The strength of our study is its random selection of our samples from people in the local community with very little bias in the process. NILS-LSA is one of the few major epidemiological studies investigating the aging mechanism that is designed to select subjects in a completely random manner. The results of this study should therefore reveal characteristics of the entire Japanese population.

In summary, we investigated the meaning of aBMD changes in aging through separate analyses of BMC and area change. The results revealed that the significance of aBMD changes were very divergent among the sites measured, and between sexes. This may explain the dissociation of aBMD change and bone strength, which encourages one to be more cautious when interpreting the meaning of aBMD change.

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EPIDEMIOLOGY

Relationship between Physical Activity and Brain Atrophy Progression

ATSUMU YUKI[1], SUNGCHUL LEE[1], HEUNGYOUL KIM[2], RUMI KOZAKAI[1,3], FUJIKO ANDO[4], and HIROSHI SHIMOKATA[1]

[1]*Department for Development of Preventive Medicine, Center for Development of Advanced Medicine for Dementia, National Center for Geriatrics and Gerontology, Obu City, Aichi Prefecture, JAPAN;* [2]*Department of Human Wellness, Tokaigakuen University, Miyoshi, Aichi Prefecture, JAPAN;* [3]*Gerontology Research Center, University of Jyvaskyla, Jyvaskyla, FINLAND; and* [4]*Department of Health and Medical Sciences, Aichi Shukutoku University, Nagakute, Aichi Prefecture, JAPAN*

ABSTRACT

YUKI, A., S. LEE, H. KIM, R. KOZAKAI, F. ANDO, and H. SHIMOKATA. Relationship between Physical Activity and Brain Atrophy Progression. *Med. Sci. Sports Exerc.*, Vol. 44, No. 12, pp. 2362–2368, 2012. **Introduction**: Brain atrophy is associated with impairment in cognitive function and learning function. The aim of this study was to determine whether daily physical activity prevents age-related brain atrophy progression. **Methods**: The participants were 381 men and 393 women who had participated in both the baseline and the follow-up surveys (mean duration = 8.2 yr). Magnetic resonance imaging of the frontal and temporal lobes was performed at the time of the baseline and follow-up surveys. The daily physical activities and total energy expenditures of the participants were recorded at baseline with uniaxial accelerometry sensors. Multiple logistic regression models were fit to determine the association between activity energy expenditure, number of steps, and total energy expenditure variables and frontal and temporal lobe atrophy progression while controlling for possible confounders. **Results**: In male participants, the odds ratio of frontal lobe atrophy progression for the fifth quintile compared with the first quintile in activity energy expenditure was 3.408 (95% confidence interval = 1.205–9.643) and for the number of steps was 3.651 (95% confidence interval = 1.304–10.219). Men and women with low total energy expenditure were at risk for frontal lobe atrophy progression. There were no significant differences between temporal lobe atrophy progression and physical activity or total energy expenditure. **Conclusion**: The results indicate that physical activity and total energy expenditure are significant predictors of frontal lobe atrophy progression during an 8-yr period. Promoting participation in activities may be beneficial for attenuating age-related frontal lobe atrophy and for preventing dementia.
Key Words: LONGITUDINAL STUDY, MIDDLE AGED AND ELDERLY, ACCELEROMETRY SENSORS, MRI

Atrophy of brain structures is associated with impairment in cognitive function and learning function (the extreme case is Alzheimer disease) (21). Brain atrophy progresses with aging (17). The gray matter volume decreases by approximately 15%, from the 20s through the 70s (38). A previous study reported that a decline in cognitive function is associated with the progression rate of brain atrophy for 6 yr in normal elderly people (33). Thus, preventing brain atrophy may be a promising strategy for preventing cognitive impairment and decline.

Physical exercise appears to induce neurogenesis in the brain not only in animals but also in humans (11). The practice of juggling for 3 months increases the volume of gray matter in the bilateral midtemporal area and in the left posterior intraparietal sulcus in young people (10). Similarly, the increase in brain volume in the anterior cingulate gyrus and frontal pole caused by juggling occurs in elderly people (3). In particular, aerobic exercise appears to suppress global and regional brain atrophy to effectively increase brain volume (14). Relatively little brain structural atrophy is seen in elderly people with high aerobic capacity (7). Six months of aerobic exercise increases the volume of the frontal lobe, temporal lobe, and hippocampus (8). Aerobic capacity is correlated with the preservation of gray matter in the medial–temporal, parietal, and frontal areas in elderly people (18). Aerobic quick-step walking suppresses hippocampal atrophy and improves cognitive function in elderly people (15). These reports suggest the possibility that aerobic exercise prevents brain atrophy.

Address for correspondence: Atsumu Yuki, Ph.D., Department for Development of Preventive Medicine, Center for Development of Advanced Medicine for Dementia, National Center for Geriatrics and Gerontology, 35 Gengo, Morioka, Obu city, Aichi prefecture, 474-8511, Japan; E-mail: ats.yuki.73@gmail.com.
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We hypothesized that brain atrophy progression can be prevented in middle-age and elderly people with a high level of daily physical activity. Daily physical activities are correlated with aerobic capacity in middle-age and elderly people (2,6). In cross-sectional studies, high physical activity levels are related to larger superior frontal volumes (5). Increased physical activity is associated with greater average brain tissue volumes in the white matter of the corona radiata, extending into the parietal–occipital junction (19). Although daily physical activities may prevent brain atrophy progression, there has been no specific longitudinal analysis showing that daily physical activity maintained at a high level prevents brain atrophy. Recent longitudinal studies have reported that elderly people with high levels of daily physical activity have a low risk of decline in cognitive function (26,34). A demonstration of the prevention of brain atrophy progression by high levels of physical activity in a longitudinal study may support the association between daily physical activity and cognitive function.

The aim of this study was to determine whether high levels of daily physical activity prevent brain atrophy progression with aging. We assessed the progression of frontal and temporal lobe atrophy with aging using 8-yr follow-up surveys and magnetic resonance imaging (MRI) of middle-age and elderly people. We also recorded the amount of physical activity (activity energy expenditure and number of steps) and total energy expenditure using a uniaxial accelerometry sensor. We evaluated the association between brain atrophy progression and daily physical activity and total energy expenditure in 774 community-living, middle-age, and elderly Japanese people using longitudinal analysis.

METHODS

Participants. The participants in this study were derived from the National Institute for Longevity Sciences, Longitudinal Study of Aging (NILS-LSA), which involves ongoing population-based biennial examinations of a cohort of approximately 2300 persons. The participants in the NILS-LSA were randomly selected from resident registrations and stratified by both decade of age and sex. The NILS-LSA is a comprehensive and interdisciplinary study to observe age-related changes and consists of various gerontological and geriatric measurements, including medical examinations, blood chemical analysis, body composition, anthropometry, nutritional analysis, psychological tests, physical function, and physical activity. Details of the NILS-LSA have been described elsewhere (35).

