Table 1
FDG activations and deactivations during treadmill walking in the low step-length variability group.

(a) FDG activation during treadmill walking in the low step-length variability group (vs. resting condition)

Cerebral hemispheres	BA	Cluster	Z	T	p	x	y	z
Left cerebellum, anterior lobe, culmen		5196	6.57	12.26	<0.001	−20	−52	−16
Right cerebellum, anterior lobe, culmen			6.46	11.75	<0.001	12	−46	−16
Right cerebellum, posterior lobe, inferior semi-lunar lobule			5.83	9.4	<0.001	4	−68	−38
Right cerebrum, frontal lobe, precentral gyrus		936	5.44	8.22	0.001	10	−30	66
Left cerebrum, parietal lobe, postcentral gyrus	3		4.84	6.69	0.014	−10	−32	66
Right cerebrum, occipital lobe, inferior occipital gyrus	19	39	5.17	7.48	0.004	56	−72	−2
Right cerebellum, posterior lobe		57	4.89	6.8	0.011	20	−50	−58
Left cerebrum, occipital lobe, superior occipital gyrus, cuneus	17	130	4.82	6.63	0.015	−14	−78	12
Right cerebrum, occipital lobe, cuneus	18	147	4.68	6.31	0.027	8	−84	16
Left cerebellum, posterior lobe		4	4.64	6.24	0.03	−24	−84	−46
Left cerebellum, posterior lobe		23	4.63	6.21	0.032	−20	−52	−56
Right cerebrum, occipital lobe, middle or lateral occipital gyrus	19	1	4.54	6.02	0.045	28	−86	38

(b) FDG deactivation during treadmill walking in the low step-length variability group (vs. resting condition)

Cerebral hemispheres	BA	Cluster	Z	T	p	x	y	z
Right cerebrum, frontal lobe, genu of the corpus callosum		5	4.82	6.64	0.015	12	40	0

(Table 3, Fig. 1H) showed relative deactivation in the middle and superior temporal gyrus white matter ($P = 0.03$) and hippocampus ($P = 0.03$) during treadmill walking compared with resting than did the LSV group (Table 3, Fig. 1G). There were no significant differences in occipital lobe, cerebellum, frontal lobe, posterior cingulate cortex, and pons between groups.

4. Discussion

This study examined changes in whole brain glucose metabolism using FDG-PET during rest and unaccustomed treadmill walking in healthy elderly females, classified as either low or high step-length variability walkers. The main findings of the study were that females with high step-length variability showed relative deactivations in the supplementary motor areas and dorsolateral prefrontal cortex compared to rest and that females with low step-length variability exhibited greater relative activations in the primary motor area during treadmill walking compared to the HSV group. The HSV group showed greater relative deactivations in the temporal lobe, especially in the hippocampus, during treadmill walking compared with the LSV group.

Hanakawa [23] proposed a hypothesis regarding the neural mechanisms that control human bipedal gait. This author postulated that multiple channels from the basal ganglia–thalamocortical system and basal ganglia–brainstem system are involved in the regulation of the central pattern generator (CPG) in the spinal cord (Fig. 2). In the present study, the most prominent relative activations during treadmill walking were found in the primary sensorimotor areas, occipital lobe, and cerebellar areas for both groups. The primary motor area projects to the spinal cord through the corticospinal tract, and it is believed that the primary motor area is involved in the precise control of limb movement during walking. The coordination of limb and trunk movements to adjust for a shift in the center of gravity associated with locomotion may be one of the primary functions of the cerebellum in gait control. Previous neuroimaging experiments have shown that the cerebellar vermis and the anteromedial part of the cerebellar hemispheres are bilaterally activated during walking in healthy individuals [9,11,12]. The cerebellum is able to make immediate alterations in ongoing movement patterns [24]. It functions as a real-time sensory processing device and modulates motor responses in a reactive or feedback manner based on sensory perturbations [25].

Our findings also suggest that the cerebellum plays an important role in gait adaptation to unfamiliar environments, such as walking on a treadmill. The occipital lobe, including the

Table 2
FDG activations and deactivations during treadmill walking in the high step-length variability group.

(a) FDG activation during treadmill walking in the high step-length variability group (vs. resting condition)

Cerebral hemispheres	BA	Cluster	Z	T	p	x	y	z
Right cerebellum, anterior lobe, culmen		3715	6.54	12.12	<0.001	0	−50	−18
Right cerebrum, parietal lobe, postcentral gyrus	6	1878	6.37	11.38	<0.001	8	−32	72
Left cerebrum, parietal lobe, postcentral gyrus	3		5.75	9.16	<0.001	−10	−34	72
Left cerebrum, parietal lobe, postcentral gyrus white matter			5.4	8.09	0.001	−14	−28	54
Right cerebrum, occipital lobe, cuneus		1402	5.52	8.46	0.001	2	−84	18
Left cerebrum, occipital lobe, cuneus			5.47	8.29	0.001	−6	−82	14
Right cerebrum, occipital lobe, middle or lateral occipital gyrus		60	5.06	7.2	0.005	52	−78	4
Left cerebellum, posterior lobe		40	4.74	6.45	0.017	−22	−46	−52
Right cerebellum, posterior lobe		7	4.67	6.3	0.022	36	−84	−40
Right cerebrum, occipital lobe, middle or lateral occipital gyrus	17	3	4.52	5.99	0.039	26	−100	−12

(b) FDG deactivation during treadmill walking in the high step-length variability group (vs. resting condition)

Cerebral hemispheres	BA	Cluster	Z	T	p	x	y	z
Left cerebrum, frontal lobe, superior frontal gyrus		5131	6.31	11.14	<0.001	−18	46	40
Right cerebrum, frontal lobe, superior frontal gyrus white matter			5.74	9.13	<0.001	10	60	6
Right cerebrum, frontal lobe, superior frontal gyrus	8		5.7	8.98	<0.001	12	54	40
Left cerebrum, temporal lobe, inferior temporal gyrus		397	5.62	8.74	<0.001	−52	−44	−14
Right cerebrum, frontal lobe, middle frontal gyrus	6	113	5.38	8.04	0.001	30	22	58

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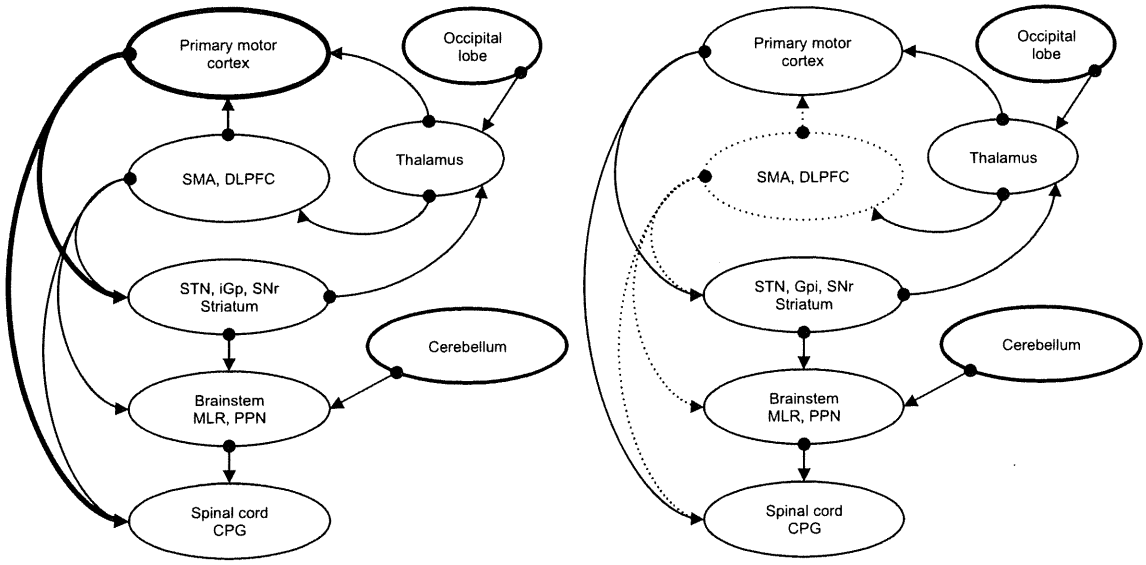

Fig. 2. Differences in neural mechanisms controlling treadmill walking in LSV compared to HSV individuals. Multiple channels from the 'basal ganglia–thalamo-cortical system' and 'basal ganglia–brainstem system' are both involved in regulating the central pattern generator (CPG) in the spinal cord. The primary motor cortex and non-primary motor areas such as supplementary motor areas constitute multiple parallel circuits with the basal ganglia counterparts. (a) Left panel displays our hypothesized neural network for the LSV group. The projections from M1 increased during walking to adapt to the unaccustomed environment (treadmill walking). (b) Right panel displays our hypothesized neural network for the HSV group. The HSV group deactivated FDG uptakes in SMA during treadmill walking and the deactivations may lead to dysfunction of 'basal ganglia–thalamo-cortical system' and 'basal ganglia–brainstem system'. *Abbreviations*: STN, subthalamic nucleus; iGP, internal segment of globus pallidus; SNr, substantia nigra pars reticulata; MLR, midbrain locomotor region; PPN, pedunculopontine nucleus.

cuneus (BA 17) and precuneus (BA 7/31), is believed to play a role in visuomotor coordination. The areas which showed relative activation were compatible with those reported in a previous activation study using FDG–PET [10]. In addition, online visual feedback was the requisite for locomotor adaptation [26] and was thought to override internal model predictions of control during locomotion [27]. Our study further supports the hypothesis that locomotor adaptation requires neuronal activation in the region related to visuomotor coordination.

In the HSV group, relative deactivations in FDG uptake were observed over a broad area of the prefrontal cortex, including the supplementary motor area and the dorsolateral prefrontal cortex. Cortical locomotor commands originating from the premotor and supplementary motor cortices are conveyed to the brainstem locomotor centers via the basal ganglia. The structure of the dorsolateral prefrontal cortex is important for selecting and planning voluntary movements [28] or simulating motor actions [29]. The relative deactivation of the supplementary motor area and dorsolateral prefrontal cortex may be associated with the finding that the participants in the HSV group might have found it difficult to adapt to an unfamiliar environment, i.e., treadmill walking.

Detailed group comparison revealed that the LSV group had a more prominent relative activation in the primary sensorimotor area compared to the HSV group and that the HSV group exhibited relative deactivation in the hippocampus compared to the LSV group during treadmill walking. The relative activation of the primary motor area may improve projection to the basal ganglia and to the CPG in the spinal cord, thus facilitating the strengthening of the basal ganglia–thalamocortical system during walking (Fig. 2). Regarding relative deactivation in the hippocampus, Zimmerman et al. (2009) found that increased variability in step length was associated with poorer hippocampal metabolism in elderly individuals. The authors suggested

Table 3
A region of interest analysis based on the standardized uptake value as the relative difference in gait-induced glucose uptake changes between groups.

	LSV group Mean (SD)	HSV group Mean (SD)	*p* value
Walk>Rest			
Primary sensorimotor area (BA 3, 4)	13.56 (3.01)	10.93 (2.16)	0.02
Occipital lobe (BA 17, 18, 19)	11.42 (4.29)	9.25 (3.55)	0.19
Cerebellum (vermis, anterior and posterior lobe)	17.18 (4.85)	17.36 (4.07)	0.92
Rest>Walk			
Orbitofrontal cortex (BA 11)	3.85 (3.18)	3.67 (2.94)	0.89
Superior frontal gyrus (BA 10)	4.16 (2.54)	4.76 (2.83)	0.59
Dorsolateral prefrontal cortex (BA 9, 46)	3.16 (2.09)	4.45 (2.25)	0.16
Supplementary motor area (BA 6, 8)	3.79 (1.74)	4.12 (1.83)	0.65
Middle and superior temporal gyrus white matter	1.85 (1.45)	3.07 (1.15)	0.03
Posterior cingulate cortex (BA 31)	3.01 (2.16)	3.67 (3.58)	0.59
Pons	2.40 (1.89)	1.84 (0.94)	0.37
Hippocampus	1.24 (1.31)	2.44 (1.29)	0.03

LSV: high step-length variability; HSV: low step-length variability.

