Research Article

Correlation between cognition and symptomatic severity in patients with late-life somatoform disorders

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Cognition in elderly patients with somatoform disorders

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Abstract

Objectives: Various aging-associated factors, such as functional decline, psychosocial problems, and cognitive dysfunction, are risk factors for somatoform disorders (SDs) in the elderly. The aim of the present study was to evaluate how cognition is correlated with the severity of late-life SDs from a neuropsychological viewpoint.

Methods: Fifty-three patients over 60 years of age who had been diagnosed as having SDs were examined in this study. The severity of the somatic symptoms was assessed using the Hamilton Anxiety Rating Scales (HAMA). Cognitive functions were assessed using the Mini-mental State Examination (MMSE), the Frontal Assessment Battery (FAB), and the Japanese version of the Neurobehavioral Cognitive Examination (J-COGNISTAT). **Results**: The J-COGNISTAT subtest score for attention was below the cut-off point (8) points) but was not correlated with the severity of the somatic symptoms in the patients with late-life SDs. The severity of anxiety as assessed using the HAMA was significantly correlated with the calculation scores (P < 0.005) among the J-COGNISTAT subtests, the FAB total (P < 0.05), and the FAB subtest scores (similarities and motor series) (P < 0.01). Other factors, including the benzodiazepine dosage, antidepressant dosage, the duration of illness, and the onset age, were not significantly correlated with the symptomatic severities. **Conclusion:** Patients with late-life SDs showed attention deficits, but no correlation was seen between the attention deficits and symptomatic severities. Attention deficits might be associated with the appearance of symptoms. Executive dysfunction and working memory might be associated with the severity of symptoms.

INTRODUCTION

According to the current concepts of the Diagnostic and Statistical Manual of Mental Disorders (4th edition, text revision) (DSM-IV-TR), somatoform disorders (SDs) are mainly characterized by chronic multiple physical symptoms that cannot be explained in terms of an underlying organic pathology (American Psychiatric Association, 2000). Thus, patients with SDs often visit medical facilities to elucidate their pathogenesis and to receive treatment. Somatization is defined as a tendency to experience medically unexplained somatic symptoms, to attribute them to physical illness, and to seek medical help for them (Lipowski, 1988). Various beliefs or perceptions may contribute to the process of somatization, including heightened bodily sensations, physical abnormalities resulting in a heightened awareness of bodily sensations, and inappropriate illness beliefs or sickness behavior. The current view of somatization has been regarded to result from complex interactive etiological factors, including psychosocial and/or neuropsychological factors (Mayou, Bass & Sharpe, 1995). Cognitive-behavioral models of SDs emphasize the role of inadequate body-related interpretations and health-related beliefs (Salkovskis & Warwick 2001).

From psychosocial viewpoints, late-life SDs are related to various factors characterized by the aging process, such as a decline in bodily functions, an increase in physical illness, psychosocial problems, and life events (Harwood, Prince, Mann & Ebrahim, 1998). The occasional experience of medically unexplainable symptoms (such as dizziness, an upset stomach, or palpitations) is common under stressful circumstances, such as various social adversities, life events, or physical illnesses, especially among the elderly. A previous study has reported that the attendance of older people with somatization is as common as that of younger people (Sheehan, Bass, Briggs & Jacoby, 2003).

Previous studies have shown age-associated differences in the prevalence of SDs. Altamura et al. reported that the prevalence of undifferentiated SD tends to increase with

age (Altamura, Carta, Tacchini, Musazzi & Pioli, 1998). Kuwabara et al. found that the age of onset is higher in patients with hypochondriasis or pain disorder than in patients with somatization disorder or body dysmorphic disorder (Kuwabara et al., 2007). The reason why such anxiety or stress-related disorders are dependent on aging has remained unclear.

From a neuropsychological viewpoint, several studies have investigated the neuropsychological performance of subjects with late-life anxiety disorder and have hypothesized that the presence or severity of anxiety is associated with a lower cognitive performance in the elderly (Beaudreau & O'Hara, 2008). According to this report, we hypothesized that cognitive functions might be related to the etiology of SDs. Cognitive functions decline with aging (Nilson, 2003), especially memory, attention, and executive functions (Buckner, 2004). Among several neuropsychological tests, the Mini-Mental State Examination (MMSE) and the Frontal Assessment Battery (FAB) are useful screening tests for measuring general cognition including memory, attention, and executive functions in elderly people (M.F. Folstein, S.E. Folstein & McHugh, 1975) (Dubois, Slachevsky, Litvan & Pillon, 2000). The Japanese version of the neurobehavioral cognitive examination (J-COGNISTAT) is a brief but comprehensive test that can be used to assess multiple cognitive domains. J-COGNISTAT is a sensitive diagnostic tool for dementia (Matsuda & Nakatani, 2004). These tests are easy to administer and can be completed at the patient s bedside within a comparatively short period. These three neuropsychological tests have been established as a convenient means of screening patients and may be useful for the testing of our hypothesis.