The baseline participants of this study were 1526 middle-age and elderly people (773 men and 753 women) who completed the second wave examinations of NILS-LSA between April 2000 and May 2002. Of these, 942 (61.6%, 481 men and 461 women) participated in the 8-yr follow-up surveys (NILS-LSA sixth wave examination from July 2008 to July 2010). The dropouts were 584 participants (292 men and 292 women). In male and female participants, the age at baseline of the dropouts was significantly higher than that of the participants who completed both examinations (*t*-test, $P < 0.0001$). In male participants, the ratios of stroke and ischemic heart disease histories in dropouts were significantly higher than those in participants who completed both examinations (chi-square test: stroke, $P = 0.0002$; ischemic heart disease, $P = 0.0019$). In female participants, there were no differences in the ratios of stroke and ischemic heart disease histories between the dropouts and the participants who completed both examinations. In male and female participants, the ratio of diabetes histories in dropouts was significantly higher than that in participants who completed both examinations (chi-square test: men, $P = 0.0077$; women, $P = 0.0369$). There were no differences in the ratios of hypertension and hyperlipidemia histories between the dropouts and the participants who completed both examinations in men or women. There were no differences in the ratios of severe atrophy in the frontal and temporal lobe between the dropouts and the participants who completed both examinations in men or women.

Participants with severe atrophy in the second wave examination were excluded because severe atrophy was of a high-end grade that cannot be used to determine further atrophy progression. Participants in their 40s were also excluded because few participants of this age show brain atrophy progression. Participants with a current medical history of Parkinson disease, dementia, or open head surgery were also excluded. Finally, the participants for this study were 381 men and 393 women.

The study protocol was approved by the Ethics Committee of the National Center for Geriatrics and Gerontology, and written informed consent was obtained from all participants.

Brain MRI examination. Brain MRI was performed on participants at the second and sixth wave examinations using a 1.5-T scanner (Toshiba Visart, Tokyo, Japan) at the National Center for Geriatrics and Gerontology. Each participant's head was oriented in the scanner and stabilized during the scanning procedure by a head support. To establish slice orientation, the first scanning sequence consisted of a T1-weighted sagittal series (repetition time (TR) = 500 ms, echo time (TE) = 15 ms, 256 × 256 matrix) centered along the midline to define the orbitomeatal line. The second series of T1-weighted axial images (TR = 500 ms, TE = 15 ms, thickness = 8 mm, gap = 1.5 mm, 256 × 256 matrix) and T2-weighted axial images (TR = 4000 ms, TE = 120 ms, thickness = 8 mm, gap = 1.5 mm, 320 × 320 matrix) were oriented parallel to the orbitomeatal line. Fourteen slices were taken during each examination.

The presence and the degree of brain atrophy in the frontal and temporal lobes were assessed as no atrophy (I), mild atrophy (II), moderate atrophy (III), and severe atrophy (IV) (25,36). The participants were divided into two groups on the basis of results from the MRI in the second wave examination and sixth wave examination: the brain atrophy progression group (progress: degree of brain atrophy in the second wave < sixth wave) and the brain atrophy non-progression group.

Daily physical activities and total energy expenditure assessments. We recorded the daily physical activities and total energy expenditures of the participants at the second wave examinations using a uniaxial accelerometry sensor (Lifecorder; Suzuken, Aichi, Japan). Lifecorder can assess two types of activity energy expenditure by activity level: energy expenditure of activities (with body movements) and energy expenditure of minor activities (working at a desk or reading a book). In this study, the activity energy expenditure was estimated as the energy expenditure of both types of activities. The total energy expenditure was determined as the sum of basal metabolism, energy expenditure of activities, energy expenditure of minor activities, and thermic effects of food. Participants wore the Lifecorder constantly (except while sleeping or bathing) for a 7-d period. We calculated the mean activity energy expenditure, the number of steps, and the total energy expenditure from 5 d of records (the maximum and the minimum records were excluded).

Other parameters. Body height and weight were measured using a digital scale. Body mass index (BMI) was calculated as weight divided by height squared ($kg \cdot m^{-2}$). Body fat mass was assessed by dual x-ray absorptiometry (QDR-4500A; Hologic, Bedford, MA). Lifestyle factors (including alcohol intake, smoking habit, and education levels), medical history, and use of medications were assessed with questionnaires. These questionnaires were confirmed by a physician at the medical examinations. All prescribed and nonprescribed medications used during the previous 2 wk were documented and brought by the participants; the physicians confirmed and coded them. Users of antihypertensive, antilipemic, or hypoglycemic medications were considered participants with hypertension, hyperlipidemia, and diabetes histories, respectively.

Statistical analysis. The results are shown as the mean ± SD or mean ± SE. Differences in continuous and class variables between the progression and the nonprogression groups were assessed with *t*-tests and chi-square tests, respectively. Cochran–Mantel–Haenszel statistics were used to examine the relationship between the age group and the brain atrophy progression. Multiple logistic regression models were fit to determine the associations of activity energy expenditure, number of steps, and total energy expenditure variables with frontal and temporal lobe atrophy progression while controlling for the baseline decade of age group (38), BMI (19), education history (19), medical history (stroke, ischemic heart disease, hypertension, hyperlipidemia, and diabetes) (4,12,24), and current smoking and alcohol intake as possible confounders (9,37). Activity energy expenditure, number of steps, and total energy expenditure were modeled as sex-specific quintiles. Statistical testing was performed using the Statistical Analysis System release 9.1.3 (SAS Institute Inc., Cary, NC). Significant probability levels were considered to be less than 0.05.

RESULTS

Characteristics of the participants. Table 1 shows elementary statistics of the study variables in male and female participants. The mean follow-up durations of all participants were 8.2 ± 0.3 yr. There were no significant differences in baseline age, BMI, or number of steps between male and female participants. Body height and weight, alcohol intake, and education history were significantly higher in male participants than those in female participants (each, $P < 0.0001$). The percentage of body fat in female participants was significantly higher than that in male participants ($P = 0.0126$). The activity and total energy expenditures in men were significantly higher than those in women (each, $P < 0.0001$). There were no sex differences in the ratios of stroke, ischemic heart disease, and hypertension histories. The ratio of hyperlipidemia history in female participants was significantly higher than that in male participants ($P = 0.0060$). The ratios of diabetes history and smoking habits in male participants were significantly higher than that in female participants (diabetes history, $P = 0.0126$; smoking habits, $P < 0.0001$).