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that the hippocampus plays an important role in the timing or rhythmicity of locomotion, which may be compromised in elderly adults [30]. Additionally, PET study showed that imagined walking with obstacles was associated with increased prefrontal and parahippocampal activation, suggesting that higher brain centers become progressively engaged when the locomotor task demands increased cognitive and sensory information processing [31]. Beauchet et al. (2003) reported that stride-to-stride variability increased significantly in older subjects with the interfering task of counting, although there was no significant change in young subjects. The authors suggested the involvement of higher cortical regions for the motor control of gait under a dual-task in older adults [32]. Our findings therefore support and extend previous research via the identification of an association between FDG–PET activation/deactivation and gait *variability* in an unfamiliar environment in elderly adults. Walking task used a treadmill, as a stimulator to increase cognitive demand may be beneficial tool for identifying the involvement of cortical regulation in gait of the older adults.

Limitations of our study were that the sample was drawn from a larger study of community-dwelling adults over the age of 75 years, and we were not able to examine the relationships between brain activity and cognitive functions across the entire adult lifespan.

In conclusion, FDG PET revealed that the most prominent relative activations during treadmill walking were the primary sensorimotor areas, occipital lobe, and cerebellar areas. The high step-length variability group exhibited a lesser relative activation in the primary sensorimotor area and a greater relative deactivation in the white matter of the middle and superior temporal gyrus and hippocampus during treadmill walking than the low step-length variability group. These results suggested the involvement of cortical regulation in gait adaptation of the older adults. Additional studies are necessary to examine the longitudinal sequence and relationships of gait, cognitive status, and presynaptic functional changes that emerge across the spectrum from normal aging to advanced functional decline.

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Conflict of interest statement

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References

[1] Hausdorff JM, Edelberg HK, Mitchell SL, Goldberger AL, Wei JY. Increased gait unsteadiness in community-dwelling elderly fallers. Archives of Physical Medicine and Rehabilitation 1997;78:278–83.
[2] Maki BE. Gait changes in older adults: predictors of falls or indicators of fear. Journal of the American Geriatrics Society 1997;45:313–20.
[3] Hausdorff JM, Nelson ME, Kaliton D, Layne JE, Bernstein MJ, Nuernberger A, et al. Etiology and modification of gait instability in older adults: a randomized controlled trial of exercise. Journal of Applied Physiology 2001;90:2117–29.
[4] Schaafsma JD, Giladi N, Balash Y, Bartels AL, Gurevich T, Hausdorff JM. Gait dynamics in Parkinson's disease: relationship to Parkinsonian features, falls and response to levodopa. Journal of the Neurological Sciences 2003;212:47–53.
[5] Sheridan PL, Solomont J, Kowall N, Hausdorff JM. Influence of executive function on locomotor function: divided attention increases gait variability in Alzheimer's disease. Journal of the American Geriatrics Society 2003;51:1633–7.
[6] Alexander NB. Postural control in older adults. Journal of the American Geriatrics Society 1994;42:93–108.
[7] Schultz AB. Mobility impairment in the elderly: challenges for biomechanics research. Journal of Biomechanics 1992;25:519–28.
[8] Ishii K, Senda M, Toyama H, Oda K, Ishii S, Ishiwata K, et al. Brain function associated with bipedal gait: a PET study. Journal of Cerebral Blood Flow and Metabolism Official Journal of the International Society of Cerebral Blood Flow and Metabolism 1993;13:S521.
[9] Mishina M, Senda M, Ishii K, Ohyama M, Kitamura S, Katayama Y. Cerebellar activation during ataxic gait in olivopontocerebellar atrophy: a PET study. Acta Neurologica Scandinavica 1999;100:369–76.
[10] la Fougere C, Zwergal A, Rominger A, Forster S, Fesl G, Dieterich M, et al. Real versus imagined locomotion: a [18F]-FDG PET-fMRI comparison. Neuroimage 2010;50:1589–98.
[11] Fukuyama H, Ouchi Y, Matsuzaki S, Nagahama Y, Yamauchi H, Ogawa M, et al. Brain functional activity during gait in normal subjects: a SPECT study. Neuroscience Letters 1997;228:183–6.
[12] Hanakawa T, Katsumi Y, Fukuyama H, Honda M, Hayashi T, Kimura J, et al. Mechanisms underlying gait disturbance in Parkinson's disease: a single photon emission computed tomography study. Brain 1999;122(Pt 7):1271–82.
[13] Iseki K, Hanakawa T, Hashikawa K, Tomimoto H, Nankaku M, Yamauchi H, et al. Gait disturbance associated with white matter changes: a gait analysis and blood flow study. Neuroimage 2010;49:1659–66.
[14] Matsas A, Taylor N, McBurney H. Knee joint kinematics from familiarised treadmill walking can be generalised to overground walking in young unimpaired subjects. Gait and Posture 2000;11:46–53.
[15] Savelberg HH, Vorstenbosch MA, Kamman EH, van de Weijer JG, Schambardt HC. Intra-stride belt-speed variation affects treadmill locomotion. Gait and Posture 1998;7:26–34.
[16] van Ingen Schenau GJ. Some fundamental aspects of the biomechanics of overground versus treadmill locomotion. Medicine and Science in Sports and Exercise 1980;12:257–61.
[17] Taylor NF, Evans OM, Goldie PA. Angular movements of the lumbar spine and pelvis can be reliably measured after 4 minutes of treadmill walking. Clinical Biomechanics (Bristol Avon) 1996;11:484–6.
[18] Wass E, Taylor NF, Matsas A. Familiarisation to treadmill walking in unimpaired older people. Gait and Posture 2005;21:72–9.
[19] Friston KJ, Ashburner J, Frith CD, Poline J-B, Heather JD, Frackowiak RSJ. Spatial registration and normalization of images. Human Brain Mapping 1995;3:165–89.
[20] Genovese CR, Lazar NA, Nichols T. Thresholding of statistical maps in functional neuroimaging using the false discovery rate. Neuroimage 2002;15:870–8.
[21] Sadato N, Tsuchida T, Nakaumra S, Waki A, Uematsu H, Takahashi N, et al. Non-invasive estimation of the net influx constant using the standardized uptake value for quantification of FDG uptake of tumours. European Journal of Nuclear Medicine 1998;25:559–64.
[22] Oishi K, Faria A, van Zijl PC, Mori S. MRI atlas of human white matter. Burlington: Elsevier; 2011.
[23] Hanakawa T. Neuroimaging of standing and walking: special emphasis on Parkinsonian gait. Parkinsonism and Related Disorders 2006;12:S70–5.
[24] Shimansky Y, Wang JJ, Bauer RA, Bracha V, Bloedel JR. On-line compensation for perturbations of a reaching movement is cerebellar dependent: support for the task dependency hypothesis. Experimental Brain Research Experimentelle Hirnforschung Experimentation Cerebrale 2004;155:156–72.
[25] Bower JM. Control of sensory data acquisition. International Review of Neurobiology 1997;41:489–513.
[26] Marigold DS, Patla AE. Visual information from the lower visual field is important for walking across multi-surface terrain. Experimental Brain Research Experimentelle Hirnforschung Experimentation Cerebrale 2008;188:23–31.
[27] Torres-Oviedo G, Bastian AJ. Seeing is believing: effects of visual contextual cues on learning and transfer of locomotor adaptation. The Journal of Neuroscience The Official Journal of the Society for Neuroscience 2010;30:17015–22.
[28] Frith CD, Friston K, Liddle PF, Frackowiak RS. Willed action and the prefrontal cortex in man: a study with PET. Proceedings Biological Sciences/The Royal Society 1991;244:241–6.
[29] Decety J, Perani D, Jeannerod M, Bettinardi V, Tadary B, Woods R, et al. Mapping motor representations with positron emission tomography. Nature 1994;371:600–2.
[30] Zimmerman ME, Lipton RB, Pan JW, Hetherington HP, Verghese J. MRI- and MRS-derived hippocampal correlates of quantitative locomotor function in older adults. Brain Research 2009;1291:73–81.
[31] Malouin F, Richards CL, Jackson PL, Dumas F, Doyon J. Brain activations during motor imagery of locomotor-related tasks: a PET study. Human Brain Mapping 2003;19:47–62.
[32] Beauchet O, Kressig RW, Najafi B, Aminian K, Dubost V, Mourey F. Age-related decline of gait control under a dual-task condition. Journal of the American Geriatrics Society 2003;51:1187–8.

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Original Study

Combined Prevalence of Frailty and Mild Cognitive Impairment in a Population of Elderly Japanese People

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A B S T R A C T

Objective: Preventive strategies for frailty and mild cognitive impairment (MCI) are important for avoiding future functional decline and dementia in older adults. The purpose of this study was to use a population-based survey to ascertain the single and combined prevalence of frailty and MCI and to identify the relationships between frailty and MCI in older Japanese adults.
Design: Cross-sectional study.
Setting: General community.
Participants: A total of 5104 older adults (aged 65 years or older, mean age 71 years) who were enrolled in the Obu Study of Health Promotion for the Elderly (OSHPE).
Measurements: Each participant underwent detailed physical and cognitive testing to assess frailty and MCI. We considered the frailty phenotype to be characterized by limitations in 3 or more of the following 5 domains: mobility, strength, endurance, physical activity, and nutrition. Screening for MCI included a standardized personal interview, the Mini-Mental State Examination, and the National Center for Geriatrics and Gerontology-Functional Assessment Tool (NCGG-FAT), which included 8 tasks used to assess logical memory (immediate and delayed recognition), word list memory (immediate and delayed recall), attention and executive function (tablet version of Trail Making Test-part A and B), processing speed (tablet version of digit symbol substitution test), and visuospatial skill (figure selection).
Results: The overall prevalence of frailty, MCI, and frailty and MCI combined was 11.3%, 18.8%, and 2.7%, respectively. We found significant relationships between frailty and MCI (the odds ratio adjusted for age, sex, and education was 2.0 (95% confidence interval 1.5–2.5).
Conclusions: Using the OSHPE criteria, we found more participants with MCI than with frailty. The prevalence of frailty and MCI combined was 2.7% in our population. Future investigation is necessary to determine whether this population is at increased risk for disability or mortality.

The rate of frailty and mild cognitive impairment (MCI), which increases with age, is a major risk factor for dependency, institutionalization, and mortality.[1,2,3,4] Individuals with disabilities have greater health care needs compared with those without.[5] The elderly population is highly heterogeneous, such that elderly people in the same age range may have a widely varied risk of disability. To prevent disability, population-based intervention programs should be targeted at those in the population with an increased risk of frailty and MCI.