The clarification of which neuropsychological functions are associated with symptomatic severity in patients with late-life SDs may be important for understanding their relation with aging. Therefore, the aim of the present cross-sectional study was to determine which cognitive functions are associated with disease severity in patients with late-life SDs using comparatively simple neuropsychological screening tests.

METHODS

Participants

Fifty-three consecutive Japanese patients with undifferentiated SD who were over 60 years of age and had been referred to The Jikei University Kashiwa Hospital outpatient clinic for psychiatry were enrolled in this study. All the patients were recruited from a private general medicine practice, and the absence of any physical disease capable of explaining the somatic symptoms was confirmed. All the patients were diagnosed as having undifferentiated SD according to the DSM-IV-TR by an expert geriatric psychiatrist. Undifferentiated SD was operationalized according to whether the sufferer was unable to perform mundane activities of daily living (ADL). Focusing on undifferentiated SD seemed reasonable, since SD often appears initially as undifferentiated SD (Altamura, Carta, Tacchini, Musazzi & Pioli, 1998; Al Lawati et al., 2000). The exclusion criteria for the study were (1) the diagnosis of another significant Axis I disorder (e.g., another anxiety-related disorder, major depressive disorder, substance abuse, somatization disorder, hypochondriasis, or pain disorder), (2) a history of major depression or other anxiety-related disorder during the last 5 years, (3) the presence of mild cognitive impairment (MCI) according to the diagnostic criteria for amnestic MCI (Petersen et al., 2001), (4) the presence of dementia or some other brain organic syndrome according to the DSM-IV-TR, (5) the presence of severe physical illness, or (6) the presence of psychiatric comorbidity. The present retrospective study was approved by the Ethics Committee of the Jikei University School of Medicine. Written informed consent was obtained from the patients or their designated representatives.

Psychological assessment

The severity of the somatic symptoms was assessed using the Hamilton Anxiety Scales

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(HAMA) (Hamilton, 1959). HAMA can be used as a scale for rating the severity of anxiety-related disorders. HAMA consists of two subscores: psychic anxiety (HAMA-PSY) (ranging from 0 to 28 points), and somatic anxiety (HAMA-SOM) (ranging from 0 to 28 points). HAMA-PSY consists of the following items: anxious mood, tension, fears, insomnia, intellectual retardation, and behavior at interview. HAMA-SOM consists of the following items: muscular symptoms, sensory symptoms, cardiovascular symptoms, respiratory symptoms, gastrointestinal symptoms, genitourinary symptoms, and autonomic symptoms (ranging from 0 to 4 points). HAMA and its subscores are reliable and valid for anxiety-related disorders (Maier, Buller, Philipp & Heuser, 1988), and HAMA and HAMA-SOM have proven to be sensitive measures for evaluating the severity of SDs (Maier, Buller, Philipp & Heuser, 1988; van Riezen & Segal, 1988). Many previous studies have used HAMA to measure the severity of SDs (Volz, Möller, Reimann & Stoll, 2000; Volz, Murck, Kasper & Möller, 2002; Müller, Mannel, Murck, & Rahlfs, 2004), and we believe that HAMA is the most appropriate tool for measuring the severity of SDs.

Neuropsychological assessment

Mini-mental State Examination (MMSE): The MMSE is a well-known and widely used test for screening cognitive impairment. Possible scores range from 0 to 30. A score of 28 is the median for normal octogenarians with more than 12 years of education. Patients with a MMSE score <24 were regarded as having dementia and were excluded from the present study.

Frontal Assessment Battery (FAB): The FAB was recently introduced as a short screening test for exploring various functions of the frontal lobes and for evaluating executive functions (Dubois, Slachevsky, Litvan & Pillon, 2000). The Japanese FAB version consists of six subtests: (i) similarities (conceptualization); (ii) lexical fluency (mental flexibility); (iii) motor series (programing); (iv) conflicting instructions (sensitivity of interference); (v)