TABLE 1. The characteristics of participants at the time of the second wave examination of the NILS-LSA, 2000–2002.

	Male (n = 381)	Female (n = 393)	P
Mean follow-up (yr)	8.2 ± 0.3	8.2 ± 0.3	0.5777
Age (yr)	60.4 ± 7.3	60.8 ± 7.6	0.5421
Body height (cm)	164.7 ± 5.4	152.2 ± 5.2	<0.0001
Body weight (kg)	62.5 ± 7.1	52.7 ± 7.0	<0.0001
BMI ($kg \cdot m^{-2}$)	23.0 ± 2.4	22.7 ± 2.9	0.1279
% body fat	21.0 ± 4.0	31.3 ± 4.9	<0.0001
Alcohol intake ($g \cdot d^{-1}$)	16.6 ± 20.9	2.7 ± 6.1	<0.0001
Education (yr)	12.3 ± 2.7	11.4 ± 2.3	<0.0001
Activity energy expenditure ($kcal \cdot d^{-1}$)	215.1 ± 78.5	175.1 ± 64.8	<0.0001
No. of steps per day	7993.2 ± 2588.0	7925.6 ± 2297.1	0.7011
Total energy expenditure ($kcal \cdot d^{-1}$)	1932.3 ± 168.5	1607.5 ± 150.0	<0.0001
With medical history, n (%)			
Stroke	14 (3.7%)	7 (1.8%)	0.1050
Ischemic heart disease	13 (3.5%)	19 (4.8%)	0.3203
Hypertension	40 (10.5%)	40 (10.2%)	0.8836
Hyperlipidemia	61 (16.0%)	94 (23.9%)	0.0060
Diabetes	32 (8.4%)	16 (4.1%)	0.0126
Smoking habit	102 (26.8%)	27 (6.9%)	<0.0001

Values are presented as mean ± SD. P values were obtained using the *t*-test for continuous data and the chi-square test for categorical data.

TABLE 2. The ratio of frontal and temporal lobe atrophy progression in participants from the second (2000–2002) to the sixth (2008–2010) wave examination of the NILS-LSA.

	Frontal Lobe Atrophy			Temporal Lobe Atrophy		
	Nonprogression	Progress	Trend *P*	Nonprogression	Progress	Trend *P*
Male, *n* (%)						
Age group						
50s	176 (95.1%)	9 (4.9%)	<0.001	156 (84.3%)	29 (15.7%)	<0.001
60s	112 (79.4%)	29 (20.6%)		87 (61.7%)	54 (38.3%)	
70s	38 (69.1%)	17 (30.9%)		38 (69.1%)	17 (30.9%)	
Total	326 (85.6%)	55 (14.4%)		281 (73.8%)	100 (26.3%)	
Female, *n* (%)						
Age group						
50s	191 (96.0%)	8 (4.0%)	<0.001	188 (94.5%)	11 (5.5%)	<0.001
60s	117 (90.0%)	13 (10.0%)		92 (70.8%)	38 (29.2%)	
70s	50 (78.1%)	14 (21.9%)		35 (54.7%)	29 (45.3%)	
Total	358 (91.1%)	35 (8.9%)		315 (80.2%)	78 (19.8%)	

The trend *P* values were obtained using the Cochran–Mantel–Haenszel test.

Progress of frontal and temporal lobe atrophy. Table 2 shows comparisons of the incidence of frontal and temporal lobe atrophy progression in each age group. Frontal lobe atrophy progression from the second wave examination to the sixth wave examination was present in 55 (14.4%) of 381 male participants and 35 (8.9%) of 393 female participants. The ratio of participants with frontal lobe atrophy progression in male participants was significantly higher than that in female participants ($P = 0.0213$). Aging raised the percentage of participants with frontal lobe atrophy progression in men and women (P trend <0.0001).

Temporal lobe atrophy progression from the second wave examination to the sixth wave examination was present in 100 (26.3%) of 381 male participants and 78 (19.8%) of 393 female participants. The ratio of participants with temporal lobe atrophy progression in male participants was significantly higher than that in female participants ($P = 0.0344$). Aging raised the percentage of participants with temporal lobe atrophy progression in men and women (P trend <0.0001).

Brain atrophy progression and physical activity level. Table 3 shows the activity energy expenditure, number of steps, and total energy expenditure in the frontal and temporal lobe atrophy progression and nonprogression groups. In the frontal lobe, activity energy expenditure ($P = 0.0095$), number of steps ($P = 0.0131$), and total energy expenditure ($P < 0.0001$) were significantly higher in the male nonprogression group than the progression group. In female participants, total energy expenditure was significantly higher in the nonprogression group than that in the progression group ($P = 0.0097$). There were no differences in the activity energy expenditure or number of steps between the female nonprogression and progression groups.

In the temporal lobe, there were no differences in the activity energy expenditure or number of steps between the nonprogression and the progression groups in male or female participants. The total energy expenditure was significantly higher in the nonprogression group than that in the progression group in male ($P = 0.0028$) and female ($P = 0.0096$) participants.

Risk of brain atrophy progression according to physical activity level differences. The results of multiple logistic regression analyses for risk of brain atrophy progression according to differences in the physical activity level in men and women are shown in Tables 4 and 5, respectively. In male participants, the odds ratio of frontal lobe atrophy progression for the comparison between the fifth quintile in activity energy expenditure and the first quintile was 3.408 (95% confidence interval (CI) = 1.205–9.643). The odds ratio of frontal lobe atrophy progression for the comparison between the fifth quintile in number of steps and the first quintile was 3.651 (95% CI = 1.304–10.219). The odds ratios of frontal lobe atrophy progression for the comparison between the fifth quintile in total energy expenditure and the first and third quintiles were 4.816 (95% CI = 1.037–22.376) and 4.639 (95% CI = 1.191–18.067), respectively.

In female participants, there were no significant differences between frontal lobe atrophy progression and physical activity parameters. The odds ratios of frontal lobe atrophy progression for the comparison between the fifth quintile in total energy expenditure and the first to the third quintiles

TABLE 3. Mean activity energy expenditure, number of steps, and total energy expenditure per day in each group.