Many studies have worked within research and clinical settings to identify target populations with frailty and MCI. For instance, the Interventions on Frailty Working Group assessed various methods for screening, recruiting, evaluating, and retaining frail elderly individuals in clinical trials.[6] They reported that most researchers focused on the following domains when identifying physical frailty: mobility,

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such as lower-extremity performance and gait abnormalities; muscle weakness; poor exercise tolerance; unstable balance; and factors related to body composition, such as weight loss, malnutrition, and muscle loss.[6] Participants with MCI in a community cohort were described by a group of investigators from the Mayo Clinic in 1999, who then produced a series of diagnostic criteria.[7] A conference of international MCI experts then revised these criteria,[8] and the National Institute on Aging joined the Alzheimer's Association to revise the diagnostic criteria for the symptomatic predementia phase of Alzheimer disease (AD). They outlined the following factors for the identification of MCI: concern regarding a change in cognition, impairment in one or more cognitive domains, preservation of independence in functional abilities, and absence of dementia.[9]

Using the frailty criteria developed by the Cardiovascular Health Study (CHS), the overall prevalence of frailty in community-dwelling adults aged 65 or older in the United States has been found to range from 7% to 12%. In the CHS, the prevalence of frailty increased with age from 3.9% in the 65 to 74 age group to 25.0% in the 85+ age group, and was greater in women than in men (8% vs 5%).[10] Using the MCI criteria in the CHS cognition study, the overall prevalence of MCI was found to be 18.8%, and the prevalence increased with age from 18.8% in participants younger than 75 years to 28.9% in those older than 85 years.[11]

Several cross-sectional studies have reported an association between physical frailty and cognitive function.[6,10,12,13] In addition, longitudinal studies have revealed that a higher level of physical frailty is associated with an increased risk of incident AD[14] and MCI.[15] These studies suggest that in some older adults, physical frailty is associated with the development of MCI. Older adults who show signs of both physical frailty and MCI may be more likely to exhibit functional decline than those with either frailty or MCI. However, the combined prevalence of frailty and MCI and the relationships between frailty and MCI in the Japanese population has not been clearly established. Thus, the purpose of this study was to ascertain the combined prevalence of frailty and MCI and to identify the relationships among frailty, MCI, and demographics including age, sex, and education in the Japanese population, using a community-based survey.

Methods

Participants

Our national study assessed 5104 individuals 65 years and older (mean age 71 years) who were enrolled in the Obu Study of Health Promotion for the Elderly (OSHPE). Each individual was recruited from Obu, Japan, which is a residential suburb of Nagoya. Inclusion criteria required each participant to be 65 years or older at the time of examination (2011 or 2012), and to reside in Obu city. Based on previous reports, we excluded participants with a history of Parkinson disease, stroke, or Mini-Mental State scores less than 18, as these conditions could produce characteristics of frailty.[3,10,16] We also excluded participants who had participated in similar studies, those with severe disabilities, and those with missing data values regarding determinants for frailty and MCI. In the present study, we examined the prevalence of frailty in 4745 participants, MCI in 5025 participants, and the combined prevalence of frailty and MCI in 4681 participants. Informed consent was obtained from all participants before their inclusion in the study, and the Ethics Committee of the National Center for Gerontology and Geriatrics approved the study protocol.

Measurements

The assessments were conducted by well-trained staff who had nursing, allied health, or similar qualifications. Before commencement of the study, all staff received training from the authors in the correct protocols for administering the assessment measures.

Operationalization of the Frailty Phenotype in OSHPE

We considered the frailty phenotype to be characterized by limitations in 3 or more of the following 5 domains: mobility, strength, endurance, physical activity, and nutrition. Mobility was measured in seconds using a stopwatch. Participants were asked to walk on a flat and straight surface at a comfortable walking speed. Two markers were used to indicate the start and end of a 2.4-meter walk path, with a 2-meter section to be traversed before passing the start marker so that participants were walking at a comfortable pace by the time they reached the timed path. Participants were asked to continue walking for an additional 2 meters past the end of the path to ensure a consistent walking pace while on the timed path. A low level of mobility was established according to a cutoff (<1.0 m/s). Grip strength was measured in kilograms using a Smedley-type handheld dynamometer (GRIP-D; Takei Ltd., Niigata, Japan). Low grip strength was established according to a sex-specific cutoff (male: <26 kg, female: <17 kg). Endurance was assessed via a self-report of exhaustion, which included questions from the Geriatric Depression Scale,[17] such as: "Do you feel full of energy?" If participants answered "no" to this question, we classified them as low endurance. We evaluated the role of physical activity by asking the following questions about time spent engaged in sports and exercise: (1) "Do you engage in moderate levels of physical exercise or sports aimed at health?" and (2) "Do you engage in low levels of physical exercise aimed at health?" If participants answered "no" to both of these questions, we considered them to be physically inactive. Nutritional status was established according to self-reports of weight loss in response to the following question: "In the past 2 years, have you lost more than 5% of your body weight irrespective of intent to lose weight?" Patients with impairments in at least 3 of the 5 domains were considered to be frail.

Operationalization of the MCI in OSHPE

We defined MCI based on previous studies,[18,19,20] using the following criteria: subjective memory complaints, cognitive impairment (indicated by an age-adjusted score at least 1.5 SDs below the reference threshold of any of the tests, all of which are commonly used for detailed neuropsychological assessments); no evidence of functional dependency (no need for supervision or external help in performing activities in daily life); and exclusion from the clinical criteria for dementia. Screening for MCI included a standardized personal interview for collection of sociodemographic, lifestyle, medical history, and functional status (activities of daily living) data, along with cognitive screening that was conducted using the Mini-Mental State Examination (MMSE)[21] and the National Center for Geriatrics and Gerontology-Functional Assessment Tool (NCGG-FAT).[22] Individuals with 23 or fewer points on the MMSE were considered to have a general cognitive impairment.[23] The NCGG-FAT consists of 8 tasks used to assess logical memory (immediate and delayed recognition), word list memory (immediate and delayed recall), attention and executive function (tablet version of Trail Making Test-part A and B), processing speed (tablet version of Digit Symbol Substitution Test), and visuospatial skill (figure selection). The participants were given 20 to 30 minutes to complete the battery, which consisted of the previously mentioned 8 tasks. High test-retest reliability and moderate to high validity were confirmed in community-dwelling older adults for all task components of the NCGG-FAT.[22] All tests used in this study had previously established

standardized thresholds for the definition of impairment in the corresponding domain (score <1.5 SDs below the age-specific mean) for population-based OSHPE cohort consisting of older adults.

Statistical Analysis

We compared age-, sex-, and education-specific prevalence, as well as the combined prevalence rates of frailty and MCI using χ^2 tests. The prevalence of frailty and MCI were explored in 4745 and 5025 participants, respectively. In calculating the combined prevalence, we found that 4681 participants did not meet the exclusion criteria for frailty or MCI. A multivariate logistic regression model was used to determine the odds ratios of MCI or frailty with respect to age category, sex, and education level. Participants with low general cognitive function were excluded from the multivariate analysis. As a result, the multivariate analysis included data from 3497 participants. All data management and statistical computations were performed using the IBM SPSS Statistics 19.0 software package (SPSS Inc., Chicago, IL).

Results

The OSHPE identified 538 (11.3%) elderly participants who had symptoms of frailty and 945 (18.8%) who had MCI (Table 1). Figures 1 and 2 show our findings regarding the prevalence of frailty and MCI, respectively. We found that the prevalence of frailty increased with advancing age. Of the 538 participants who were classified as frail, 192 (34.9%) were 80 years and older. The prevalence of frailty was higher in women than in men ($P < .05$), and a lower level of education was significantly associated with prevalence of frailty ($P < .01$). Participants who reported 9 or fewer years of education had a 16.4% rate of frailty, whereas in those who reported at least 13 years of education, this rate was 7.7% (Table 1 and Figure 1).

The OSHPE found young-old, 65 to 74 years, participants to have a higher rate of MCI than old-old, 75 years and older, participants. Educational level was significantly associated with MCI ($P < .01$). Participants who reported 9 or fewer years of education had a 23.4% rate of MCI, whereas this rate was reduced to 14.1% in participants who reported at least 13 years of education (Table 1 and Figure 2). The OSHPE found no significant sex-specific differences in the prevalence of MCI.

Table 1 shows the distribution of the combined prevalence of frailty and MCI by age, sex, and educational level. The OSHIPE revealed 126 (2.7%) participants with a combined incidence of frailty and MCI. Combined prevalence increased with age, with the highest rate found in the age group containing participants who were 80 years and older (6.9%). Participants with a low educational level had a higher rate of MCI combined with frailty (4.4% for 9 or fewer years) than those with higher education (1.3% for 13 years and more). No clear pattern emerged for any sex-specific differences in the prevalence of combined frailty and MCI (Table 1).

Our multivariate analysis found 3497 participants from the OSHPE cohort who did not meet the exclusion criteria for frailty and MCI and who maintained objective cognitive function. We found several significant relationships between frailty and MCI (odds ratio [OR] = 2.0, 95% confidence interval [95% CI] 1.5–2.5). In terms of the relationship between frailty and sociodemographics, participants aged 65 to 69 years were less likely to be frail than older participants (OR = 2.7, 95% CI 1.9–3.8, for the group 75 to 79 years of age, and OR = 6.9, 95% CI 4.9–9.7, for the group 80 years and older). There were no significant associations observed between frailty and sex. Participants with 9 or fewer years of education had a higher OR (1.4) than participants with at least 13 years of education (Table 2).

In terms of the relationship between MCI and sociodemographics, female participants had a significantly lower OR (0.8, 95% CI 0.7–1.0) than male participants. There was an evident relationship between MCI and educational level. In comparison with participants with at least 13 years of education, participants with a lower level of education were more likely to have MCI (OR = 1.5, 95% CI 1.2–1.8, for those with 10–12 years of education, and OR = 3.2, 95% CI 2.5–4.0, for those with 9 or fewer years of education) (Table 2).

Discussion

This study presents original data regarding vulnerability for physical and cognitive decline in a sample of 5104 elderly community dwellers in Japan. To our knowledge, this is the first study about frailty and MCI in this region of the world. Japan has a rapidly aging population in comparison with North, Central, and South America, as well as Europe. An examination of the differences in levels of frailty and MCI between countries may be useful in developing health care policies, especially in countries where the population is expected to rapidly age in the near future.

Growing evidence has indicated that there is a connection between frailty and cognitive impairment. Several studies have reported a longitudinal association between frailty and rate of MCI in elderly community-dwelling individuals. Boyle et al[15] reported, in an assessment that used 12 years of annual follow-up data, that physical frailty was associated with a high risk of MCI, such that each 1-unit (grip strength, timed walk, body composition, and fatigue) increase in physical frailty was associated with a 63% increase in the risk of MCI. Auyeung et al[24] identified that physical frailty, as indicated by

Table 1
Number of Participants and Prevalence of Frailty and Mild Cognitive Impairment (MCI)

	Frailty (n = 4745)			MCI (n = 5025)			Combined (n = 4681)
	Without Frailty	With Frailty	Prevalence	Without MCI	With MCI	Prevalence	Prevalence
All participants	4207	538	11.3%	4080	945	18.8%	2.7%
Age, y			$P < .01$			$P < .02$	
65–69	1794	106	5.6%	1583	390	19.80%	1.6%
70–74	1344	105	7.2%	1221	307	20.10%	2.2%
75–79	711	135	16.0%	771	145	15.80%	3.4%
≥80	358	192	34.9%	505	103	16.90%	6.9%
Sex			$P < .05$			$P < .05$	
Females	2157	302	12.3%	2073	489	19.10%	3.0%
Males	2050	236	10.3%	2007	456	18.50%	2.4%
Educational level, y			$P < .01$			$P < .01$	
≤9	1420	279	16.4%	1414	431	23.40%	4.4%
10–12	1812	179	9.0%	1712	357	17.30%	2.0%
≥13	963	80	7.7%	943	155	14.10%	1.3%

