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Causal Relationship Between Behavioral and Psychological Symptoms of Dementia and Autonomic Nervous Activity: A Covariance Structure Analysis

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Abstract

The purpose of this research was to clarify the causal relationship between both behavioral and psychological symptoms of dementia (BPSD) and psychosocial factors (stress state). Cognitive function and BPSD were evaluated using the Revised Hasegawa's Dementia Scale and Neuropsychiatric Inventory, respectively, and stress was measured by the autonomic nervous activity and heart rate variability analysis. Using observations and latent variables, we constructed a causal hypothesis model that aggregated the causal relationship between cognitive function and stress state in one system. This model was analyzed using structural equation modeling. The results showed that cognitive function had a strong influence on autonomic nervous activity via BPSD; however, autonomic nervous activity had little influence on BPSD.

Keywords: Autonomic nervous activity • Dementia • Psychosocial factors • Stress

Abbreviations: BPSD, Behavioral and psychological symptoms of dementia; SEM, structural equation modeling; GFI, goodness-of-fit; AGFI, adjusted GFI; NFI, normed fit index; TFI, Tucker-Lewis index; CFI, comparative fit index; RMSEA, root mean square error of approximation; NPI, Neuropsychiatric Inventory; HDS-R, Revised Hasegawa's Dementia Scale; LF, low-frequency component; HF, high-frequency component; Ln, logarithmic value; AD, Alzheimer's disease.

Introduction

Behavioral and psychological symptoms of dementia (BPSD) is a concept proposed by the International Psychogeriatric Association [1] that encompasses aggression, restlessness, apathy, excitement, depression, hallucinations, delusions, anxiety, and depression, all frequently found in patients with dementia. BPSD is an important clinical condition that impairs patients' daily lives and associated with relative's care burden, early admission to a care facility, cognitive impairment, and so on [1]. BPSD is thought to appear due to the progression of cognitive dysfunction (memory, disorientation, etc.) associated with the underlying dementia, and psychological and social factors are strongly related [2]. In previous research, these psychological and social factors were regarded as stressors, and the relationship between BPSD and stress evaluated using salivary cortisol. As such, we would assume that BPSD is likely to manifest when stress matches the progression of cognitive dysfunction [2].

Under stress, sympathetic and parasympathetic nerve activity are overactive [3–5], which compromises homeostasis. Stress indicators typically used imply measuring cortisol levels in the blood and saliva. However, in recent years, the reliability and validity of stress assessments that measure autonomic nervous activity by heart rate variability analyses has been reported [3–5].

In our previous research, stress was evaluated by autonomic nervous activity (heart rate variability analysis), BPSD using the Neuropsychiatric Inventory (NPI), and their relevance examined. We found that stress and parasympathetic hyperactivity were related to BPSD, and a causal relationship wherein BPSD is favored when parasympathetic hyperactivity overlaps with the progression of cognitive dysfunction, was assumed [6,7]. Most diseases causing dementia are difficult to treat, and so is to improve cognitive dysfunction. However, if we assume that the cause of BPSD is the stress caused by the psychological and social factors of cognitive dysfunction, rehabilitation as an alternative complementary therapy for relieving stress may prevent, improve, or eliminate BPSD [1].

On the other hand, in recent years, the neural basis of BPSD has received attention. For example, it has been shown that attention and BPSD are related to behavioral disorders, aggression, and circadian rhythm disorder; further, both BPSD and attention are improved by the administration of risperidone, an atypical antipsychotic drug [8]. In another study, Bruen et al. [9] reported that the left frontal lobe, right frontal cortex, and left anterior lesion are involved in delusions. In addition, they asserted that BPSD in Alzheimer's disease (AD) refers to the association between personal memory, reality monitoring, reward processing receptor sensation, and neural degeneration of the areas that process subjective emotional experiences. These studies have suggested that cognitive dysfunction is a direct factor in BPSD and the neurological basis for cognitive dysfunction. In other words, BPSD is not simply caused by psychological and social stressors added to cognitive dysfunction; rather, cognitive dysfunction is a direct factor. If the cause of BPSD is cognitive dysfunction, and a neural basis is assumed for cognitive dysfunction, then root treatment should be prioritized.