	Frontal Lobe Atrophy			Temporal Lobe Atrophy		
	Nonprogression	Progress	*P*	Nonprogression	Progress	*P*
Male (*n*)	326	55		281	100	
Activity energy expenditure (kcal·d^{-1})	219.3 ± 4.4	189.7 ± 9.9	0.0095	217.3 ± 4.6	208.8 ± 8.1	0.3503
No. of steps per day	8128.0 ± 143.6	7194.3 ± 327.4	0.0131	7983.1 ± 155.1	8021.8 ± 256.6	0.8979
Total energy expenditure (kcal·d^{-1})	1947.0 ± 9.2	1845.22 ± 1.2	<0.0001	1945.6 ± 10.1	1895.0 ± 15.9	0.0097
Female (*n*)	358	35		315	78	
Activity energy expenditure (kcal·d^{-1})	176.4 ± 3.4	161.6 ± 10.1	0.1965	176.7 ± 3.7	169.4 ± 6.9	0.3664
No. of steps per day	7984.9 ± 121.8	7318.7 ± 365.6	0.1016	7997.4 ± 130.1	7699.5 ± 254.6	0.3043
Total energy expenditure (kcal·d^{-1})	1614.5 ± 7.9	1535.4 ± 21.8	0.0028	1616.5 ± 8.3	1567.7 ± 17.8	0.0096

Values are presented as means ± SE. The *P* values were obtained using the *t*-test.

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TABLE 4. Adjusted odds ratios of frontal and temporal lobe atrophy progression in male participants distributed into quintiles of physical activity and total energy expenditure data.

	Odds Ratio, 95% CI				
	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5
Frontal lobe (*n*)	76	76	76	76	77
Activity energy expenditure (kcal·d^{-1})	3.408, 1.205–9.643 (<143.2)	1.054, 0.321–3.462 (143.2 to <184.4)	1.623, 0.523–5.035 (184.4 to <226.2)	2.054, 0.691–6.904 (226.2 to <284.4)	1.00, referent (≥284.4)
No. of step per day	3.651, 1.304–10.219 (<5736.0)	1.216, 0.383–3.863 (5736.0 to <6955.0)	1.487, 0.471–4.689 (6955.0 to <8261.4)	2.403, 0.819–7.052 (8261.4 to <10,407.4)	1.00, referent (≥10,407.4)
Total energy expenditure (kcal·d^{-1})	4.816, 1.037–22.376 (<1771.4)	2.758, 0.652–11.672 (1771.4 to <1897.4)	4.639, 1.191–18.067 (1897.4 to <1983.4)	2.275, 0.553–9.358 (1983.4 to <2091.2)	1.00, referent (≥2091.2)
Temporal lobe (*n*)	76	76	76	76	77
Activity energy expenditure (kcal·d^{-1})	1.015, 0.473–2.178 (<143.2)	1.293, 0.617–2.708 (143.2 to <184.4)	0.800, 0.364–1.756 (184.4 to <226.2)	0.845, 0.390–1.833 (226.2 to <284.4)	1.00, referent (≥284.4)
No. of step per day	0.938, 0.435–2.024 (<5736.0)	1.100, 0.519–2.330 (5736.0 to <6955.0)	1.142, 0.538–2.425 (6955.0 to <8261.4)	1.123, 0.528–2.389 (8261.4 to <10,407.4)	1.00, referent (≥10,407.4)
Total energy expenditure (kcal·d^{-1})	1.045, 0.388–2.816 (<1771.4)	1.303, 0.554–3.065 (1771.4 to <1897.4)	1.229, 0.537–2.810 (1897.4 to <1983.4)	1.006, 0.439–2.307 (1983.4 to <2091.2)	1.00, referent (≥2091.2)

Odds ratios were controlled for age, BMI, education history, medical history (stroke, ischemic heart disease, hypertension, hyperlipidemia, and diabetes), current smoking, and alcohol intake in a multinomial logistic regression model.

were 12.363 (95% CI = 1.029–148.594), 12.743 (95% CI = 1.292–125.792), and 21.539 (95% CI = 2.381–194.839), respectively.

We also evaluated temporal lobe atrophy progression using the adjustment model, similar to the frontal lobe atrophy progression analysis. There were no significant differences between temporal lobe atrophy progression and physical activities or total energy expenditure (Tables 4 and 5) in any groups of participants.

DISCUSSION

Using longitudinal analyses, we showed that a high level of physical activity and total energy expenditure suppressed the frontal lobe atrophy progression that is induced by aging.

An inactive daily life appears to be a risk factor for frontal lobe atrophy progression. In male participants, those with the lowest activity energy expenditure (first quintile, <143.2 kcal) had a 3.408-fold risk of frontal lobe atrophy progression compared with those with the highest activity energy expenditure (fifth quintile, ≥284.4 kcal) (Table 4). Similarly, men with the fewest number of steps (first quintile, <5736.0 steps) had a 3.651-fold risk of frontal lobe atrophy progression compared with those with the most number of steps (fifth quintile, ≥10,407.4 steps) (Table 4). An activity energy expenditure of 143.2 kcal is equivalent to activity in 4 METs (e.g., raking the lawn and table tennis) for 33 min in 62.5-kg men (1). Thirty minutes of middle-intensity or greater activities per day, such as 5700 steps or more walking per day, may be necessary to reduce the risk of frontal lobe atrophy progression. In addition, daily physical activity decreases with aging (27). An increase in planned physical activities may be necessary to prevent frontal lobe atrophy progression in older people.

Not only the expenditure of energy with physical activity but also the energy metabolic rate of the whole body appears to be associated with frontal lobe atrophy. Low total energy expenditure tended to be a risk for frontal lobe atrophy in male and female participants (Tables 4 and 5). In a study of prosimians and anthropoid apes and humans, brain volume is correlated with basal metabolism (23). The amount of basal metabolism may determine frontal lobe atrophy progression. It is well known that basal metabolism decreases with aging (32). Age-related skeletal muscle loss (sarcopenia) may be a risk factor for frontal lobe atrophy progression due to decreasing basal metabolism. Physical activity may compensate for a reduction in basal metabolism in the elderly.

TABLE 5. Adjusted odds ratios of frontal and temporal lobe atrophy progression in female participants distributed into quintiles of physical activity and total energy expenditure data.