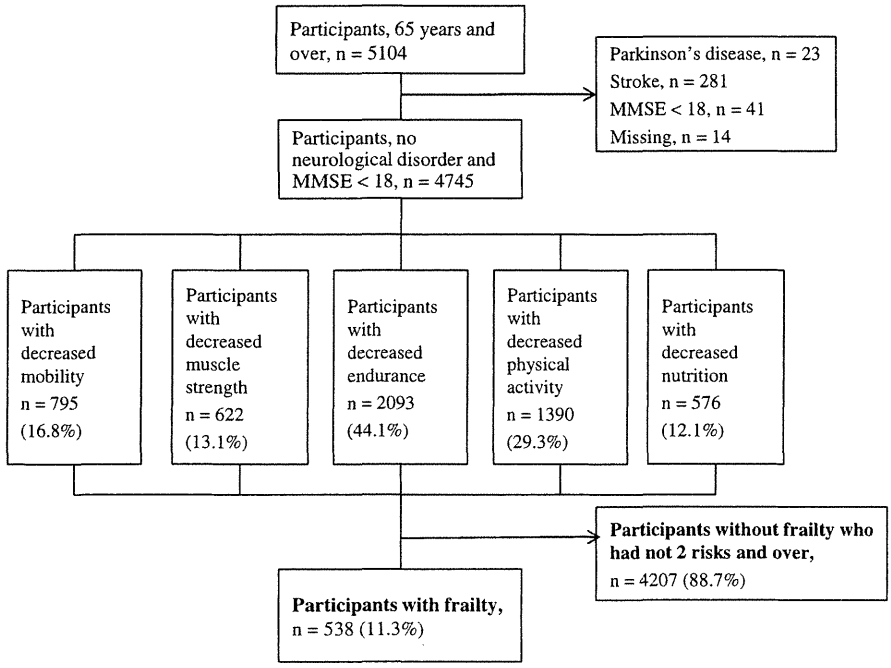

Fig. 1. Participants' flow to find frail older adults.

low body weight, weaker grip strength, slower performance in the chair-stand test, and shorter step-length in men and weaker grip strength in women, was associated with a decline in MMSE score over a 4-year period. Similarly, low cognitive function was independently associated with an increased risk of frailty in older adults. Raji et al. reported that nonfrail participants with a poor MMSE score (<21) at baseline had a 9% probability per year of becoming frail over a 10-year period, compared to individuals with normal cognition (MMSE

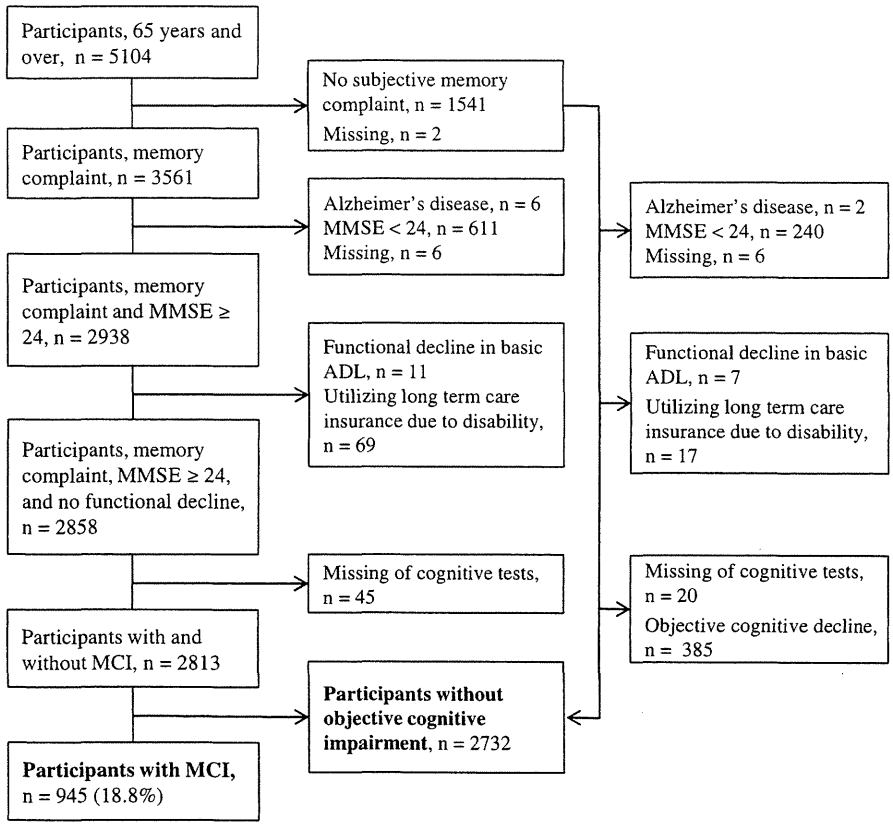

Fig. 2. Participants' flow to find MCI older adults.

Table 2
Relationships Between Frailty, Mild Cognitive Impairment (MCI), and Sociodemographics

	Frailty		MCI	
	Odds Ratio (95% Confidence Interval)	*P*	Odds Ratio (95% Confidence Interval)	*P*
MCI	2.0 (1.5–2.5)	<.01		
Frailty			2.0 (1.5–2.5)	<.01
Age, y	*P* for trend	<.01	*P* for trend	>.05
65–69	1		1	
70–74	1.2 (0.9–1.7)	.30	1.0 (0.8–1.2)	.95
75–79	2.7 (1.9–3.8)	<.01	0.7 (0.6–0.9)	.01
≥80	6.9 (4.9–9.7)	<.01	0.9 (0.7–1.2)	.54
Sex				
Males	1		1	
Females	1.1 (0.9–1.4)	.45	0.8 (0.7–1.0)	.04
Educational level, y	*P* for trend	.02	*P* for trend	<.01
≥13	1		1	
10–12	1.0 (0.7–1.4)	.85	1.5 (1.2–1.8)	<.01
≤9	1.4 (1.0–2.0)	<.05	3.2 (2.5–4.0)	<.01

21+).[25] Although the criteria for determining frailty and MCI vary slightly between studies, our results were in accordance with previous findings, and thus add support to the association between frailty and MCI.

The prevalence of frailty was 11.3% in our participant group, a rate slightly higher than that of previous studies that also used the CHS frailty criteria. In the American Cardiovascular Health Study, the prevalence of frailty among 5317 community-dwelling men and women aged 65 years and older was 6.9%, and frailty was associated with older age, male gender, being African American, having lower education and income, poorer health, and higher rates of comorbid chronic disease and disability.[10] The French Three-City Study demonstrated a frailty prevalence of 7% among 6078 community-dwelling men and women aged 65 years and older, and frailty was associated with older age, female gender, lower education, lower income, a poorer self-reported health status, and more chronic disease in addition to incident disability.[26] The Hertfordshire Cohort Study (HCS), UK, reported that the prevalence of frailty, as defined by CHS frailty criteria, among 638 community-dwelling participants aged 64 to 74 years was 8.5% for women and 4.1% for men.[27] The principal difference in the frailty criteria used by the CHS and OSHPE is the cutoff point for walking speed: in the CHS it is set at 0.65 m/s (height ≤173 cm) and in the OSHPE it is 1.0 m/s. This difference may be one explanation for the higher prevalence observed in studies using the OSHPE. The Survey of Health, Aging, and Retirement in Europe (SHARE) studied 16,584 men and women aged 50 years and older, and found that the prevalence of frailty in the nondisabled population aged 65 years and over ranged from 3.9% to 21.0%. The SHARE study demonstrated a higher prevalence of frailty in southern (9.3% to 21.0%) compared with northern Europe (<9.0%).[28] The SHARE study defined slowness using the following 2 questions regarding mobility: "Because of a health problem, do you have difficulty [expected to last more than 3 months] walking 100 meters" and "... climbing 1 flight of stairs without resting." Gait velocity has consistently been reported to differentiate between participants with and without functional decline, as frail elderly individuals walk significantly slower than their nonfrail peers.[29,30] Thus, gait velocity has been found to be a strong predictor of adverse events, such as disability,[31-37] mortality,[32,33,38,39] hospitalization,[32,33,35,40] and falls.[40,41] The cutoff point for walking speed in the present study was 1.0 m/s, which appears to be a critical point for predicting future functional decline in community-dwelling elderly individuals.[32,33,35,36,37] These results suggest that walking speed may be the most useful measurement for determining frailty and predicting future functional decline in older adults.[42,43]

It is likely that the reported prevalence of MCI varies between studies as a result of different diagnostic criteria, as well as different sampling and assessment procedures. Despite some methodological differences, most previous studies report prevalence figures for MCI or for cognitive impairment without dementia ranging from 11% to 23%. The Women's Cognitive Impairment Study used global and domain-specific cognitive measures and found the prevalence of MCI or cognitive impairment without dementia to be 23.2% in a sample of 1299 participants aged 85 years and older.[19] The Mayo Clinic Study of Aging diagnosed 329 of 1969 study participants (16.7%) with MCI or cognitive impairment without dementia using the Clinical Dementia Rating Scale, a neurologic evaluation, and neuropsychological testing to assess 4 cognitive domains: memory, executive function, language, and visuospatial skills.[44] A study from Leipzig, Germany, that used a 55-point composite instrument found the overall prevalence of MCI or cognitive impairment without dementia to be 19.3% in participants aged 75 years and older.[45] The Cardiovascular Health Study found the overall rate of MCI or cognitive impairment without dementia to be 19% in participants aged 75 years and older.[11] In the Aging, Demographics, and Memory Study, an estimated 5.4 million people (22.2% of the total population of the country) in the United States aged 71 years or older were found to have cognitive impairment without dementia.[46] In a Japanese study, MCI was diagnosed in 271 of 1433 study participants (18.9%).[47] In the above-mentioned study, a diagnosis of MCI was contingent on cognitive performance 1.0[44,45,47] or 1.5 SDs[11,19,46] below at least one test measure. In the present study, we found the prevalence of MCI to be 18.8%, which is similar to previous studies that used multiple cognitive tests to detect MCI.

In the present study, we found the combined prevalence of frailty and MCI to be 2.7% among 4681 community-dwelling elderly participants. Our analyses of the relationships among frailty, MCI, and sociodemographics revealed a significant relationship between frailty and MCI (OR 2.0). These results suggest that frailty may coincide with MCI in older adults who exhibit vulnerability factors for both conditions. Many researchers believe that the definition of frailty should include mental health as well as physical functioning. The Frailty Operative Definition-Consensus Conference Project reported that experts agreed on the importance of a more comprehensive definition of frailty that should include assessment of physical performance, including gait speed and mobility, nutritional status, mental health, and cognition.[48] The results of the present study were in line with the new concept of frailty, which included cognition. Individuals with a co-occurrence of frailty and MCI may face a higher risk of incidence disability than healthy older adults or older adults with either frailty or MCI. The French Three-City Study established that frail persons with a cognitive impairment are significantly more likely to develop disabilities in activities of daily living (ADL) and instrumental ADL disabilities.[49] Moreover, the Hispanic Established Populations for the Epidemiologic Study of the Elderly demonstrated that frailty and cognitive impairment affect mortality differently when they occur independently compared with when they are present together. For instance, individuals with cognitive impairment and frailty had higher mortality compared with individuals with either frailty or cognitive decline.[50] Further longitudinal study is needed to clarify the ways in which frailty and MCI might affect vulnerability among older adults.

Our multivariate analysis indicated that the participants with the highest risk of developing frailty were 80 years and older or had received fewer than 9 years of education. Many studies have reported relationships among frailty, age, and education. For instance, the Women's Health Initiative Observational Study found

that age is significantly correlated with incident frailty. In contrast, the previously mentioned study found no clear relationship between MCI and age. The MCI criteria in the OSHPE is based on cognitive score (ie, <1.5 SDs below the age-specific mean of healthy peers). Our inability to find a relationship between MCI and age may have been because of our use of age-specific criteria.

Our logistic model revealed that participants with the highest risk of MCI were predominantly male and had received 9 or fewer years of education. The Mayo Clinic Study of Aging reported that the prevalence OR for MCI in men was 1.54 (95% CI 1.21–1.96; adjusted for age, and education). Several other studies have reported a higher rate of MCI in older adults who received fewer years of education.[19,20,44,51] In one study, this result remained essentially unchanged after adjusting for several demographic and clinical variables, as well as the Apolipoprotein E genotype, suggesting that this association is not due to comorbid conditions or to a differential rate of MCI in men compared with women.[44] Our results support these previous discoveries while adding the finding that ethnic differences do not explain the higher prevalence of MCI in men than in women. There is a clear relationship between educational level and prevalence of MCI. Indeed, our results suggest that educational level is more closely associated with MCI risk than age in the OSHPE criteria.

