
Openness	3.8	(1.3)	3.6	(1.2)	3.5	(1.2)	4.0	(1.2)

Note: Data show mean and (standard deviation).

Health Literacy Scores Among Patients with the Major Psychiatric Diseases

Table 2 shows the health literacy scores among the three groups (patients with schizophrenia, mood disorders, and anxiety disorders). Fifty-two percent of patients with schizophrenia, 51% of patients with mood disorders, and 38% of patients with anxiety disorders were classified as having "limited" (0–33 points) health literacy according to the GEN-HL; 49% of patients with schizophrenia, 50% of patients with mood disorders, and 40% of patients with anxiety disorders were classified as having "limited" health literacy according to the HC-HL. According to the DP-HL, 46% of patients with schizophrenia, 43% of patients with mood disorder, and 34% of patients with anxiety disorder had 'limited' health literacy. Finally, according to the HP-HL, 44% of patients with schizophrenia, 44% of patients with mood disorder, and 35% of patients with anxiety disorder had 'limited' health literacy.

Table 2 Results of the Health Literacy Indices Among Three Metal Illness

HL Index	Schizophrenia n=211		Mood Disorders n=261		Anxiety Disorders n=234		Significance
GEN-HL standardized	33.3	(10.7)	33.3	(9.2)	35.2	(8.9)	p=0.055
Categorized index (N, %)							
Excellent	47	22%	50	19%	48	21%	p=0.012
Sufficient	55	26%	79	30%	97	41%	
Problematic	70	33%	92	35%	63	27%	
Inadequate	39	18%	40	15%	26	11%	
Limited	**109**	**52%**	**132**	**51%**	**89**	**38%**	**p=0.005**

(*Continued*)

Table 2 (Continued).

HL Index	Schizophrenia n=211		Mood Disorders n=261		Anxiety Disorders n=234		Significance
HC-HL standardized	33.6	(11.5)	33.7	(10.1)	35.2	(10.0)	p=0.189
Categorized index (N, %)							
Excellent	46	22%	49	19%	67	29%	p=0.090
Sufficient	62	29%	81	31%	74	32%	
Problematic	58	27%	85	33%	59	25%	
Inadequate	45	21%	46	18%	34	15%	
Limited	**103**	**49%**	**131**	**50%**	**93**	**40%**	**p=0.046**
DP-HL standardized	33.8	(11.5)	34.6	(10.5)	36.5	(10.5)	p=0.023
Categorized index (N, %)							
Excellent	50	24%	60	23%	67	29%	p=0.199
Sufficient	63	30%	90	34%	87	37%	
Problematic	46	22%	57	22%	42	18%	
Inadequate	52	25%	54	21%	38	16%	
Limited	**98**	**46%**	**111**	**43%**	**80**	**34%**	**p=0.026**
HP-HL standardized	34.1	(14.0)	33.3	(11.8)	35.5	(12.4)	p=0.171
Categorized index (N, %)							
Excellent	52	25%	54	21%	62	26%	p=0.205
Sufficient	67	32%	92	35%	90	38%	
Problematic	41	19%	61	23%	45	19%	
Inadequate	51	24%	54	21%	37	16%	
Limited	**92**	**44%**	**115**	**44%**	**82**	**35%**	**p=0.081**

Notes: Bold shows where there were significant differences. Data show mean and (standard deviation). Limited show sum of Problematic and Inadequate.

Abbreviations: Gen-HL, general health literacy; HC-HL, Healthcare literacy; DP-HL, disease prevention literacy; HP-HL, Health promotion literacy.

Health Literacy Scores Between Patients with Different Mood Disorders (Major Depressive Disorder and Bipolar Disorder)

Table 3 shows the health literacy scores for patients with major depressive disorder and those with bipolar disorder. Among patients with bipolar disorder and major depressive disorder, 51% and 50% were classified as having "limited" health literacy according to the GEN-HL, 49% and 50% according to the HC-HL, 37% and 44% according to the DP-HL, and 42% and 45% according to the HP-HL, respectively.

Table 3 Results of the Health Literacy Indices Between Bipolar Disorders and Major Depressive Disorders

HL Index	Bipolar Disorders n=59		Major Depressive Disorders n=202		Significance
GEN-HL standardized	33.6	(8.7)	33.3	(9.4)	p=0.779
Categorized index (N, %)					
Excellent	11	19%	39	19%	p=0.823
Sufficient	18	31%	61	30%	
Problematic	23	39%	69	34%	
Inadequate	7	12%	33	16%	
Limited	**30**	**51%**	**102**	**50%**	**p=0.962**

(*Continued*)

Table 3 (Continued).