	Odds Ratio, 95% CI				
	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5
Frontal lobe (*n*)	78	79	78	79	79
Activity energy expenditure (kcal·d^{-1})	1.442, 0.421–4.945 (<119.6)	1.422, 0.435–4.644 (119.6 to <148.4)	0.610, 0.148–2.520 (148.4 to <182.8)	1.233, 0.362–4.199 (182.8 to <226.4)	1.00, referent (≥226.4)
No. of step per day	1.559, 0.420–5.791 (<5825.2)	2.269, 0.627–8.209 (5825.2 to <7090.0)	0.826, 0.181–3.769 (7090.0 to <8374.0)	1.887, 0.505–7.053 (8374.0 to <9910.4)	1.00, referent (≥9910.4)
Total energy expenditure (kcal·d^{-1})	12.363, 1.029–148.594 (<1495.6)	12.743, 1.292–125.792 (1495.6 to <1570.2)	21.539, 2.381–194.839 (1570.2 to <1639.6)	4.261, 0.430–42.214 (1639.6 to <1722.0)	1.00, referent (≥1722.0)
Temporal lobe (*n*)	78	79	78	79	79
Activity energy expenditure (kcal·d^{-1})	0.978, 0.362–2.645 (<119.6)	1.023, 0.400–2.614 (119.6 to <148.4)	1.569, 0.591–4.162 (148.4 to <182.8)	1.547, 0.617–3.876 (182.8 to <226.4)	1.00, referent (≥226.4)
No. of step per day	0.879, 0.355–2.178 (<5825.2)	0.789, 0.311–2.005 (5825.2 to <7090.0)	0.825, 0.317–2.147 (7090.0 to <8374.0)	1.206, 0.489–2.974 (8374.0 to <9910.4)	1.00, referent (≥9910.4)
Total energy expenditure (kcal·d^{-1})	0.881, 0.260–2.984 (<1495.6)	1.127, 0.405–3.138 (1495.6 to <1570.2)	0.948, 0.337–2.668 (1570.2 to <1639.6)	1.285, 0.499–3.305 (1639.6 to <1722.0)	1.00, referent (≥1722.0)

Odds ratios were controlled for age, BMI, education history, medical history (stroke, ischemic heart disease, hypertension, hyperlipidemia, and diabetes), current smoking, and alcohol intake in a multinomial logistic regression model.

Although a low-activity energy expenditure and a low number of steps were risk factors for frontal lobe atrophy progression in male participants, they were not risk factors in female participants (Tables 4 and 5). Generally, there are many more men with brain atrophy than women (38). In this study, the ratios of frontal lobe atrophy progression were different between male and female participants (Table 2). Sex hormones may also affect the relationship between physical activity and frontal lobe atrophy. Androgens and estrogens are associated with brain volume (13,24), and the adaptability of the brain to physical activity may be higher in men than that in women.

In contrast to activity energy expenditure, total energy expenditure was associated with frontal lobe atrophy progression in both men and women. Basal metabolism is the maximal occupation ratio in total energy expenditure. The brain metabolic rate is included in the basal metabolism. In women, total energy expenditure including basal metabolism appears to be a better index of the risks for frontal lobe atrophy progression compared with physical activity parameters. However, because some of the odds ratios were exceedingly large in female participants, our logistic regression model may not have precisely estimated the risk of frontal lobe atrophy. There were 55 male participants with frontal lobe atrophy progression (Table 2), but only 35 female participants had frontal lobe atrophy progression (Table 2). These sex differences in the brain atrophy progression rate may have influenced estimation of the odds ratio. In women in particular, further investigations may be needed to determine the association of frontal lobe atrophy progression with total energy expenditure.

Brain atrophy is caused in part by obesity (19), metabolic syndrome, and its components (4,12). A high level of physical activity improves obesity and metabolic syndrome (29). Cross-sectional research suggests that prevention of obesity by physical activity causes the relationship between physical activity and brain volume (19). However, in this study, frontal lobe atrophy progression was associated with the physical activity level in logistic regression models that controlled for BMI. Physical activity or the total energy expenditure may be independent factors for preventing frontal lobe atrophy progression, regardless of obesity.

In this study, the activity energy expenditure, the number of steps, and the total energy expenditure were quantitative data collected by an accelerometer. The objectivity of our study is higher than that of past studies that estimated the physical activity level with a questionnaire (5,19).

A limitation of this study is the noninvasive approach using MRI. We could not elucidate the mechanism of frontal lobe atrophy progression induced by a low level of physical activity or total energy expenditure. In an animal study, the beta amyloid cumulative dose is active mass dependent in mouse brain (22). The death of neurons may be inhibited by physical activity. Some growth factors, such as nerve growth factor or brain-derived neurotrophic factor, contribute to neuronal survival or neurogenesis (31,39). The serum level of nerve growth factors fluctuates with physical exercise (16), and thus, exercise stimulus with physical activity may modify expression of nerve growth factors.

Exercise and physical activity have been reported to change the volume of every region of the brain, including the frontal lobe, the temporal lobe, the parietal lobe, and the hippocampus (3,5,8,19). Interestingly, our results showed associations between brain atrophy progression and physical activity or total energy expenditure only in the frontal lobe, but not in the temporal lobe. We hypothesize that the regional differences in brain atrophy progression were due to differences in the patterns of physical activities (including types, intensities, or frequencies). A previous study suggests that increased blood flow in the brain due to physical exercise promotes neurogenesis (30). Blood flow in the brain varies with exercise type and intensity (20,28). In this study, because the activity energy expenditure, the number of steps, and the total energy expenditure data were collected as the total amount per day with accelerometer sensors, the differences in the patterns of physical activities between participants were not determined. Further investigations that define these details may clearly uncover an association between physical activities and regional differences in brain atrophy progression.

In summary, using the longitudinal design of the NILS-LSA cohort, we evaluated the association between brain atrophy progression and daily physical activity and total energy expenditure in 774 community-living, middle-age, and elderly Japanese people with an 8-yr follow-up duration. Our data confirm that low levels of physical activity and total energy consumption are significant predictors of the risk for brain atrophy, and the effect of atrophy suppression is seen only in the frontal lobe. Promoting participation in physical activities may be beneficial in attenuating age-related frontal lobe atrophy and in preventing dementia.

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The authors report no conflict of interest.

The results of the present investigation do not constitute endorsement by the American College of Sports Medicine.

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第53回日本老年医学会学術集会記録
〈若手企画シンポジウム2：サルコペニア―研究の現状と未来への展望―〉

1. 日常生活機能と骨格筋量，筋力との関連

下方　浩史　　安藤富士子

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1. 日常生活機能と骨格筋量，筋力との関連

下方　浩史[1)]　安藤富士子[2)]

要　約　サルコペニアは高齢者の日常生活機能を低下させ，健康長寿の障害となる．われわれは無作為抽出された地域在住中高年者コホートのデータを使用して，日常生活機能と筋力，筋量との関連について検討した．男女ともに40歳以降，握力，下肢筋力は年間約1パーセントずつ低下していた．どの年代でも男性は女性よりも筋力が強く，80代の男性の筋力は40代の女性の筋力にほぼ等しかった．筋力の低下は女性の日常生活機能により大きな影響を与える可能性がある．一方，四肢の筋量は男性では加齢とともに低下するが，女性では加齢による低下はほとんどなかった．このことは女性では筋肉の量的な変化よりも，質的な変化が問題になっていることを示している．日常生活機能は筋肉のパフォーマンスの影響を受け，握力と歩行速度で推定することが可能であった．高齢者の脆弱を予防するためには，これらの評価によりハイリスクの集団を見つけることが重要であろう．