One strength of the present study is the size of the cohort assessed in a specific community. Our findings are backed by comprehensive geriatric assessments intended to identify frailty and cognitive impairments. To our knowledge, this is the first study to demonstrate the combined prevalence of frailty and MCI in a large sample of older adults. We identified MCI using the NCGG-FAT, which is useful for multidimensional cognitive screening in population-based samples to assess the risk of cognitive decline. In a hospital setting, psychologists, neurologists, and other specialists are available to perform psychological tests. It can be difficult to assemble specialists in Japan for assessments in a community setting. The NCGG-FAT is easily administered using a tablet PC with the instructions shown on the display. Therefore, it is not necessary for those collecting the data to have a thorough knowledge of neurocognitive measures, and the identity of the person administering the questionnaire will not strongly affect the results.

An important limitation of our study is that participants were not recruited randomly to complete the OSHPE. This may lead to an underestimation of the prevalence of frailty and MCI, as the participants were relatively healthy elderly persons who were able to access the health checkup from their homes. Second, for some participants, we were not able to contact an informant, such as family member, to verify medical records, lifestyle information, and asymptomatic aberrant behavior.

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References

1. Fried LP, Ettinger WH, Lind B, et al. Physical disability in older adults: A physiological approach. Cardiovascular Health Study Research Group. J Clin Epidemiol 1994;47:747–760.
2. Ensrud KE, Ewing SK, Taylor BC, et al. Frailty and risk of falls, fracture, and mortality in older women: The study of osteoporotic fractures. J Gerontol A Biol Sci Med Sci 2007;62:744–751.
3. Woods NF, LaCroix AZ, Gray SL, et al. Frailty: Emergence and consequences in women aged 65 and older in the Women's Health Initiative Observational Study. J Am Geriatr Soc 2005;53:1321–1330.
4. Gnjidic D, Stanaway FF, Cumming R, et al. Mild cognitive impairment predicts institutionalization among older men: A population-based cohort study. PLoS One 2012;7:e46061.
5. Guralnik JM, Fried LP, Simonsick EM, et al. The Women's Health and Aging Study: Health and Social Characteristics of Older Women With Disability. Bethesda, MD: National Institute of Aging; 1995. NIH Pub. No: 95–4009.
6. Ferrucci L, Guralnik JM, Studenski S, et al. Designing randomized, controlled trials aimed at preventing or delaying functional decline and disability in frail, older persons: A consensus report. J Am Geriatr Soc 2004;52:625–634.
7. Petersen RC, Smith GE, Waring SC, et al. Mild cognitive impairment: Clinical characterization and outcome. Arch Neurol 1999;56:303–308.
8. Winblad B, Palmer K, Kivipelto M, et al. Mild cognitive impairment—beyond controversies, towards a consensus: Report of the International Working Group on Mild Cognitive Impairment. J Intern Med 2004;256:240–246.
9. Albert MS, DeKosky ST, Dickson D, et al. The diagnosis of mild cognitive impairment due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimers Dement 2011;7:270–279.
10. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: Evidence for a phenotype. J Gerontol A Biol Sci Med Sci 2001;56:M146–M156.
11. Lopez OL, Jagust WJ, DeKosky ST, et al. Prevalence and classification of mild cognitive impairment in the Cardiovascular Health Study Cognition Study: Part 1. Arch Neurol 2003;60:1385–1389.
12. Fried LP, Ferrucci L, Darer J, et al. Untangling the concepts of disability, frailty, and comorbidity: Implications for improved targeting and care. J Gerontol A Biol Sci Med Sci 2004;59:255–263.
13. Mitnitski AB, Song X, Rockwood K. The estimation of relative fitness and frailty in community-dwelling older adults using self-report data. J Gerontol A Biol Sci Med Sci 2004;59:M627–M632.
14. Buchman AS, Boyle PA, Wilson RS, et al. Frailty is associated with incident Alzheimer's disease and cognitive decline in the elderly. Psychosom Med 2007; 69:483–489.
15. Boyle PA, Buchman AS, Wilson RS, et al. Physical frailty is associated with incident mild cognitive impairment in community-based older persons. J Am Geriatr Soc 2010;58:248–255.
16. Santos-Eggimann B, Cuenoud P, Spagnoli J, Junod J. Prevalence of frailty in middle-aged and older community-dwelling Europeans living in 10 countries. J Gerontol A Biol Sci Med Sci 2009;64:675–681.
17. Yesavage JA, Brink TL, Rose TL, et al. Development and validation of a geriatric depression screening scale: A preliminary report. J Psychiatr Res 1982;17: 37–49.
18. Jungwirth S, Weissgram S, Zehetmayer S, et al. VITA: Subtypes of mild cognitive impairment in a community-based cohort at the age of 75 years. Int J Geriatr Psychiatry 2005;20:452–458.
19. Yaffe K, Middleton LE, Lui LY, et al. Mild cognitive impairment, dementia, and their subtypes in oldest old women. Arch Neurol 2011;68:631–636.
20. Hanninen T, Hallikainen M, Tuomainen S, et al. Prevalence of mild cognitive impairment: A population-based study in elderly subjects. Acta Neurol Scand 2002;106:148–154.
21. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975; 12:189–198.
22. Makizako H, Shimada H, Park H, et al. Evaluation of multidimensional neurocognitive function using a tablet personal computer: Test-retest reliability and validity in community-dwelling older adults [published online ahead of print December 12, 2012]. Geriatr Gerontol Int doi:10.1111/ggi.12014.
23. Anthony JC, LeResche L, Niaz U, et al. Limits of the 'Mini-Mental State' as a screening test for dementia and delirium among hospital patients. Psychol Med 1982;12:397–408.
24. Auyeung TW, Lee JS, Kwok T, Woo J. Physical frailty predicts future cognitive decline—a four-year prospective study in 2737 cognitively normal older adults. J Nutr Health Aging 2011;15:690–694.
25. Raji MA, Al Snih S, Ostir GV, et al. Cognitive status and future risk of frailty in older Mexican Americans. J Gerontol A Biol Sci Med Sci 2010;65:1228–1234.
26. Avila-Funes JA, Helmer C, Amieva H, et al. Frailty among community-dwelling elderly people in France: The three-city study. J Gerontol A Biol Sci Med Sci 2008;63:1089–1096.
27. Syddall H, Roberts HC, Evandrou M, et al. Prevalence and correlates of frailty among community-dwelling older men and women: Findings from the Hertfordshire Cohort Study. Age Ageing 2010;39:197–203.
28. Santos-Eggimann B, Cuenoud P, Spagnoli J, Junod J. Prevalence of frailty in middle-aged and older community-dwelling Europeans living in 10 countries. J Gerontol A Biol Sci Med Sci 2009;64:675–681.
29. Shimada H, Suzukawa M, Tiedemann A, et al. Which neuromuscular or cognitive test is the optimal screening tool to predict falls in frail community-dwelling older people? Gerontology 2009;55:532–538.
30. Tiedemann A, Shimada H, Sherrington C, et al. The comparative ability of eight functional mobility tests for predicting falls in community-dwelling older people. Age Ageing 2008;37:430–435.
31. Guralnik JM, Ferrucci L, Pieper CF, et al. Lower extremity function and subsequent disability: Consistency across studies, predictive models, and value of gait speed alone compared with the short physical performance battery. J Gerontol A Biol Sci Med Sci 2000;55:M221–M231.
32. Cesari M, Kritchevsky SB, Penninx BW, et al. Prognostic value of usual gait speed in well-functioning older people—results from the Health, Aging and Body Composition Study. J Am Geriatr Soc 2005;53:1675–1680.

33. Cesari M, Kritchevsky SB, Newman AB, et al. Added value of physical performance measures in predicting adverse health-related events: Results from the Health, Aging And Body Composition Study. J Am Geriatr Soc 2009;57:251–259.
34. Onder G, Penninx BW, Ferrucci L, et al. Measures of physical performance and risk for progressive and catastrophic disability: Results from the Women's Health and Aging Study. J Gerontol A Biol Sci Med Sci 2005;60:74–79.
35. Studenski S, Perera S, Wallace D, et al. Physical performance measures in the clinical setting. J Am Geriatr Soc 2003;51:314–322.
36. Simonsick EM, Newman AB, Visser M, et al. Mobility limitation in self-described well-functioning older adults: Importance of endurance walk testing. J Gerontol A Biol Sci Med Sci 2008;63:841–847.
37. Shinkai S, Watanabe S, Kumagai S, et al. Walking speed as a good predictor for the onset of functional dependence in a Japanese rural community population. Age Ageing 2000;29:441–446.
38. Markides KS, Black SA, Ostir GV, et al. Lower body function and mortality in Mexican American elderly people. J Gerontol A Biol Sci Med Sci 2001;56:M243–M247.
39. Studenski S, Perera S, Patel K, et al. Gait speed and survival in older adults. JAMA 2011;305:50–58.
40. Montero-Odasso M, Schapira M, Soriano ER, et al. Gait velocity as a single predictor of adverse events in healthy seniors aged 75 years and older. J Gerontol A Biol Sci Med Sci 2005;60:1304–1309.
41. Dargent-Molina P, Favier F, Grandjean H, et al. Fall-related factors and risk of hip fracture: The EPIDOS prospective study. Lancet 1996;348:145–149.
42. Abellan van Kan G, Rolland Y, Andrieu S, et al. Gait speed at usual pace as a predictor of adverse outcomes in community-dwelling older people an International Academy on Nutrition and Aging (IANA) Task Force. J Nutr Health Aging 2009;13:881–889.
43. Vermeulen J, Neyens JC, van Rossum E, et al. Predicting ADL disability in community-dwelling elderly people using physical frailty indicators: A systematic review. BMC Geriatr 2011;11:33.
44. Petersen RC, Roberts RO, Knopman DS, et al. Prevalence of mild cognitive impairment is higher in men. The Mayo Clinic Study of Aging. Neurology 2010;75:889–897.
45. Busse A, Hensel A, Guhne U, et al. Mild cognitive impairment: Long-term course of four clinical subtypes. Neurology 2006;67:2176–2185.
46. Plassman BL, Langa KM, Fisher GG, et al. Prevalence of cognitive impairment without dementia in the United States. Ann Intern Med 2008;148:427–434.
47. Sasaki M, Kodama C, Hidaka S, et al. Prevalence of four subtypes of mild cognitive impairment and APOE in a Japanese community. Int J Geriatr Psychiatry 2009;24:1119–1126.
48. Rodriguez-Manas L, Feart C, Mann G, et al. Searching for an operational definition of frailty: A Delphi method based consensus statement: The frailty operative definition-consensus conference project. J Gerontol A Biol Sci Med Sci 2013;68:62–67.
49. Avila-Funes JA, Amieva H, Barberger-Gateau P, et al. Cognitive impairment improves the predictive validity of the phenotype of frailty for adverse health outcomes: The three-city study. J Am Geriatr Soc 2009;57:453–461.
50. Cano C, Samper-Ternent R, Al Snih S, et al. Frailty and cognitive impairment as predictors of mortality in older Mexican Americans. J Nutr Health Aging 2012;16:142–147.
51. Nie H, Xu Y, Liu B, et al. The prevalence of mild cognitive impairment about elderly population in China: A meta-analysis. Int J Geriatr Psychiatry 2011;26:558–563.

