Leisure-Time Physical Inactivity Associated with Vascular Depression or Apathy in Community-Dwelling Elderly Subjects: The Sefuri Study

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Background: Although physical inactivity is a major public health problem, the causative factors for physical inactivity per se are poorly understood. To address this issue, we investigated the relationship between deep white matter lesions (DWMLs) on magnetic resonance imaging, apathy, and physical activities using structural equation modeling (SEM). *Methods:* We examined 317 community-dwelling elderly subjects (137 men and 180 women with a mean age of 64.5 years) without dementia or clinically apparent depression. Physical activity was assessed with a questionnaire consisting of 3 components (leisure-time, work, and sport activities). *Results:* The mean score from the apathy scale (a visual analogue version of Starkstein's apathy scale) of the Grades 2-3 DWML group was 420 (95% confidence interval [CI] 379-461), which was lower (more apathetic) than the Grade 0 DWML group score of 478 (95% CI 463-492) after adjustment for education as a covariate. SEM showed that the direct paths from DWMLs or education to apathy were significant, and the direct path from apathy to leisure-time activity was highly significant ($\beta = .25$, $P < .001$). The degree of apathetic behavior was negatively associated with sport activity in female subjects and positively associated with TV watching in male subjects. *Conclusions:* The results of the study show that DWMLs are one of the major factors that cause apathetic behavior and that apathy has significant negative effects on leisure-time physical activity in community-dwelling elderly subjects. Even a minor level of apathy without major depression would have a significant impact on activities of daily living and quality of life. **Key Words:** Physical activity—apathy—vascular depression—vascular cognitive impairment—white matter lesions—magnetic resonance imaging—small vessel disease—silent stroke.

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Introduction

Physical inactivity causes 6%-10% of the major noncommunicable diseases such as obesity, coronary heart disease, diabetes, cancer, and Alzheimer's disease.[1-3] An earlier study on the risk factors of vascular and Alzheimer-type dementia (the Hisayama study) and a recent review have shown that physical activity is a robust preventive factor for Alzheimer's disease.[4,5] Physical inactivity may exert adverse effects on vascular risk factors and may cause a lower integrity of the cerebral white matter.[6] Physical activity is obviously important in common diseases; nonetheless the causative factors for physical inactivity per se are poorly understood.

Several studies, including ours, have reported that white matter lesions (WMLs) contribute to depressive symptoms or apathy in healthy elderly subjects,[7-13] supporting the concept of vascular depression.[14] Of note, Brookes et al. found that a major factor for depression in patients with small vessel disease was WMLs, not physical disability.[13] Older persons with depressive symptoms and apathy were at risk of subsequent decline in physical performance or disability in activities of daily living.[15-19] However, no study so far has examined the relationship between neuropsychiatric syndrome, deep white matter lesions (DWMLs), and physical activities. Recently, a systematic review found that key barriers to participating physical activities included lack of social support, previous sedentary habits, competing priorities, accessibility, and apathy.[20] These findings lead us to the hypothesis that DWMLs cause apathy, which may subsequently impair physical activities. To address this issue, we examined a structural equation modeling (SEM) of DWMLs, apathy, and physical activities.

Subjects and Methods

Study Design and Participants

This is a cross-sectional observational investigation of SEM in community-dwelling people. Between 2010 and 2014, we examined 350 volunteers aged 40-89 years who were living in the rural community of Sefuri village (Saga, Japan) with a total population of approximately 1100 aged 40 years or older. They were independent in their daily life without apparent dementia. A total of 32 subjects were excluded because of psychiatric disorders, including depression (n = 5); claustrophobia or contraindications to magnetic resonance imaging (MRI) (n = 5); a history of stroke (n = 11); brain tumor (n = 1); chronic subdural hematoma (n = 2); malignant neoplasm (n = 1); a history of head trauma (n = 4); chronic renal failure (n = 2); and insufficient clinical information (n = 1). One subject with excessive alcohol intake (199 units per week) was also excluded from the present study. Finally, we analyzed 317 subjects in the present study. The National Hospital Organization Hizen Psychiatric Center Institutional Review Board approved the study (approval number: 24-4), and written informed consent was obtained from the participants.

The participants underwent a structured clinical interview, biochemistry tests, and an electrocardiogram. Vascular risk factors were defined as previously described.[21] Briefly, arterial hypertension was considered present if the subject had a history of repeated blood pressure recordings above 140/90 mmHg or the subject was being treated for hypertension. Diabetes mellitus was characterized by fasting plasma glucose greater than 7.77 mmol/L and/or HbA1c greater than 6.5% or a previous diagnosis of diabetes mellitus. Metabolic syndrome was defined according to the proposed criterion for metabolic syndrome in Japanese.[22] We defined alcohol habit as consuming 4 drinks or more (1 drink as 10 g of ethanol) per week. Smoking was defined as present if the subject smoked at least an average of 10 cigarettes per day.

Assessment of MRI Findings

Imaging was performed on a 1.5T MRI scanner (Achieva, Philips, The Netherlands) using the T1- and T2-weighted, fluid-attenuated inversion recovery, and T2*-weighted images. The definitions and imaging methods were basically in line with the neuroimaging standards for research into small vessel disease.[23] The WMLs were defined as isointense with normal brain parenchyma on T1-weighted images, and high signal intensity areas on T2-weighted images. We used the validated rating scale of DWMLs by Fazekas et al.: Grade 0, absent; Grade 1, punctate foci; Grade 2, beginning confluence of foci; and Grade 3, large confluent areas.[24] For periventricular hyperintensities (PVHs), we determined the presence and severity (Grade 0, absent; Grade 1, pencil thin; and Grade 2, smooth halo lining) using fluid-attenuated inversion recovery (FLAIR) images. Two authors (H.Y. and A.U.), who were blinded to all clinical data, independently reviewed all scans.

Physical Activity

Physical activity was assessed with a questionnaire modified from the Baecke questionnaire on habitual physical activity.[25] The questionnaire consisted of 3 components: leisure-time, work, and sport activities (Table 1). Items concerning leisure-time and work activities were coded on 5-point scales. Leisure-time index was assessed through 5 questions on comparison with others, sweat, sport, walking, and television (TV) viewing. Because the association between TV score and total score for leisure activities was relatively weak ($r = .34$), this question was used as a separate item. Higher TV scores indicated higher leisure activities (i.e., less TV viewing). Work index was assessed through 4 questions on standing, walking, heavy loads, and sweat after excluding the 3 original items (sitting, fatigue, and comparison with others) because of the relatively weak associations ($r < .6$) of these questions with total score. Sport index was expressed as reported hours