Key words：サルコペニア，日常生活機能，筋量，筋力，老化

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はじめに

老化に伴う筋量減少（サルコペニア）は，高齢者のADLを低下させ，健康長寿を実現の大きな障害となる[1)2)]．しかし，老化に伴う筋量減少の実態は明らかでなく，またサルコペニア自体の簡便な基準がない．臨床の現場や住民調査などで使用できる簡便なサルコペニアの基準が必要である．これらの検討を一般住民のコホートのデータを使用して行った．

研究方法

対象は「国立長寿医療研究センター・老化に関する長期縦断疫学研究（NILS-LSA）」第5次調査参加者で，40歳から88歳までの無作為抽出された地域在住中高年者2,419名（男性1,200名，女性1,219名）である[3)]．上腕囲，臍高腹囲，大腿囲，下腿囲を身体指標として計測し，また体力の指標として，普通歩速度，速歩速度，上体起こし，膝伸展筋力，脚伸展パワー，握力を計測した．日常生活機能として健康関連QOL尺度であるSF36の身体機能項目を用いた．サルコペニア指標として，Dual-energy X-ray absorptiometry（DXA）（QDR 4500, Hologic）によって四肢除脂肪・除骨重量測定し，これを四肢筋量とした．Baumgartnerら[1)]の方法に準じ，四肢筋量（kg）を身長（m）の二乗で除した値をSkeletal Muscle Index（SMI）とし，サルコペニアの指標とした．その判定基準には同じQDR 4,500で測定したSanadaら[4)]によるYAM（Young Adult Mean：18～40歳）の－2SD（男性6.87 kg/m^2，女性5.46 kg/m^2）を用いた．

サルコペニアの性・年代別頻度

DXAによるSMIでの診断基準で求めたサルコペニアの有無を，性・年齢別の分布をみた（図1）．男性では25.0パーセントが，女性では24.2パーセントがサルコペニアであり，全体の割合には性差はなかった．年代別の検討では，男性では加齢とともにサルコペニアの頻度は高くなっていたが（p trend<0.0001），女性では有意な加齢変化はなかった．男性のSMIの平均値±SDは7.42±0.83 kg/m^2，女性は5.96±0.73 kg/m^{2}であり，男性の方が有意に高い値であった（p<0.0001）．男性では加齢とともにSMIは低下していたが（p trend<0.0001），女性では有意な加齢変化はなかった．男女ともに年齢が高いほど握力は低下していた（p trend<0.0001）．男性の方が低下率は大きかったが，80代でも女性の40代の握力よりも大きかった．膝伸展筋力についても握力と同様に，

1) H. Shimokata：国立長寿医療研究センター予防開発部
2) F. Ando：愛知淑徳大学健康医療科学部スポーツ・健康医科学科

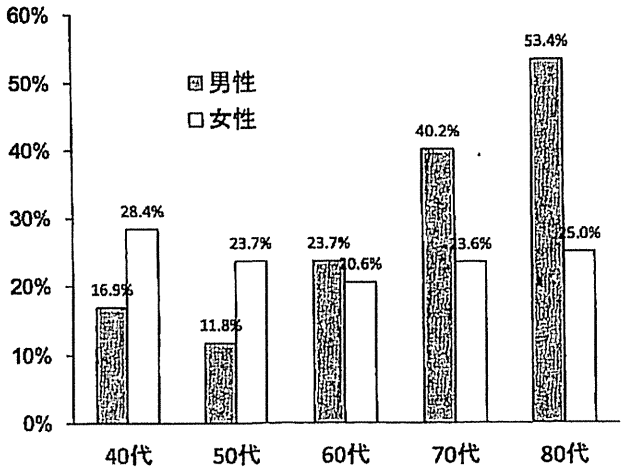

図1　サルコペニアの性・年代別頻度
DXAによるSMIでの診断基準（YAMの－2SD）での判定を行った．男性では加齢とともにサルコペニアの頻度は高くなっていたが（p　trend<0.0001），女性では有意な加齢変化はなかった．

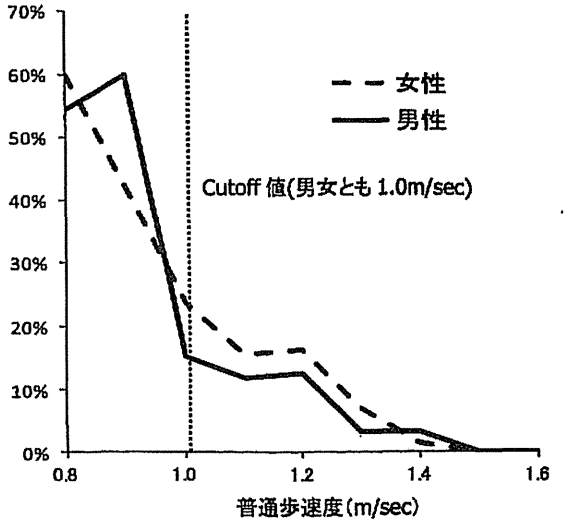

図2　普通歩速度と数百メートル以上歩くことに困難を感じる割合（65歳以上）

男女ともに加齢とともに低下していた．男性の方が低下率は大きかったが，男性の80代でも女性の40代とほぼ同じ値であった．

SMIに影響を与える変数を求めるとともに，SMIを推定するための簡便な式の作成を行うために，SMIと身体測定値，アルブミンとの相関解析を行った．SMIは上腕囲，下腿囲，大腿囲，腹囲BMIと強い正の相関があったがアルブミンとは相関はなく，体脂肪率とは弱い正の相関が認められた．SMIと最も相関が強かったのはBMIであり，相関係数は男性で0.77，女性で0.73と高かった．周囲長では女性で下腿囲が最も相関が強く，男性では上腕囲，下腿囲，大腿囲で相関係数はほぼ同じ値となった．

65歳以上の男女について，年齢，BMI，下腿からSMIを推定する重回帰式の作成を試みた．その結果，以下の回帰式を得ることができた．

男性：SMI＝－0.1026×年齢＋0.1341×BMI＋0.6034×下腿囲＋2.5653（r^2＝0.651）

女性：SMI＝－0.0413×年齢＋0.0513×BMI＋0.4438×下腿囲＋0.5509（r^2＝0.558）

骨格筋量，筋力と日常生活機能

65歳以上の男女についてサルコペニアの有無とSF36での身体機能との関連を検討した．男性では一部の項目でサルコペニアがあると身体機能は低下していたが，その差は大きくなかった．女性ではサルコペニアによる身体機能の有意な低下はなかった．身体機能の障害の有無とSMIとの関連については，男性では身体機能の障害の有無によるSMIの差はいくつかの項目で認められたものの，その差はそれほど大きくはなかった．女性では身体機能の障害の有無によるSMIの差はほとんどなかった．