公衆衛生 Up-To-Date ・8

[国立長寿医療研究センター発信：その2]

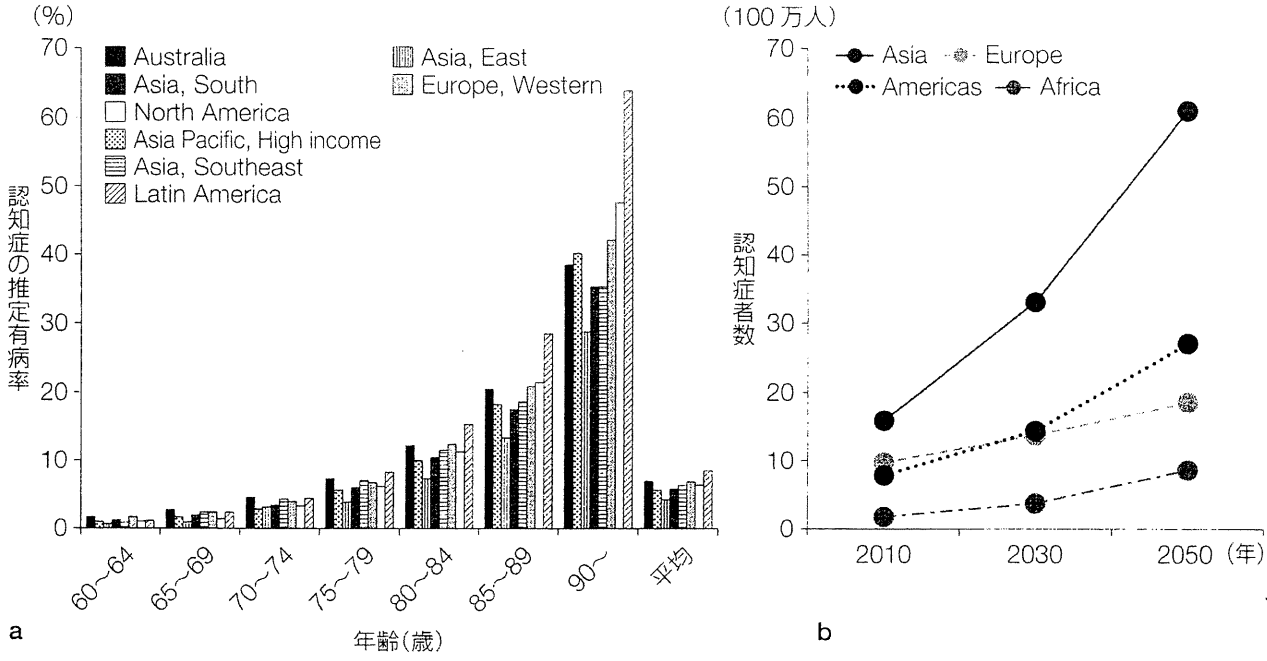
認知症の危険因子と予防に関するエビデンス

島田 裕之

認知症の危険因子

認知症は加齢とともに増加し，80歳代から急激に有病率が向上し，90歳以上では地域にかかわらず30%以上の高齢者が認知症を有すると推定されている（図1，a）[1]．特にアジアにおける高齢者数の増大は，今後40年間において認知症者の著しい増大を迎えると予想されている（図1，b）[1]．アルツハイマー病および認知症の危険因子は，加齢の過程に伴い出現し，変化し，あるいは幾重にも重なり，その結果，高齢期における脳の機能的予備力を低下させる原因となるが，この20年間に行動，社会科学的側面からアルツハイマー病および認知症の危険因子が多数報告され，一定の見解がまとまりつつある．

例えば，2004年に報告されたFratiglioni ら[2]のレビューを参考に認知症の危険因子と保護因子をまとめると，図2のようになる．若年期におい



文献1）より作図

図1　認知症の推定有病率と人数の推移

しまだ ひろゆき：国立長寿医療研究センター老年学・社会科学研究センター自立支援開発研究部自立支援システム開発室室長　連絡先：〒474-8511 愛知県大府市森岡町源吾35

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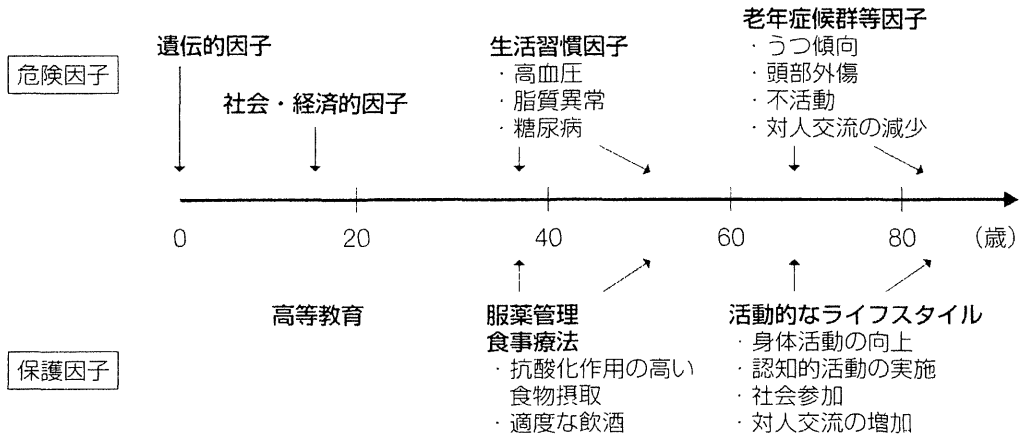

文献2)を参考に作成

図2　認知症の危険因子と保護因子

ては遺伝的あるいは社会・経済的な危険因子が存在し，教育を受ける機会が減少すると認知的予備力を十分蓄えることができないことなどが，将来の認知症の発症に関連すると考えられている．成人期においては，高血圧，脂質異常，糖尿病などの生活習慣に関連した危険因子が現れる．これらは脳血管疾患のみではなくアルツハイマー病の危険因子でもあり，将来の認知症を予防するためには，服薬管理と食事療法[3]を実践することが重要な課題となる．

高齢期になると老年症候群と呼ばれるうつ傾向，転倒による頭部外傷や不活動に伴う対人交流の減少が起こり，これらが認知症の発症を促進する．そのため，高齢期においては，定期的な運動の促進[4]，社会参加，知的活動，生産活動への参加[5]，社会的ネットワークの向上[6]などの活動的なライフスタイルの確立が，認知症予防のために重要であると考えられる．

認知症予防の焦点

認知症ではないが正常ともいい難い軽度の認知機能低下を有する状態は，軽度認知障害(mild cognitive impairment：MCI)と呼ばれ，認知症を発症する危険性が高い[7]．MCIは認知症に移行する危険性が高い反面，正常の認知機能に回復する場合もあり[8,9]，認知症予防を積極的に推進すべき状態と考えられる．

例えば，記憶に問題を有する健忘型MCI高齢者の半数，および記憶以外の認知機能にも問題を持つMCI高齢者の3分の2が，3年間の追跡期間中にアルツハイマー病へ移行することが示されている[10]．また，Petersenら[11]の報告によると正常な認知機能を有する高齢者のアルツハイマー病への移行率は年間1～2%であったのに対してMCIからのアルツハイマー病の発症率は年間10～15%であり，MCIはアルツハイマー病の前駆状態として重要な介入時期であるとされている．一方，38.5%のMCI高齢者は，5年後に正常な認知機能へと回復するとした報告もあり[12]，MCIの状態から脱却することが認知症を予防もしくは発症を遅延させることにつながるものと考えられる．

そのため，認知症予防を目的とした介護予防においては，特にMCI高齢者に焦点を当てた取組みが重要であり，その効果が期待される．筆者らが実施した5,104名の高齢者を対象としたMCIのスクリーニング検査[13]では，地域における約19%の高齢者がMCIと判定された．

MCI高齢者に対する認知症予防対策

MCI高齢者を対象とした認知症の予防対策の中で，運動介入プログラムは比較的低コストで実施でき，短期間で効果を得ることが期待できることから，認知症予防事業の中核をなす可能性を

っている．

筆者らは愛知県大府市在住の65歳以上のMCI高齢者100名を対象として，運動介入の効果を検証するためのランダム化比較試験を実施した．研究に参加した100名の対象者を健忘型MCIで層化して，無作為に健康講座群(対照群)と運動教室群(介入群)とに割り付けて1年間の介入を実施した．運動教室群の介入は，週2回，1回につき90分間．計80回実施した．教室は理学療法士1～2名，運動補助員4名で介入を実施した．運動プログラムには，先行研究において効果が認められている有酸素運動に加え，記憶や思考を賦活する運動課題を取り入れた．また，健康行動を促進する目的で，加速度センサー付きの歩数計と記録手帳の配布，ホームエクササイズの指導，健康講座の開催などを定期的に行った．記憶と思考を賦活する運動課題には，例えばステップ運動としりとりを同時に行う課題，屋外を歩きながら俳句を考える課題，ラダー(はしご)トレーニングのように，決められたパターンに従って正確なステップを踏む課題などが含まれ，対象者に応じてその方法や難易度を変化させた．健康講座群には，介護や疾病予防に関する健康講座(60～90分間)を3回実施した．

介入開始から6か月後の中間評価においては，週2回の運動を実施した群に処理速度や言語能力の向上が認められた．また，健忘型MCI高齢者($n=50$)に限定した分析では，全般的な認知機能(mini mental state examination)の低下抑制，記憶力の向上や，脳萎縮の進行抑制効果も認められた[14]．これらの効果は1年後の最終評価においても継続した[15]．

現在，認知症を予防できる明確な方法は明示されていないが，発症遅延を実現できる可能性のある介入として運動を推奨することができるだろう．高齢期における運動は，筋骨格系の機能保持，呼吸循環機能の向上，血圧の低下，脂質代謝の改善，ストレス軽減，転倒予防など多様な効果を持つことが明らかであり，心身の健康保持に有益であることは間違いない．

文　献

1) World Health Organization, Alzheimer's Disease International: Dementia: a public health priority. WHO Press, 2012
2) Fratiglioni L, et al: An active and socially integrated lifestyle in late life might protect against dementia. Lancet Neurol **3**(6): 343-353, 2004
3) Morris MC, et al: Dietary intake of antioxidant nutrients and the risk of incident Alzheimer disease in a biracial community study. JAMA **287**(24): 3230-3237, 2002
4) Verghese J, et al: Leisure activities and the risk of dementia in the elderly. N Engl J Med **348**(25): 2508-2516, 2003
5) Wilson RS, et al: Participation in cognitively stimulating activities and risk of incident Alzheimer disease. JAMA **287**(6): 742-748, 2002
6) Fratiglioni L, et al: Influence of social network on occurrence of dementia: a community-based longitudinal study. Lancet **355**(9212): 1315-1319, 2000
7) Petersen RC, et al: Current concepts in mild cognitive impairment. Arch Neurol **58**(12): 1985-1992, 2001
8) Larrieu S, et al: Incidence and outcome of mild cognitive impairment in a population-based prospective cohort. Neurology **59**(10): 1594-1599, 2002
9) Matthews FE, et al: Two-year progression from mild cognitive impairment to dementia: to what extent do different definitions agree? J Am Geriatr Soc **56**(8): 1424-1433, 2008
10) Palmer K, et al: Mild cognitive impairment in the general population: occurrence and progression to Alzheimer disease. Am J Geriatr Psychiatry **16**(7): 603-611, 2008
11) Petersen RC, et al: Mild cognitive impairment: clinical characterization and outcome. Arch Neurol **56**(3): 303-308, 1999
12) Ishikawa T, et al: A longitudinal study regarding conversion from mild memory impairment to dementia in a Japanese community. Int J Geriatr Psychiatry **21**(2): 134-139, 2006
13) Shimada H, et al: Combined Prevalence of Frailty and Mild Cognitive Impairment in a Population of Elderly Japanese People. J Am Med Dir Assoc, 2013
14) Suzuki T, et al: A randomized controlled trial of multicomponent exercise in older adults with mild cognitive impairment. PLoS One **8**(4): e61483, 2013
15) Suzuki T, et al: Effects of multicomponent exercise on cognitive function in older adults with amnestic mild cognitive impairment: a randomized controlled trial. BMC Neurol **12**: 128, 2012

認知症に対する非薬物的介入としての臨床美術
—近赤外線分光法による前頭葉脳活動の検討—

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原著

認知症に対する非薬物的介入としての臨床美術*
—近赤外線分光法による前頭葉脳活動の検討—

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近藤正樹**　中川正法**

Key Words : clinical art therapy, dementia, frontal lobe, near infrared spectroscopy (NIRS)