HL Index	Bipolar Disorders n=59		Major Depressive Disorders n=202		Significance
HC-HL standardized	34.7	(9.4)	33.4	(10.3)	p=0.404
Categorized index (N, %)					
Excellent	12	20%	37	18%	p=0.793
Sufficient	18	31%	63	31%	
Problematic	21	36%	64	32%	
Inadequate	8	14%	38	19%	
Limited	**29**	**49%**	**102**	**50%**	**p=0.856**
DP-HL standardized	34.4	(10.4)	34.7	(10.5)	p=0.862
Categorized index (N, %)					
Excellent	13	22%	47	23%	p=0.708
Sufficient	24	41%	66	33%	
Problematic	11	19%	46	23%	
Inadequate	11	19%	43	21%	
Limited	22	37%	89	44%	p=0.355
HP-HL standardized	33.0	(11.3)	33.4	(12.0)	p=0.799
Categorized index (N, %)					
Excellent	12	20%	42	21%	p=0.927
Sufficient	22	37%	70	35%	
Problematic	12	20%	49	24%	
Inadequate	13	22%	41	20%	
Limited	**25**	**42%**	**90**	**45%**	**p=0.767**

Notes: Bold shows where there were significant differences. Data show mean and (standard deviation). Limited show sum of Problematic and Inadequate.
Abbreviations: Gen-HL, general health literacy; HC-HL, Healthcare literacy; DP-HL, disease prevention literacy; HP-HL, Health promotion literacy.

Factors Associated with Health Literacy

Logistic regression analysis was conducted to identify the determinants of general health literacy (Table 4 and Table 5). Female gender and four of the five personality factors, namely, extraversion, agreeableness, neuroticism, and openness, were identified as determinants of health literacy. Extraversion and agreeableness were associated with health literacy that was sufficient or above, while neuroticism and openness were associated with limited health literacy. In addition, anxiety disorders were associated with health literacy that was sufficient or above.

Table 4 Odds Ratio for General Health Literacy by Patient Characteristics in Logistic Regression Analysis

	Wald	Exp (B)	95% CI	
Age	15.05	0.975***	0.524	1.045
Gender	2.91	0.740	0.962	0.987
Marriage state				
Married	2.57	0.169	0.019	1.485
Unmarried	3.49	0.124	0.014	1.110
Divorced	1.92	0.210	0.023	1.910
Bereaved	1.33	0.262	0.027	2.554

(*Continued*)

Table 4 (Continued).

	Wald	Exp (B)	95% CI	
Academic career (years)	0.59	1.029	0.956	1.109
Smoking	2.09	0.752	0.511	1.106
Drinking habits		1.205	0.831	1.747
Diagnosis	0.97			
Schizophrenia	0.56	1.259	0.690	2.295
Mood disorders	0.14	1.119	0.617	2.031
Anxiety disorders	4.12	1.846*	1.021	3.337
Personality Trait				
Extraversion	18.98	1.335***	1.172	1.520
Agreeableness	17.76	1.358***	1.178	1.566
Conscientiousness	0.21	0.971	0.856	1.102
Neuroticism	5.50	0.854*	0.748	0.974
Openness	5.30	0.852*	0.743	0.977

Notes: *P<0.05, ***p<0.005.

Table 5 Odds Ratio for Subitems of Health Literacy by Patient Characteristics in Logistic Regression Analyses

	HC-HL	95% CI		DP-HL	95% CI		HP-HL	95% CI	
Age	0.981**	0.969	0.994	0.972***	0.960	0.985	0.990	0.977	1.003
Gender	0.990	0.703	1.394	0.799	0.566	1.127	0.678*	0.481	0.955
Marriage state									
Married	0.175	0.020	1.528	0.234	0.027	2.047	0.572	0.105	3.130
Unmarried	0.127	0.014	1.135	0.150	0.017	1.343	0.459	0.082	2.571
Divorced	0.212	0.024	1.915	0.316	0.035	2.866	0.769	0.135	4.386
Bereaved	0.207	0.021	1.997	0.305	0.031	2.972	0.542	0.087	3.379
Academic career (years)	1.069	0.993	1.150	1.014	0.941	1.092	1.057	0.982	1.138
Smoking	0.881	0.603	1.288	0.735	0.499	1.082	0.797	0.544	1.168
Drinking habits	1.272	0.881	1.835	1.071	0.737	1.555	1.395	0.961	2.026
Diagnosis									
Schizophrenia	0.771	0.426	1.395	1.318	0.725	2.395	1.154	0.638	2.088
Mood disorders	0.647	0.359	1.166	1.315	0.727	2.379	0.999	0.555	1.798
Anxiety disorders	1.029	0.574	1.847	1.778	0.985	3.211	1.559	0.868	2.800
Personality Trait									
Extraversion	1.274***	1.121	1.447	1.284***	1.127	1.463	1.197**	1.054	1.360
Agreeableness	1.297***	1.128	1.491	1.337***	1.160	1.541	1.267**	1.103	1.455
Conscientiousness	0.986	0.870	1.116	1.015	0.893	1.153	0.961	0.848	1.090
Neuroticism	0.829**	0.727	0.944	0.847*	0.741	0.968	0.814**	0.713	0.929
Openness	0.857*	0.750	0.981	0.869*	0.758	0.996	0.974	0.852	1.113

Notes: *P<0.05, **p<0.01, ***p<0.005.
Abbreviations: HC-HL, Healthcare literacy; DP-HL, disease prevention literacy; HP-HL, Health promotion literacy.