In summary, BPSD is thought to occur by the stress caused by a combination of psychological and social factors and cognitive dysfunction, and two causal relationships are possible: 1) cognitive dysfunction directly causes BPSD, thus leading to stress, or 2) cognitive dysfunction directly causes stress, which leads to BPSD. Clarifying these causal relationships could facilitate more effective interventions for BPSD. Therefore, the purpose of this study was to clarify the possible two-way causal relationship between BPSD and stress.

Materials and Methods

Participants

Of the 42 elderly people diagnosed with dementia at a nursing home health facility in Gifu Prefecture, Japan, 35 individuals, without defects in cognitive function or BPSD, participated in the study (mean age = 85.4 ± 6.1 years; 9 men and 26 women). Inclusion criteria were a diagnosis of dementia and the ability to communicate verbally. Exclusion criteria were a history of cerebrovascular disease, depression, or heart disease; a diagnosis of Lewy body dementia or frontotemporal dementia; and communication difficulties.

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Methods

Cognitive function was evaluated using the Revised Hasegawa's Dementia Scale (HDS-R), BPSD with the NPI, and stress state with heart rate fluctuation analysis (TAS 9 VIEW; manufactured by YKC Co., Ltd.).

The HDS-R was created to screen elderly people with dementia and is designed to detect the presence or absence of general cognitive impairment by focusing on memory. It includes nine question items that can be implemented in about 5 to 10 minutes if the date of birth of the respondent can be confirmed [10].

The NPI is a method used by caregivers to assess mental symptoms. It consists of 10 items: delusions, hallucinations, excitement, depression, anxiety, euphoria, absence, depression, irritability, and abnormal behavior. The frequency of each was evaluated in four stages (1 to 4), and its severity in three (1 to 3). Higher scores indicate higher frequency and severity. The scores for each item are expressed by frequency × severity (1 to 12 points); therefore, total scores range from 1 to 120 [11,12].

The TAS 9 VIEW is an instrument used to evaluate autonomic nervous activity by measuring an acceleration pulse wave from the fingertip. Heart rate variability was measured at RR intervals, and the underlying specific frequency component determined by fast Fourier transform, low-frequency component (LF; 0.04–0.15 Hz), and high frequency component (HF; 0.16–0.40 Hz). Next, the LF and HF components can be analyzed [13]. In this study, we used LF and HF as parameters for autonomic nervous activity. For each parameter, a logarithmic value (Ln) was used. In other words, LnLF represents sympathetic activity and LnHF represents parasympathetic activity [14].

Measurements were conducted based on previous studies [6,7]. The evaluation was performed by two occupational therapists (18 and 4 years of experience, respectively). Both had NPI evaluation experience and received instructions on how to use the TAS 9 VIEW equipment. The measurements were repeated until they could be performed smoothly and effectively.

NPI seeks to establish presence or absence of BPSD in the past month; however, in this study, we sought to establish its current state. Therefore, the two occupational therapists provided joint evaluation scores for the NPI. The environmental conditions for autonomic nerve measurement were as follows: 1) an air-conditioned room (28 °C), 2) ample illumination (conforming to Japanese Industrial Standards), and 3) sound environment below the standard value (nursing home); additionally, the odor was controlled using the air circulation by the air conditioner so that the persons did not feel uncomfortable. The measurement conditions were as follows: 1) daytime (1 p.m.), 2) only tester and participant in the room, 3) the participant sat at rest with eyes closed, and 4) adaptation time (about 2 to 3 minutes) to get used to the examination equipment. A wave sensor was then attached to the participant's finger when they were in a relaxed state [11], and the measurement was performed for 2 min and 30 s. Although guidelines recommend a measurement time of 5 min [13], the measurement time used in this research (2 min and 30 s) was the shortest measurement time possible for satisfactory reliability, according to equipment manufacturers [6,7,14]. Measurement conditions were analogous for all participants.