はじめに

高齢化社会に伴う認知症患者の増加が問題になる中，認知症の早期介入は今後の社会にとってきわめて重要な課題であるといえる．認知症進行予防の非薬物的介入の一つとして，音楽や絵画を楽しんだり，創作活動を行ったりするなどの，芸術療法が知られている．京都府立医科大学神経内科学教室では，軽度を含むAlzheimer型認知症(dementia of Alzheimer type：DAT)患者とその家族を対象として，日本臨床美術協会[1]認定臨床美術士による美術教室を開催し，認知症患者の脳活性化のためのアプローチを試みている．患者本人のみならず，付添いの家族にも大変ご好評いただいている．

われわれは，この臨床美術の教室受講中の脳活動を検証すべく，近赤外線分光法(near infrared spectroscopy：NIRS)[2][3]を用いた前頭葉血流動態を検討した．

方　法

臨床美術教室を受講中のDAT患者6名(男性5名/女性1名)を対象に，NIRS装置による前頭葉血流検査を施行した．全例が右手利きであった．平均年齢75.3歳で，検査前の認知機能評価では，平均がMini Mental State Examination(MMSE) 23.7点，Frontal Ability Battery(FAB) 14.5点，気分評価ではProfile of Mood States(POMS) 8.5点であった．

NIRS装置はOMM-3000(島津製作所，京都)[2]を使用し，測定部位は，10-20法Fpzが中央下辺にあうように3行7列のフォルダーで前額部を覆い，プローブ間の42チャンネルを測定した．測定パラメーターはoxy Hb(ヘモグロビン)およびdeoxy Hbの信号値とした．測定時の課題については，対照課題として，黒い単純な線を繰り返し描く課題1分間を行い，続いて臨床美術士の指導のもとで林檎の描画課題15分間を行い，最後に再び黒い単純な線を繰り返し描く課題1分間を行った(図1)．林檎の描画課題では，林檎を手にして，林檎にまつわるエピソードを話したり，香りや味を楽しむことで，そのイメージをふくらませながら，クレヨンを用いて林檎の絵を描いていただいた．そしてその様子を検者がそばで観察し，作業内容を秒単位で記録し，測定値変化と照らし合わせ検討した．描画課題中，臨床

* Frontal lobe activation measured by near infrared spectroscopy during clinical art therapy for patients with dementia. (Accepted April 26, 2013).

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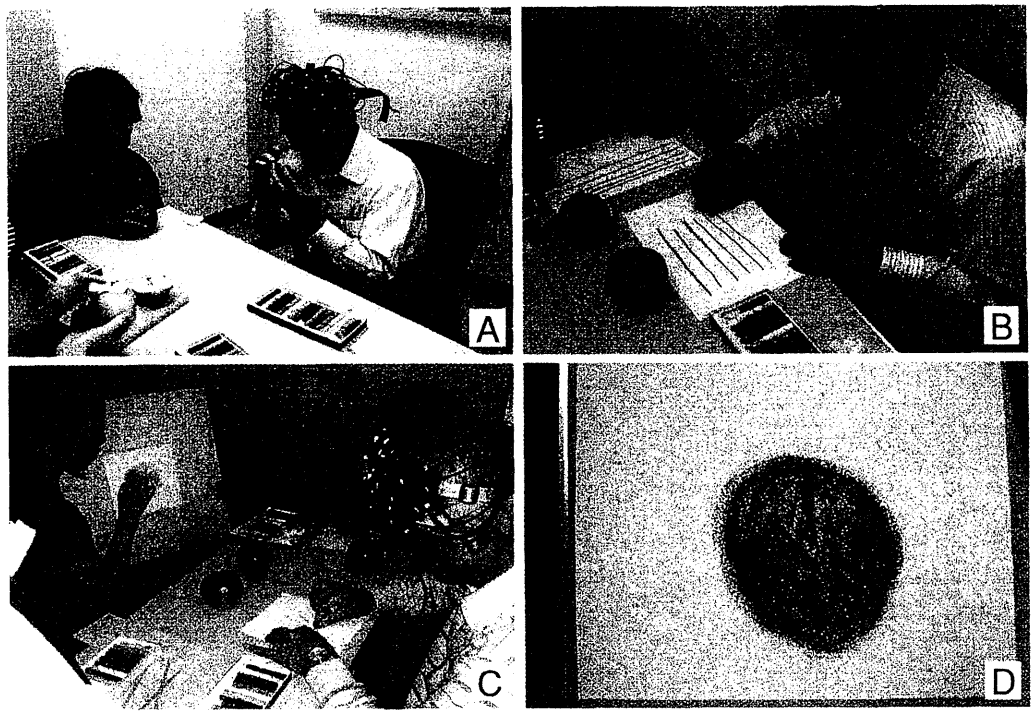

図1　認知症患者を対象にした林檎をテーマに絵を描く授業
まずは林檎についてイメージを膨らまし(A)，対照課題として黒い線を引く(B：1分)，林檎を描く(C：15分)，黒い線を引く(1分)という課題を続けて行う．その間NIRS装置で前頭葉の脳血流動態を記録する．Dはこの被験者が描いた完成の絵．

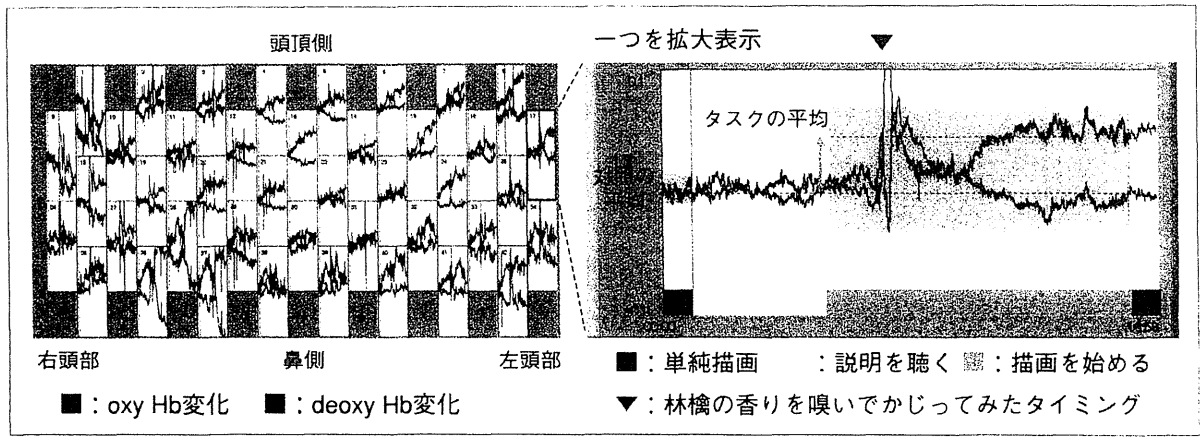

図2　課題中のNIRS装置による前頭葉血流検査
単純描画課題の時間帯をベースラインとして，林檎描画の時間帯のoxy Hb(赤)・deoxy Hb(青)信号値変化量を前頭部42カ所で測定した．

美術上に説明を受けているのみの時間帯は測定の対象外とした(図2)．

創作による脳活動を評価するためには，サブトラクション，すなわち手の動きによる脳活動を差し引いて考えなければならない．また，単純作業の対照課題中にも測定値にチャンネルそれぞれで違った変動を呈しており，描画課題中の平均変化量については，対照課題を基準にして以下のように定義した．

[平均変化量 Δ]＝{[林檎描画課題中の平均値(mM・mm)]－[対照課題中の平均値(mM・mm)]}/[対照課題中の変動の標準偏差(mM・mm)]

すなわち，林檎描画課題でHbが上昇すれば正のスコアで，Hbが低下すれば負のスコアで，チャンネルごとに表されることになる．ここでは，

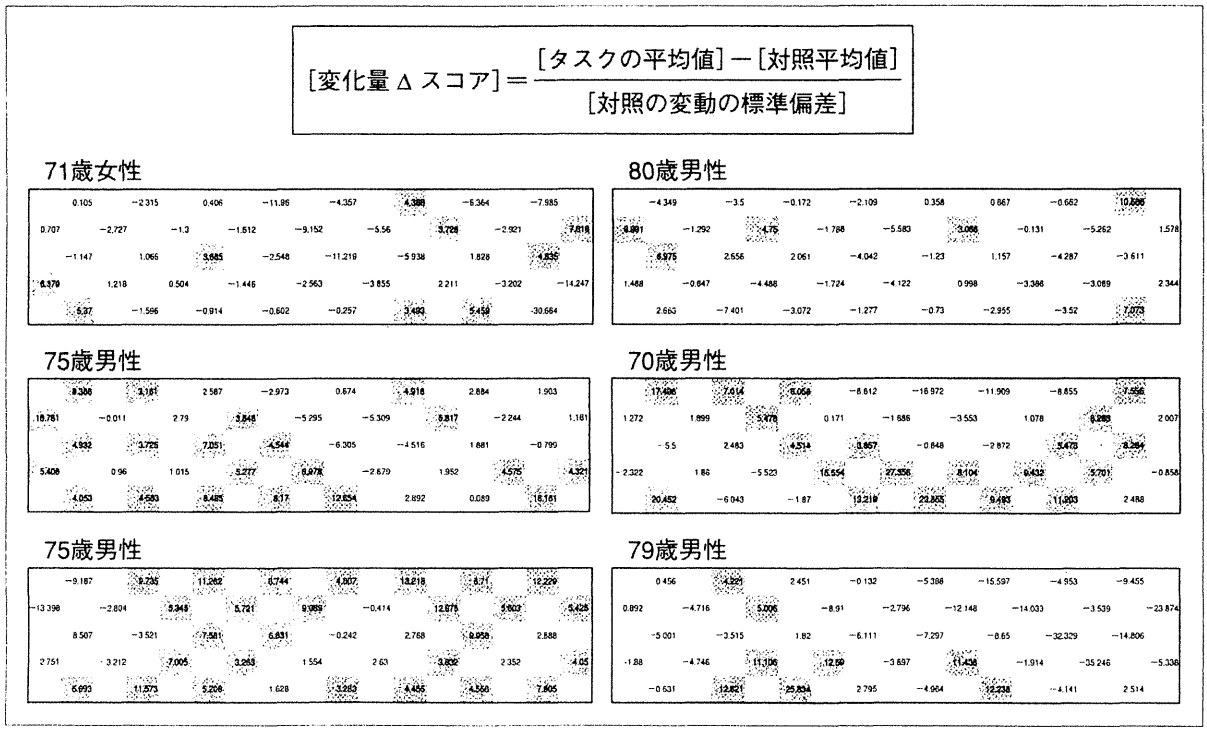

図3　臨床美術課題中の認知症患者6症例のNIRS前頭葉活動の解析結果

林檎描画中のNIRS記録は対照課題をもとに各チャンネルでの変化量Δを定義し，値が3.0以上を有意な血流上昇と考えて，そのチャンネルを灰色で示した．マッピングは，右が被験者左頭部側，左が右頭部側，上が頭側，下が鼻側を示す．

±3を超えるものを有意な上昇/低下として検討した．

結　果

Oxy Hbについては，林檎の描画(後半)の時間で，いずれの被検者も著明な上昇が認められた．また経時的にみて，味覚や触覚を合わせた瞬間(図2)に特に顕著な上昇が多くの部位で観察された．変化量の平均をみると，全例ではないが多くの症例で両側に上昇のチャンネルが認められた(図3)．