Discussion

The results of this study showed that health literacy was sufficient or above in the anxiety disorder group than in the schizophrenia and mood disorder groups among patients with psychiatric disorders. This is the first study to determine whether there are differences in health literacy by illness. Higher health literacy in anxiety disorders than those in mood disorders or schizophrenia may be because anxiety disorders are less likely to be associated with cognitive dysfunction than mood disorders or schizophrenia[22] and cognitive function is directly related to health literacy skills. Hence, more

careful physical health instruction is needed for patients with mood disorders and schizophrenia. One-way service providers may be able to address this gap is by providing more careful health instruction for patients with mood disorders and schizophrenia.

In this study, extraversion and agreeableness were associated with high health literacy, while neuroticism and openness were associated with limited health literacy. Although the results for extraversion and neuroticism are reasonable because the vectors are always reversed, the association between openness and limited health literacy differs from the findings of previous studies of healthy subjects. Previous studies have found an association between increased openness scores and higher utilization of alternative medicine[23] and use of complementary/alternative medicine,[24] while an association between increased openness scores and increased use of medical services was reported.[25] Openness is also referred to as the "ability to challenge" and is considered a measure of broadening of mental associations, diffuse thinking, and artistic sensitivity.[26]

While health literacy is important in the treatment of physical illnesses,[9] and psychiatry is more concerned with the patient's awareness of his or her illness and holistic care. Increasing health literacy for people with mental illness supports their active involvement in managing their own health and exercising their right to self-determination. The following are health literacy recommendations for people with mental illness. 1) Patients and their families need to be provided with accurate and understandable information about mental illness. It is also important to provide patients with education to help them develop self-management skills. 2) Improved communication with healthcare professionals can help patients become active participants in the healthcare process. It is important that healthcare professionals work with patients to set treatment goals and support them in the decision-making process. 3) Regular support is needed to help patients understand information and exercise self-determination. This support may take many forms and may come from different sources, including from healthcare professionals, family members and support groups. 4) To ensure that patients can achieve health literacy, the accessibility of information and services needs to be improved. This includes providing information in appropriate languages and formats, providing a barrier-free environment and providing online resources. 5) Patients can perform self-assessments to gain a better understanding of their health status and the care they need. It is important for healthcare professionals to provide patients with tools for self-assessment and to support them in managing their own health conditions.

This study has limitations. First, this was a single cross-sectional study in a single region, so causality could not be addressed. In addition, the study may have been strongly influenced by the local health care system. The areas from which participants were recruited are rural and lack adequate access to healthcare resources. Different results may be obtained in urban areas. Second, as the questionnaire was self-administered, it is not known whether the respondents answered the questions objectively and correctly. It is possible that the participants were influenced by social desirability bias, which confuses facts and wishes with statements. It is also possible that participants were strongly influenced by their own medical conditions. In other words, depression may have led to a negative portrayal of health literacy due to low self-esteem and the belief that it is a bad condition.

Conclusion

The results of this study showed that the health literacy of patients with psychiatric disorders was higher in the anxiety disorder group than in the schizophrenia and mood disorder groups. There was no difference between patients with bipolar disorder and patients with depression. Gender and four of the five factors in the personality model (extraversion, agreeableness, neuroticism, and openness) were associated with health literacy. In the future, it will be necessary to examine factors such as employment, economics, and education, as well as the relationship between health literacy and final outcomes of health and quality of life, including mortality, among persons with mental illness.

Abbreviations

ADHD, attention-deficit/hyperactivity disorder; ASD, autism spectrum disorder; DP-HL, the Disease Prevention Health Literacy Index; GEN-HL, the General Health Literacy Index; HC-HL, the Health Care Health Literacy Index; HLS-EU-Q47, European Health Literacy Survey Questionnaire; HP-HL, the Health Promotion Health Literacy Index; TIPI-J, the Japanese version of the Ten Item Personality Inventory.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics Approval and Informed Consent

The study protocol conformed with the Declaration of Helsinki and was approved by the Ethics Committee of Hirosaki University Hospital and the affiliated hospitals where it was conducted. Written informed consent was obtained from each patient to participate in the study.

Consent for Publication

Written informed consent was obtained from each patient for the publication.

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Disclosure

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