Analysis

The following statistics were used for structural equation modeling (SEM): goodness-of-fit (GFI), adjusted GFI (AGFI), Bentler-Bonett normed fit index (NFI), Tucker-Lewis index (TFI), comparative fit index (CFI), and root mean square error of approximation (RMSEA). The causal hypothesis model used in this analysis is shown in Fig 1. We constructed a causal hypothesis model where the causal structure was integrated into one system and analyzed using SEM. IBM SPSS Amos 19.0 (SPSS; IBM, Armonk, NY, USA) was used for statistical analyses. Statistical significance was set at $P < 0.05$.

Ethics

We explained the purpose and method of this study to the patients and their families, and affirmed that 1) there were no negative consequences for refusing to participate, 2) participation could be terminated at any time, and 3) their personal information would be completely protected. Informed written consent was obtained from all participants. This research was approved by the Kansai University of Welfare Science Research Ethics Committee (no. 1604) and complied with the ethical standards of the Declaration of Helsinki.

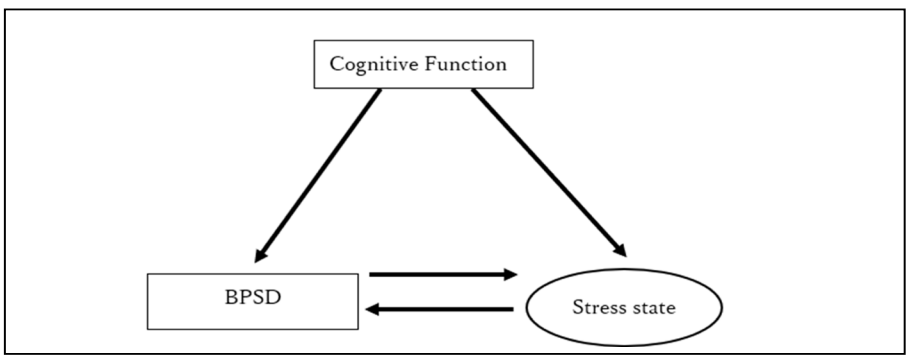
Results

The goodness-of-fit indices of the fruit model used in SEM analysis were confirmed to be within the acceptable range of fit, with $\chi 2$ values of 1.886

Table 1: Direct and indirect effects.

		Standardized coefficients
Direct effect	Cognitive function ⟶ BPSD	-0.44
	BPSD ⟶ stress state	-0.28
	Cognitive function ⟶ stress state	0.21
	Stress state ⟶ BPSD	0.29
Indirect effect	Cognitive function ⟶ BPSD ⟶ stress state	0.13
	Cognitive function ⟶ stress state ⟶ BPSD	0.06