go/no go (inhibition control); and (vi) prehension behavior (environmental autonomy). Each subtest is rated from 0 to 3, with the total score ranging from 0 to 18. Japanese version of the Neurobehavioral Cognitive Examination (J-COGNISTAT): The J-COGNISTAT is a comprehensive cognitive test that consists of 10 subtests designed to convert raw scores for each subtest into age-matched standardized scores, which are distributed with a mean of 10 and a standard deviation of 1. The cutoff point for each standardized score is set at between 8 and 9. If a subject score is not more than 8, the score is considered to indicate an impaired level (Matsuda & Nakatani, 2004). The J-COGNISTAT can also be used as a screening tool for dementia that can be easily administered at the patient bedside. However, the J-COGNISTAT can be used to evaluate multiple cognitive status profiles, which is useful for identifying how a certain domain has decreased in comparison with other domains. The validity of each domain of the J-COGNISTAT has been well examined (Matsuda & Saito, 2009). More intricate neuropsychological testing can impose a burden on patients with late-life SDs. Thus, we used the J-COGNISTAT to evaluate each cognitive domain relatively easily.

Assessment of other factors

Some previous studies have reported an increased risk of cognitive impairment in benzodiazepine users (Stewart, 2005). Thus, whether benzodiazepine dosage confounded the effect on cognitive functions was examined. Antidepressants also influence cognitive functions (Barch, 2012). The benzodiazepine and antidepressant dosage was based on the equivalent conversion table for psychometric drugs (Inagaki & Ikeda, 1999). In addition, we also evaluated the correlations between cognitive functions and other factors (onset age and duration of illness). As described previously, some studies have shown age-associated differences in the prevalence of SDs.

Statistical analysis

SPSS 19.0J for Windows (SPSS Japan Inc., Tokyo, Japan) was used for all the statistical analyses. To analyze the correlation between clinical parameters (HAMA score, HAMA-PSY score, and HAMA-SOM score) and cognitive parameters (MMSE total, subtest scores, FAB total, subtest scores, and J-COGNISTAT subtest scores), we performed a partial correlation analysis. The analyses were adjusted according to patient age and duration of education because some neuropsychological tests are strongly influenced by aging and education level. As an exploratory study was intended, the *P*-values were not initially corrected for multiple tests so that the data trends would be apparent. However, the Bonferroni-corrected *P*-value requirements (MMSE subtest scores: $P = 0.05/11 \approx 0.005$, FAB subtest scores: $P = 0.05/6 \approx 0.008$, and J-COGNISTAT subtest scores: P = 0.05/10 = 0.005) were reported and the effects of the correlations were noted. We also used a partial correlation analysis adjusted according to age and education level to evaluate the correlations between cognitive functions and other factors (benzodiazepine dosage, antidepressant dosage, onset age and duration of illness).

RESULTS

Patient characteristics

The demographic variables of the 53 late-life SDs patients aged 60 years and older are summarized in Table 1 (Table 1).

Cognitive profiles according to J-COGNISTAT

Table 2 shows the cognitive profiles according to J-COGNISTAT. The mean J-COGNISTAT subtest score for attention was 6.2 (SD = 3.0), which was below the cut-off value (8 points). None of the other subtest scores were below the cut-off values (Table 2).

Correlations between cognitive functions and disease severity

The MMSE total score was not significantly correlated with disease severity (HAMA score and HAMA-SOM score). The MMSE subtest scores were also not significantly correlated with disease severity. The FAB total score was significantly correlated with disease severity (HAMA score: P = 0.002; and HAMA-SOM score: P = 0.02). The FAB subtest scores for similarities (HAMA score: P < 0.001; and HAMA-SOM score: P < 0.001) and motor series (HAMA score: P = 0.003) were also significantly correlated with severity (Table 3). The J-COGNISTAT subtest score for calculation was significantly correlated with disease severity (HAMA score: P = 0.001) (Table 4). Other FAB subtest scores, MMSE total and subtest scores, and J-COGNISTAT subtest scores were not significantly correlated with the HAMA score.

Correlations between cognitive functions and other factors

No significant correlation between cognitive function (FAB total score, FAB similarities, FAB motor series score, and J-COGNISTAT calculation score) and benzodiazepine dosage was seen among the patients with undifferentiated SD. The antidepressant dosage also showed no correlation with cognitive functions (FAB total score, FAB similarities, FAB motor series score, and J-COGNISTAT calculation score). These cognitive functions were not correlated with either onset age or the duration of illness.

DISCUSSION

Summary of findings

In the present study, we investigated the correlations between cognitive functions and symptomatic severities in patients with SDs who were over 60 years of age. We found a decrease in the 'attention' average score among the J-COGNISTAT subscales. The HAMA scores were negatively correlated with the FAB total score, the FAB subtest score

(similarities, motor series), and the calculation score among the J-COGNISTAT subscales. However, no other neuropsychological scores were significantly correlated with the HAMA scores. Therefore, in the present study, the symptomatic severities of late-life SDs were associated with executive function as assessed using the FAB and calculation skill as assessed using the J-COGNISTAT. Moreover, cognition and symptomatic severity in late-life SDs were not significantly influenced by the dosages of psychotropic agents (e.g., benzodiazepine and antidepressants) or other factors.