一方，deoxy Hbについては，多くは変化なく，有意な傾向は認められなかった．

考　察

日本臨床美術協会[1]の展開する臨床美術とは，認知症の症状改善を目的として開発されたアートカリキュラムのことである．1996年に医師・美術家・ファミリーケアアドバイザーがチームとなって臨床美術協会を立ち上げ，実践研究がスタートした．医療・美術・福祉の壁を越えた独自のアートカリキュラムに沿って創作活動を進めるのが特徴で，アートセラピーの先進国にも例をみない先駆的な取り組みとされている．現在では認知症のみならず，発達障害の子供へのアプローチも含め子供たちの教育・福祉教育の分野でも取り入れられ，高い評価を得ている．

われわれは，臨床美術教室の効果を客観的に評価するために，臨床美術教室で6カ月のカリキュラムを受講したDAT患者5名において，神経心理学検査としてMMSE, FAB，また気分評価として日本語版気分プロフィール検査POMS[4]を，6カ月のカリキュラム前後で検査し比較した．その結果，MMSEやFABでは有意な変化は見出せなかったものの，POMSにおいて，特にvigor(活力)のsubscoreでの改善が目立って認められた(図4)．

活力，意欲につながる脳活動をつかさどるのは主に前頭葉である．では創作活動によって実際にどのように前頭葉が賦活されるか，こうした前頭葉の動態を評価するのに，NIRSを用いた検査が有用であると考えた．NIRSとは，近赤外

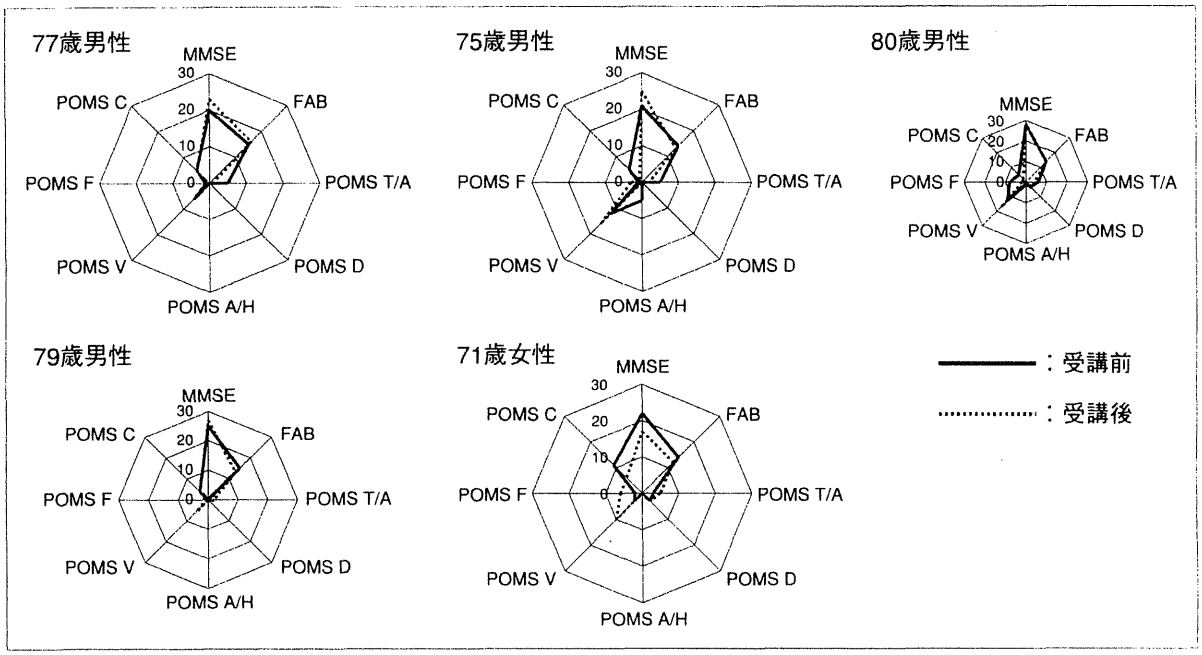

図4　認知症患者5名における神経心理検査および気分評価尺度検査の結果
6カ月間の臨床美術カリキュラム受講前後での変化を示す(前：実線，後：点線)．MMSE：Mini Mental State Examination，FAB：Frontal Ability Battery，POMS：日本語版気分プロフィール検査Profile of Mood States，T/A：tension & anxiety，D：depression & dejection，A/H：anger & hostility，V：vigor，F：fatigue，C：confusion.

光を用いて組織内Hb変化を動的かつ非侵襲的に測定し，「神経細胞の活動に比例して脳局所の血流量や代謝が増加する」というneurovascular coupling仮説に基づき，脳活動を画像化する手法である．脳活動のモニタリングにoxy Hbの上昇が重要であることはよく知られているが，脳賦活には多くの酸素代謝が必要であることからも容易に理解される．Functional MRIやPETとならんで近年注目される脳機能マッピングであり，精神神経科・脳外科領域で臨床応用もされている[3]．Functional MRIとは違って，簡便で検査時の自由度が高く，作業や描画の課題中の脳活動をみるのには適した検査といえる．

臨床美術が脳を活性化することはこれまで数々報告されている[5]が，われわれのNIRS検査では，臨床美術の受講中の描画で単純描画課題と比較して前頭葉のoxy Hbが上昇しており，前頭葉の脳活動を反映していると考えられる．対照実験として，データは提示していないが，若年健常者でも同様の課題で行い，前頭葉全般の脳活動の上昇が認められた．ただし，age-matched controlsとの比較は行っておらず，また，課題が再現性をもって反復できるものではないので，実際の脳賦活効果を評価するためにはさらなる方法論の検討が必要であると考える．

また，これまで臨床美術は，いわゆる「右脳」を活性化することが強調されてきた[5]．しかし，この場合の「右脳」は，直感や創造性，空間認識，イメージなどの中枢という意味であって，前頭葉の左右で機能局在と関連は明確ではない．今回のNIRS検査による検討でも，前頭葉は右優位ではなく両側の賦活がもたらされることが示唆された．ただし，functional MRIに比べNIRSでは優位半球を同定する感度は低いとの報告もある[6]．

さらに局在についてふれると，われわれのNIRS装置を用いた先行研究では，前頭葉機能課題を評価した際に，言語課題においても非言語課題においても同様に両側前頭葉，外側優位の賦活が示唆されている[7]．これは前頭前野，主に外側面の複雑な遂行機能を反映している[8]ものと考えられた．本検討では，内側外側にかかわらず両側前頭葉でoxy Hbの上昇が多くの症例でみられ，この描画体験で複雑な脳活動を要することが示唆される．むろん，絵を描く体験での喜びや達成感，あるいは出来映えに対して感じる違和感など，さまざまな情動をもたらすため，これら

を含めた脳活動の反映も考慮する必要がある．臨床美術の五感を使った描画体験を通じて，こうした前頭葉の活性化が，廃用性脳障害の予防やあるいは前に述べた活力の改善につながるのではないかと考える．認知症の脳活動低下に，臨床美術のような非薬物的治療のアプローチの有用性が期待される．

結　語

認知症に対する非薬物的介入としての臨床美術を紹介した．臨床美術受講中の認知症患者の前頭葉脳活動を近赤外線分光法(NIRS)装置で測定し，前頭葉全般の脳活動を捉えることができた．こうした前頭葉の活性化が，認知症の脳活動低下への介入につながるのではないかと考える．

当大学病院での取り組みと本報告に関し，「日本臨床美術協会」および「京都臨床美術をすすめる会」の皆様の多大なる協力に深謝する．なお，「臨床美術」は，日本臨床美術協会の登録商標である．

文　献

1) 日本臨床美術協会HP. 2013. Available from : URL : http://www.arttherapy.gr.jp/index.html.
2) 島津製作所HP. 2013. Available from : URL : http://www.med.shimadzu.co.jp/products/om/index. html.
3) 滝沢　龍，小池進介，高橋礼花，ほか．NIRSでみる精神疾患の前頭葉機能．神経内科 2009；71：286-94.
4) 横山和仁，荒記俊一．日本版POMS手引．東京：金子書房；1994.
5) 大橋啓一．認知症を予防・改善する臨床美術の実践—美術による地域福祉・社会貢献活動の展開！東京：日本地域社会研究所；2008.
6) 太田貴裕，鎌田恭輔，斉藤延人．非侵襲的言語優位半球同定法—fMRIとNIRSの比較検討—．神経内科 2009；71：278-85.
7) 丹羽文俊，近藤正樹，諫山玲名，ほか．近赤外線光分光法(NIRS)を用いた前頭葉機能検査におけるタスク項目の検討(会議録)．臨床神経 2010；50：1108.
8) 酒井　浩，加藤寿宏．注意制御課題実施時の前頭前野領域における血中ヘモグロビン濃度の変化—仮名拾いテストを用いた検討—．健康科学：京都大学医学部保健学科紀要 2006；3：7-15.

＜Abstract＞

Frontal lobe activation measured by near infrared spectroscopy during clinical art therapy for patients with dementia.

by
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Clinical art therapy for patients with dementia has been performed in our hospital. To evaluate the frontal lobe activation in patients with dementia, we examined frontal cerebral blood flow by near infrared spectroscopy (NIRS) in six patients with Alzheimer dementia, while asking them to draw an apple during the art therapy. As a result, the oxyhemoglobin signals increased dominantly on multiple channels in bilateral frontal cortex. NIRS demonstrated bilateral frontal cortex activity in patients with Alzheimer dementia during the art therapy sessions.

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Distribution of Amyloid Burden Differs between Idiopathic Normal Pressure Hydrocephalus and Alzheimer's Disease

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Key words: hydrocephalus, amyloid, positron-emission tomography, 11C-PIB

SUMMARY – *This study aimed to elucidate the incidence and distribution of the cortical retention of Pittsburgh compound B (PIB) in patients with idiopathic normal pressure hydrocephalus (iNPH) and clarify the differences from those in patients with Alzheimer's disease (AD). Ten patients with iNPH without any clinical signs indicative of AD were enrolled in this study. Cerebral retention of PIB in positron emission tomography (PET) in iNPH patients was compared with those in seven age-matched AD patients. The CSF levels of β-amyloid 1-42 peptide (Aβ42), which inversely decrease with cerebral amyloid burden, were also measured. Three of the ten patients with iNPH showed increased cortical PIB retention. Although the mean cortical SUV ratios were similar, the distribution of PIB retention differed widely between the patients with iNPH and AD. PIB retention was limited to the high-convexity parasagittal areas in iNPH patients, whereas it spread over the frontal and parietotemporal areas in AD. The coronal images of PIB-PET were more informative than conventional transverse images in evaluating the distribution pattern of cortical PIB retention. Two iNPH patients with higher cortical PIB retention had the lowest levels of CSF Aβ42, indicating that PIB retention in iNPH would not reflect a simple delay in PIB clearance but its binding to existing Aβ amyloid in the brain. Our results indicate that iNPH is one of the diseases exhibiting cortical PIB retention. The characteristic distribution of PIB retention in iNPH could be useful in the differential diagnosis between iNPH and AD.*

Introduction

Idiopathic normal pressure hydrocephalus (iNPH) causes gait disturbance, cognitive decline and urinary incontinence which can be ameliorated by shunt operation. One of the potential factors that may negatively influence shunt responsiveness is the presence of comorbidity, especially Alzheimer's disease (AD) that results in progressive dementia [1,2]. It is hence essential to make an accurate diagnosis on whether each patient with iNPH has comorbid AD.

Recently, positron emission tomography (PET) using ^{11}C-labeled radiotracer Pittsburgh compound B (PIB) has been widely applied for the in vivo assessment of amyloid-β (Aβ) deposition in patients with AD, with successful results [3,4]. It is thus conceivable that this PIB-PET study may be useful for the diagnosis of comorbid AD in iNPH patients. However, there remains a possibility that iNPH patients may also have PIB retention, since cortical Aβ deposition has been found in biopsied cortical tissues in 42-75 % of iNPH patients examined [2,5,6]. No previous study has investigated whether iNPH patients without comorbid AD may exhibit PIB retention. Thus, the aim of our study was to determine whether cortical PIB retention exists