BPSD: behavioral and psychological symptoms of dementia

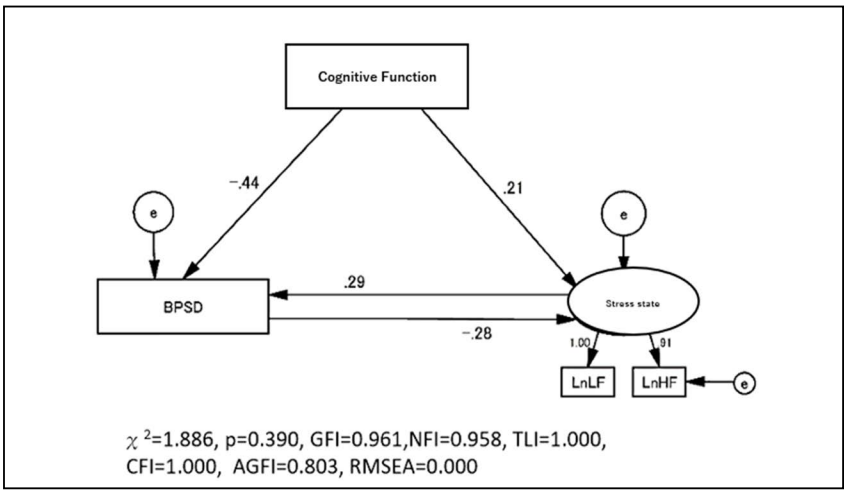


BPSD : Behavioral and psychological symptoms of dementia

: Observed variable

: Latent variable

Figure 1. Causal model.



BPSD：Behavioral and psychological symptoms of dementia

GFI: Goodness of Fit Index

AFGI: Adjusted GFI

NFI: Bentler-Bonett normed fit index

TFI: Tucker-Levis index

CFI: Comparative fit index

RMSEA: Root Mean Square Error of Approximation

：Observed variable

：Latent variable

Figure 2. Structural equation model results.

(p=0.390), GFI=0.961, AGFI=0.803, NFI=0.958, TLI=1.000, CFI=1.000, and RMSEA=0.000. Comparing the coefficients of the indirect effects, "cognitive function" had a strong influence on "BPSD" to act on "stress state," while in the direct effects, "stress state" was a factor that also influenced "BPSD" to a lesser extent.

The results of SEM analysis are shown in Fig 2. The fitness indicators were within the allowable ranges. The standardized coefficients showing the direct and indirect effects are shown in Table 1.

Discussion

In this study, a covariance structure analysis was used to analyze the bidirectional causal relationship assumed for BPSD and stress caused by cognitive dysfunction. The results showed that cognitive dysfunction is a direct cause of BPSD, and that stress is a reaction to BPSD. The cognitive dysfunction underlying BPSD is assumed to have a neural basis, and from the data, it may be interpreted that a neural-based disorder causes BPSD. Previous studies clarified the neural basis of BPSD. For example, one study shows that AD patients with delusions of object theft exhibited asymmetric enlargement of the anterior and inferior horns of the lateral ventricles, wherein the right side was significantly larger than that of healthy individuals [15]. In addition, brain imaging studies show that delusions in Alzheimer-type dementia are associated with decreased function in the right parietal lobe [16]. In Lewy-body dementia, the illusions associated with visual cognitive dysfunction are the consequence of a dysfunctional amygdala, which causes abnormal emotional reversion. As a result, patients may mistake close relatives for strangers or imposters, as in the condition called Capgra's syndrome [17]. Furthermore, in frontotemporal dementia, personality changes can be explained by frontal lobe disorders. Although the social and interpersonal problems characteristic of frontotemporal dementia are attributed to a disordered theory of mind, they may actually result from a disorder of the cranial nerve network that impairs the capacity for empathy and abstract thought [17,18]. Delusions of Lewy-body dementia and behavioral disorders related to frontotemporal dementia were specified in the diagnostic criteria [18]. These symptoms are characteristic of the disease and should be considered as core symptoms of a neural-based definition of dementia [18]. Insofar as BPSD is assumed to have a neural basis, dementia onset and BPSD expression should be regarded as a continuum.