Comparison with previous studies

In previous studies investigating cognitive declines in patients with late-life anxiety disorders, significant reductions in episodic memory and attention function were reported (Beaudreau & O'Hara, 2008). In the present study, we also found a decrease in the attention score using the J-COGNISTAT subscales, but no reduction in episodic memory was observed. The reason for this difference between the two studies is thought to be that patients with dysfunctional episodic memory were excluded from our study, based on the presence of MCI or dementia. An attention decrement was confirmed in our patients, but the decrease was not correlated with disease severity. Several possibilities may explain this result. One possibility is that a deficit in attention may have existed in our patients prior to the somatic symptoms and may have triggered the somatic symptoms, rather than being a result of the somatic symptoms. Another possibility is that attention deficits in patients with late-life SDs may be a vicarious or compensative reaction of the awareness of bodily sensations as a defense mechanism (Lipowski, 1988).

Interpretation of results

Regarding the FAB subtest score, 'similarities' reflects executive functions that enable the establishment of an abstract link between items or adherence to concrete aspects of objects.

Furthermore, 'the motor series' measures the capacity to execute a sequence of actions successively in separate tasks, resembling the 'first-palm-edge' task in Luria's motor series. Therefore, we hypothesized that such disabilities of conceptualizing or executing performances in patients with late-life SDs might reflect a distortion of self-monitoring or self-correcting for physical symptoms, which might be linked to the aggravation of convinced ideations related to anxiety or dysphoria in SD patients (Nagata et al., 2009). In patients with late-life SDs, the loss of self-correction in executive functions might influence their ability to access corrective information necessary for the modification of their irrational beliefs (Kashyap, Kumar, Kandavel, & Reddy, 2012). The J-COGNISTAT score for calculation was negatively correlated with the severity of late-life SDs patients. A poorer calculation performance is caused by a dysfunction of working memory, since the calculation skill in the J-COGNISTAT requires the patient to perform single-step calculations where instructions can be repeated at the patient's request (Gupta & Kumar, 2009). The present study showed that the severity of late-life SDs was significantly correlated with executive functions and working memory. On the other hand, attention decline was not correlated with severity. This finding suggests that attention deficits in SD patients may be a trait marker of late-life SDs; thus, impairments in executive functions and working memory may be state markers of late-life SDs.

Implications for research

From the viewpoint of coping strategies, patients with SDs may adopt somatic complaints as a mode of coping with life¢ vicissitudes, psychological needs and conflicts, feelings of guilt and anger, and low self-esteem (Lipowski, 1988). In other words, poor coping strategies can lead to somatization. Hall et al. reported that coping strategies are associated with attention, working memory, and executive functions (Hall, Kuzminskyte, Pedersen, Ørnbøl & Fink, 2011). However, the present results partially differ from this previous

report. These results suggest that working memory and executive functions may contribute to coping strategies, rather than attention, in patients with late-life SDs. Further study involving a large number of patients and detailed neuropsychological test batteries is needed to clarify this hypothesis.

Implications for practice

The reason why the other FAB subtest scores were not correlated with disease severity was thought to be due to the ceiling effect of the FAB. Patients with MCI or dementia were excluded from our sample in the present study, and the FAB is somewhat limited at examining the details of cognition. This reasoning is also thought to be applicable to the J-COGNISTAT subtests.

As described previously, the HAMA score consists of the HAMA-SOM score and the HAMA-PSY score. The HAMA total score is often used to measure the severity of SDs (Volz, Möller, Reimann & Stoll, 2000; Volz, Murck, Kasper & Möller, 2002). Therefore, we mainly used the HAMA total score to examine the severity of the SDs. Additionally, we evaluated the HAMA-SOM score to ascertain whether it can be used as an indicator of the severity of SDs. As a result, the HAMA-SOM score almost resembled the HAMA total score. However, the HAMA total score and the HAMA-SOM score were somewhat different. The HAMA total score was correlated with the 'motor series' score among the FAB subtests and with the 'calculation' score among the J-COGNISTAT subtests. On the other hand, the correlation between the HAMA-SOM score and these subtests was not statistically significant, but an associative trend was seen (former, P = 0.01; latter, P = 0.005). Some possible reasons for this difference can be considered. First, the distribution of type-I errors should be examined. To clarify this problem, further study involving a large number of patients with late-life SDs is needed. However, the HAMA total score is generally used to measure the severity of SDs (Volz, Möller, Reimann & Stoll, 2000; Volz,

Murck, Kasper & Möller, 2002), and we believe that our results are valid.