65歳以上の男女について，身体機能と歩行や筋力などの体力との正準相関係数を求めて，体力のどの項目が身体機能と関連しているのかを検討した．その結果，男女とも普通歩速度が身体機能にもっとも関連しており，筋力では脚伸展パワーの影響が男性でもっとも大きかったが，握力は男女ともに身体機能に大きな影響が与えていた．

一般住民で日常生活に影響が出るような障害は，SF36の中強度の身体活動項目に困難を感ずる障害と考え，中強度の項目のうち「数百メートル以上歩くこと」を身体機能の指標とすることとした．「数百メートル以上歩くこと」が困難になれば，日用品の買い物にも支障が生じ，独立した生活を送ることが困難となる．体力，身体計測値がどの程度まで低下すると身体機能が低下するのか，身体機能との関連が認められた項目のうち，簡便に測定できるものについてカットオフ値を求めた．図2に示すように，普通歩速度は男女ともに1 m/secよりも遅くなると身体機能が低下する割合が大きく増加した．握力に関しては，普通歩ほどカットオフ値ははっきりしなかったが，男性で25 kg，女性で20 kgをカットオフ値とした．身体計測値については，女性ではSMIが低い部分でのカットオフ値は決められなかった．男性ではカットオフ値は5.5 kg/m^2であった．BMIは女性では値

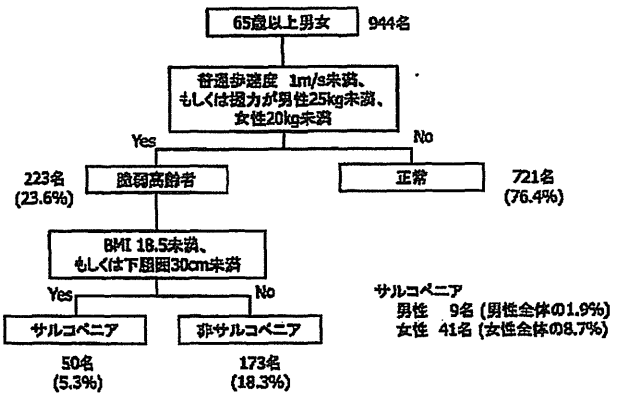

図3　サルコペニアの簡易基準案と，一般住民での分布

が小さいほど，つまりやせているほど身体機能は良くなっており，カットオフ値は決められなかったが，男性では19 kg/m²がカットオフ値であった．下腿囲も同様に女性ではカットオフ値は決められなかったが男性では30 cmであった．

サルコペニアの簡易基準の作成

サルコペニアの簡易基準の作成は，体力や身体計測値から中強度の身体機能に支障が生じる可能性のある集団を捉えることを目指した．判定に使用する項目は，簡便な器具で簡単に測定できるものとした．さらに，Muscle performanceとmuscle volumeを分けて考えることとし，Muscle performanceは普通歩速度と握力で評価し，Muscle volumeは測定に高額で放射線被曝を伴う機器が必要なSMIの代わりにBMIと下腿囲で評価することとした．また，各指標のカットオフ値は中強度の身体機能との関連で決めることとし，女性で上記の基準で決められない場合には，従来のやせの基準値や男性の値を参考に決めることとした．

European consensus[5]によるサルコペニアの簡易基準を参考に，日本人高齢者におけるサルコペニアの簡易基準の作成を試みた．図3に示すように，まず普通歩速度1 m/sec未満，もしくは握力が男性25 kg未満，女性20 kg未満である場合には脆弱高齢者と判断し，脆弱高齢者のうち，BMI 18.5 kg/m²未満もしくは下腿囲30 cm未満である場合をサルコペニアとした．

今回の検討での対象者についてこの基準を当てはめてみると，65歳以上の男女944名のうち23.6パーセント(223名)が脆弱高齢者であり，さらに全体の5.3パーセント(50名)がサルコペニアと診断された．その内訳は男性9名(男性全体の1.9パーセント)，女性41名(女性全体の8.7パーセント)と女性で割合が高くなっていた．

ここに示したサルコペニアの簡易基準案は，身長，体重，握力計とメジャー，ストップウォッチがあれば実施することができる．スクリーニング検査として有用と思われるが，さらに縦断的なデータを用いて，妥当性の検討を行っていきたい．

ま と め

40歳以上の地域住民2,419名を対象としたDXAによる判定では男性の25.0パーセントが，女性の24.2パーセントがサルコペニアに分類された．男性では加齢とともにサルコペニアの割合は増加していたが，女性では加齢による変化はなかった．サルコペニアの簡易基準の作成は，体力や身体計測値から中強度の身体機能に支障が生じる可能性のある集団を捉えることを目指した．その結果，普通歩速度1 m/sec未満もしくは握力が男性25 kg未満，女性20 kg未満である場合には脆弱高齢者と判断し，脆弱高齢者のうちBMI 18.5 kg/m²未満もしくは下腿囲30 cm未満である場合をサルコペニアとした．65歳以上の男女の5.3パーセントがサルコペニアとされた．

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Association of daily physical performance with muscle volume and strength

Hiroshi Shimokata[1] and Fujiko Ando[2]

Abstract

Sarcopenia disturbs the daily life of elderly people, and hinders healthy aging. We studied the association of daily physical performance with muscle volume and muscle strength in a randomly selected community-living population. Results: Grip power and leg muscle strength decreased about 1% per year after age 40 in both men and women. Muscle strength was greater in men than in women at every age by decade, and muscle strength in men in their 80s was similar to that in women in their 40s. Therefore, the effect of a decrease in muscle strength on daily physical performance was greater in women than men. On the other hand, the muscle volume of all limbs decreased with age in men, but there was almost no decrease in muscle volume in women. These results indicate that qualitative change in muscle was more significant than quantitative change in muscle in women. Daily physical performance was influenced by muscle performance and could be assessed based on grip power and walking speed. To prevent frailty, it may be important to determine the high-risk group for frailty using these assessments.