Research into the mechanism behind the onset of dementia is progressing on a global scale, particularly through the efforts of the Dominantly Inherited Alzheimer Network [19] and the National Institute of Medical Research and Development [20]. However, currently patients must still rely on alternative complementary therapies. Concurrently, researchers are attempting to identify the neural basis of BPSD, which remains unclear. For example, even in AD-related delusions, the related brain regions differ across studies. Delusions are complex psychological processes supported by multiple brain functions, and it is difficult to explain everything with a single cognitive impairment [17]. Therefore, rehabilitation is a valuable alternative complementary therapy for BPSD. The interventions for this rehabilitation may involve different forms and steps. We revealed the direct effect of stress on BPSD, complementing prior studies. Existing research suggests exercise [21,22]. Circulatory and respiratory functions regulated by autonomic nerves are affected by physical training. In other words, physical training may alleviate stress by affecting the autonomic nerves that control circulation and respiratory function [23–26]. For example, parasympathetic activity significantly increases when 18 middle- and old-aged men and women performed aerobic activity for 30 minutes a day, 3 times a week, for a 12-week period [27]. In addition, Earnest et al. [28] in a 6-month-long exercise intervention with 373 postmenopausal women report significantly increased parasympathetic activity in those exercising. Another study reports elevation of the parasympathetic nervous system and depression of the sympathetic nervous system after outdoor walking in patients with dementia, and that this was effective in alleviating stress [29].

In summary, it may be useful to introduce physical activities as an intervention to relieve stress in patients with BPSD. Previous research focused on physical activities such as exercise and walking to relieve stress; however, it is necessary to demonstrate whether these activities can relieve stress and suppress BPSD in separate intervention studies.

Limitations

In this study, participants were selected under exclusive conditions and diagnosed as having AD. Although objective findings such as diagnostic imaging are necessary to confirm AD, a limitation of this study is that we did not perform diagnostic imaging. In addition, data should be collected from patients at other institutions to increase the generalizability of the current results and improve the accuracy of the covariance structural analysis. Lastly, to demonstrate whether physical activities can suppress BPSD, a controlled intervention study is warranted.

Conclusion

In this study, a covariance structure analysis was conducted to clarify the bidirectional causal relationship between BPSD and stress caused by cognitive dysfunction. Our results show that while cognitive impairment strongly affects BPSD and stress, it turns out that stress does slightly affect BPSD. In the current situation, where the neural basis of all BPSD remains unclear, there is a need for exploring the feasibility and effectiveness of rehabilitation as an alternative and complementary therapy to suppress BPSD.