Limitations

The present study had some limitations. First, the sample size was comparatively small. Thus, we defined a validly statistical value using the Bonferroni correction to examine the association between symptomatic severity and cognitive functions. Second, we did not use normal sample data and instead investigated the cognitive profiles of late-life SDs patients according to the only standardized cognitive scale available, the J-COGNISTAT subscales. Third, many other neuropsychological test batteries for evaluating executive functions exist, and these test batteries might have provided useful information. However, the FAB is one of the easiest tests to administer and can be completed at bedside without requiring any tools or instruments. J-COGNISTAT is also easy and can be used with less burden to the patients. We believe that the simplicity of these tests makes them valuable tools. Finally, the HAMA is not a specific scale for SDs. The use of more specific scale for SDs would be preferable, although a standardized specific scale is not available. Furthermore, in some previous studies, the HAMA was used to measure the severity of SDs. Thus, we believe that the use of HAMA is valid.

Conclusion

In conclusion, to elucidate the pathogenesis or to investigate risk factors for late-life SDs, we focused on the correlation between symptomatic severity and cognitive function. We found that the cognitive profiles that influenced the appearance of symptoms and symptomatic severity differed. Therefore, a subgroup of patients with a poor prognosis may exist among patients with late-life SDs based on differences in pathogenesis and the appearance of symptoms. The further development of treatment strategies targeting prognostic subgroups, rather than SD itself, is needed in the future.

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CONFLICT OF INTERESTS

The authors declare that they have no conflicts of interest.

DESCRIPTION OF AUTHORS' ROLES

Keisuke Inamura designed this study, examined the subjects, and wrote the manuscript. Norifumi Tsuno, Kenji Tagai, Tomoyuki Nagata and Shunichiro Shinagawa gave advice, including suggestions regarding the analysis method, and reviewed this manuscript. Kazuhiko Nakayama reviewed and commented on the final manuscript.

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Table 1. Subject characterist	haracteristics of patients with late-life somatoform disorders	
	n = 53	
	(mean ± SD)	
Sex (male/female)	9 / 44	
Age	71.7 ± 7.2	
Education (years)	12.1 ± 2.2	
Duration of illness (years)	6.7 ± 6.4	
onset age	64.7 ± 8.6	
HAMA total score	14.8 ± 7.2	
HAMA-SOM score	8.0 ± 4.1	
HAMA-PSY score	6.8 ± 4.0	
MMSE total score	27.6 ± 2.0	
FAB total score	16.0 ± 1.5	

HAMA (The Hamilton Anxiety Scale), HAMA-SOM (The Hamilton Anxiety Scale, somatic subscore), HAMA-PSY(The Hamilton Anxiety Scale, psychic subscore), MMSE (Mini-Mental State Examination), FAB (Frontal Assessment Battery)

	J-COGNISTAT subscores	
	$(\text{mean} \pm \text{SD})$	
orientation	9.6 ± 0.9	
attention	6.2 ± 3.0	
comprehension	8.5 ± 1.9	
repetition	9.9 ± 1.3	
naming	9.8 ± 0.6	
constructive ability	8.1 ± 1.5	
memory	9.6 ± 0.7	
calculation	8.9 ± 1.4	
similarities	10.1 ± 0.8	
judgement	10.7 ± 1.1	
	(average)	
GNISTAT (The Japanese vers	tion of the neurobehavioral cognitive examin	

* Attention score was blov	w the cutoff value	of J-COGNISTAT (8	3 points).
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Table 3. Partial correlations between	ble 3. Partial correlations between FAB scores and HAMA scores	
	HAMA-SOM	HAMA total
FAB total acore	-0.33*	-0.46*
SUBTEST		
Similarities	-0.53**	-0.55**
Lexical fluency	-0.05	-0.01
Motor series	-0.36	-0.46**
Conflicting instructions	-0.08	-0.13
Go / no go	0.13	0.26
Prehension behavior	/	/
* $p < 0.05$,**Bonfferoni-corected	p < 0.05/6 = 0.008	

	HAMA-SOM	HAMA total
orientation	0.05	0.05
attention	0.23	0.16
comprehension	-0.11	-0.03
repetition	-0.20	-0.22
naming	-0.24	-0.16
constructive ability	0.17	0.10
memory	-0.16	-0.15
calculation	-0.39	-0.46*
similarities	-0.22	-0.22
judgement	0.04	0.05