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References

1. International Psychogeriatric Association. "IPA Complete Guides to Behavioral and Psychological Symptoms of Dementia (BPSD)". (2019).
2. *Dodo N. "Preliminary examinatio*n on psychoimmunological index for patients with Alzheimer's dementia (AD)". *J Jpn Soc Dement Care* 9(2010): 83-87.
3. Takai N, Yamaguchi M, Aragaki T, Eto K, Uchihashi K, et al. "Effect of psychological stress on the salivary cortisol and amylase levels in healthy young adults". *Arch Oral Biol* 49(2004): 963-968.
4. Yamaguchi M, Kanemori T, Kanemaru M, Takai N, Mizuno Y, et al. "Performance evaluation of salivary amylase activity monitor". *Biosens Bioelectron* 20(2004): 491-497.
5. Fries E, Dettenborn L, Kirschbaum C. "The cortisol awakening response (CAR): facts and future directions". *Int J Psychophysiol* 72(2009): 67-73.
6. Kimura D, Notoya M, Imai A, Ohtoshi T. "The relationship between behavioral and psychological symptoms of dementia (BPSD) and the autonomic nervous system in dementia patients". *Jpn Occupat Ther Res* 39(2018): 377-384.
7. Kimura D, Nakatani K, Notoya M, Imai A, Ohtoshi T. "The influence of behavioral and psychological symptoms of dementia on the autonomic nervous system". *World* 7(2017): 383-390.
8. Teng EL, Hasegawa K, Homma A, Imai Y, Larson E, et al. "The Cognitive Abilities Screening Instrument (CASI): a practical test for cross-cultural epidemiological studies of dementia". *Int Psychogeriatr* 6(1994): 45-58.
9. Bruen PD, McGeown WJ, Shanks MF, Venneri A. "Neuroanatomical correlates of neuropsychiatric symptoms in Alzheimer's disease". *Brain* 131(2008): 2455-2463.
10. Kato S. "Development of the revised version of Hasegawa's Dementia Scale (HDS-R)". *Jpn Geriatr Psychiatr Med* 2(1991): 1339-1347.
11. Cummings JL, Mega M, Gray K, Thompson RS, Carusi DA, et al. "The Neuropsychiatric Inventory: comprehensive assessment of psychopathology in dementia". *Neurology* 44(1994): 2308.
12. Hirono N, Mori E, Ikejiri Y, Imamura T, Shimomura T, et al. "Japanese version of the Neuropsychiatric Inventory—a scoring system for neuropsychiatric disturbance in dementia patients". *Brain Nerve* 49(1997): 266-271.
13. Malik M, Bigger JT, Camm AJ, Kleiger RE, Malliani A, et al. "Heart rate variability: standards of measurement, physiological interpretation, and clinical use". *Eur Heart J* 17(1996): 354-381.
14. Igawa J, Shiwa S, Nakanishi D, Kurumaji M, Kikumoto O, et al. "On the autonomic function evaluation of anxiety using heart rate variability. Japanese Society of Biofeedback Research". *Int Arch Occupat Environ Health* 83(2010): 521-529.
15. Geroldi C, Bresciani L, Zanetti O, Frisoni G. "Regional brain atrophy in patients with mild Alzheimer's disease and delusions". *Int Psychogeriatr* 14(2002): 365-378.
16. Fukuhara R, Ikeda M, Nebu A, Kikuchi T, Maki N, et al. "Alteration of rCBF in Alzheimer's disease patients with delusions of theft". Neuroreport 12(2001): 2473-2476.
17. Snowden JS, Gibbons ZC, Blackshaw A, Doubleday E, Thompson J, et al. "Social cognition in frontotemporal dementia and Huntington's disease". *Nezeropsychologia* 41(2003): 688-701.
18. Hashimoto M. "Association of mental symptoms and cognitive impairment in dementia". *Jpn J Geriatr Psychiatry* 22(2011): 1269-1276.
19. Bateman RJ, Xiong C, Benzinger TL, Fagan AM, Goate A, et al. "Clinical and biomarker changes in dominantly inherited Alzheimer's disease". *New Eng J Med* 367(2012): 795-804.
20. Japan Agency for Medical Research and Development." About AMED". (2019).
21. Pollock ML, Miller HS, Linnerud AC, Cooper KH. "Frequency of training as a determinant for improvement in cardiovascular function and body composition of middle aged men". *Arch Phys Med Rehabil* 56(1975): 141-145.
22. Carte H, Jones AM, Doust JH. "Effect of 6 weeks of endurance training on the lactate minimum speed". *J Sport Sci* 17(1999): 957-967.
23. Yamaji K. "Saidaisannsosessyuryou no kagaku. Kyourinsyoin". (1992):192-225.
24. Watanabe T. "Ikiteirukoto no seirigaku. Kyourinsyoin". (1988):136-334.
25. McArdle WD, Katch FI, Katch VL. "Exercise physiology". 4th ed. *Baltimore: Williams & Wilkins*; (1996):541-781.
26. Moritani, T. "Exercise and physiological functions adaptation and reversibility". (1999):123-222.
27. Amano M, Kanda T, Ue H, Moritani T. "Exercise training and autonomic nervous system activity in obese individuals: exercise training and autonomic nervous system activity in obese individuals". *Med Sci Sports Exerc* 33(2001): 1287-1291.
28. Earnest CP, Lavie CJ, Blair SN, Church TS. "Heartrate variability characteristics in sedentary postmenopausal women following six months of exercise training: the DREW study". *PLoS ONE* 3(2009): 2288.
29. Eguchi K, Koura S, Ogawa N, Eguchi N. "Effects on the autonomic nervous system of outdoor and indoor walks as an activity for patients with moderate Alzheimer's disease". *J Jpn Assoc Occupat Ther* 15(2016): 448-456.

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