Key words: *Sarcopenia, Daily physical performance, Muscle volume, Muscle strength, Aging*
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1) Department for the Development of Preventive Medicine, National Center for Geriatrics and Gerontology
2) Faculty of Health and Medical Sciences, Department of Sports and Health Sciences, Aichi Shukutoku University

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認知症の実態と予防の重要性

下方 浩史　　安藤 富士子

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第18回日本未病システム学会学術総会

●シンポジウム4「認知症予防の最前線—現在そして将来，どこまでできるか—」

認知症の実態と予防の重要性

下方　浩史[1)]
安藤　富士子[2)]

1. はじめに

認知症にはまだ根本的な治療はなく，病状は長期にわたって慢性に進行して重症に至ることが多い．進行すると徘徊や暴力などの問題行動もみられ，末期には寝たきりとなり，誤嚥性肺炎や褥創などの合併症も生じて，経済的，社会的な負担がきわめて多い．認知症の出現頻度は高齢になるほど高くなるので，わが国の社会の高齢化に伴って今後急速に患者数が増大し，介護や医療への費用負担が急騰することが予想される[1-5]．このため，認知症罹患の実態を把握し，認知症の予防を目指すことはわが国にとっての緊急の課題となっている．

2. 認知症の有病率

認知症の有病率や罹患率に関しての疫学統計が，今後の医療費予測や高齢者の介護・福祉のあり方，医療政策に関して，重要な意味を持つと思われる．しかし，今まで認知症の疫学調査は十分には行われてこなかった．それは認知症という疾患の持つ特殊性により，調査に多くの困難を伴うためである[1-4]．

認知症の有病率は比較的低いので正確な統計データを得るためには対象人数を多くしなければならない．65歳以上の高齢者は日本全体では現在約3,000万人であり，推定有病率の1％の違いが患者数推計では30万人の差となる．例えば，有病率15％を14～16％の信頼区間で得るためには4,898名の対象者が必要である．また，アルツハイマー病，血管性認知症，レビー小体型認知症，前頭側頭葉脳変性などの病型別有病率についての検討を加えるためには，さらに多くの対象者が必要である．

認知症の診断を行うためには専門的知識が必要であり，場合によってはMRIやPETなどの検査や剖検が診断のためには必要となる．認知症患者やその家族は調査に対して消極的なことが多い．認知症は高齢者に多いため，身体機能の低下を認める者が少なくなく，訪問による検査などが必要で，実際の調査が思うようにいかないことも多い．また，認知症の有病率を調べる場合，調査地域の高齢者の年代分布によって有病率が異なる可能性がある．地域在住者を調査しても，問題行動のある認知症患者は施設に入所しているために，有病率が低く出てしまうことも考えられる．

認知症の有病率については1970年代から全国のさまざまな地域において疫学調査が行われてきたが，調査は県や市町村の地域ごとに行われており，最近まで全国規模での調査は行われていなかった．日本初の全国調査は，厚生労働省認知症対策総合事業「認知症の実態把握に向けた総合的研究」として実施された[6)]．まず2009年から2010年にかけて全国7ヵ所で65歳以上の住民を対象として行われた（図1）．訪問調査員による1次調査と専門医による2次調査を基本として，さらに頭部MRIによる脳萎縮や血管性病変の評価なども行い，精度の高い診断を目指した．全国での調査結果から2008年の日本の人口を基準にして推定された有病率は12.4～20.2％（平均14.4％）であった．2008年度の65歳以上の全国人口2,822万人から，認知症患者数は406万人と推定された．しかし，施設入所者などを加えればこれよりも患者数はさらに多い可能性がある．従来の方法での患者数推計では208万人とされていたが，患者数は少な

1)（独）国立長寿医療研究センター予防開発部　2) 愛知淑徳大学健康医療科学部スポーツ・健康医科学科

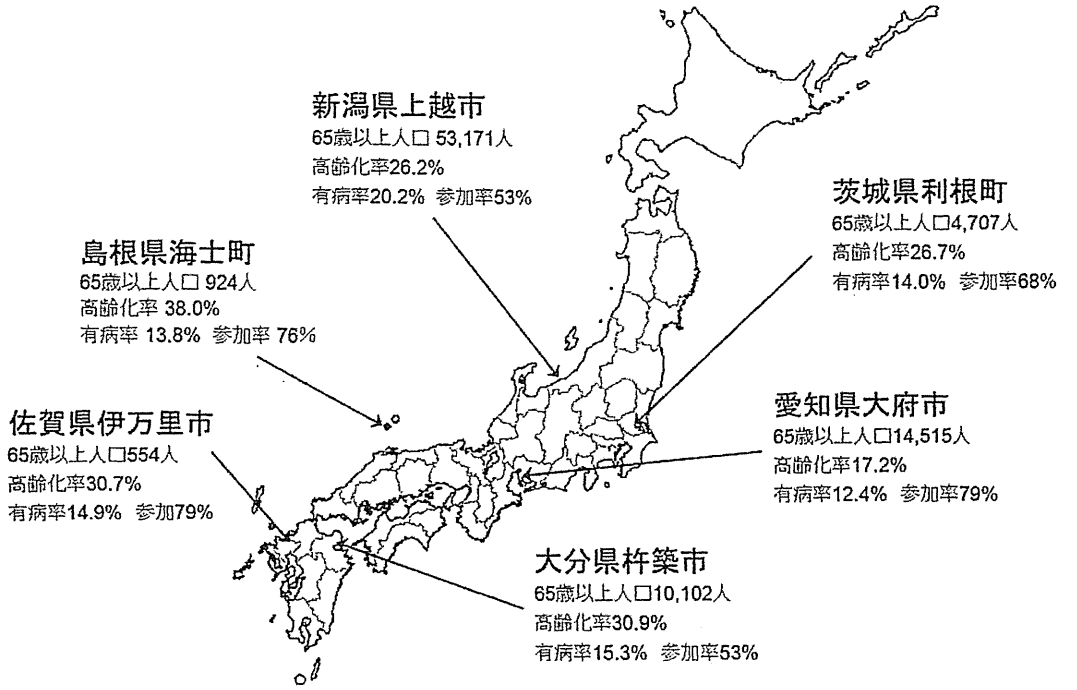


図1　認知症有病率全国調査結果（2008年度日本全国の人口構成に基づく）

くともその約2倍存在することになる．

3. 認知症の発症率

発症率を推定するためには，同一対象集団について複数年にわたっての繰り返しの調査が必要であり，有病率の推定よりも難しく，わが国の疫学調査の結果では認知症の発症率の推定はほとんど行われていない．われわれは，無作為抽出された地域住民を長期にわたって追跡した「国立長寿医療研究センター・老化に関する長期縦断疫学研究（NILS-LSA）」[7]のデータを用いて8年間の縦断的な検討から認知症の発症率の推定を行った（図2）．その結果では，60歳以上の地域住民の1.5％が毎年認知症となっていた．年齢が高くなるほど発症率は上昇し，80歳以上では毎年3.9%が認知症となっていたという結果であった．

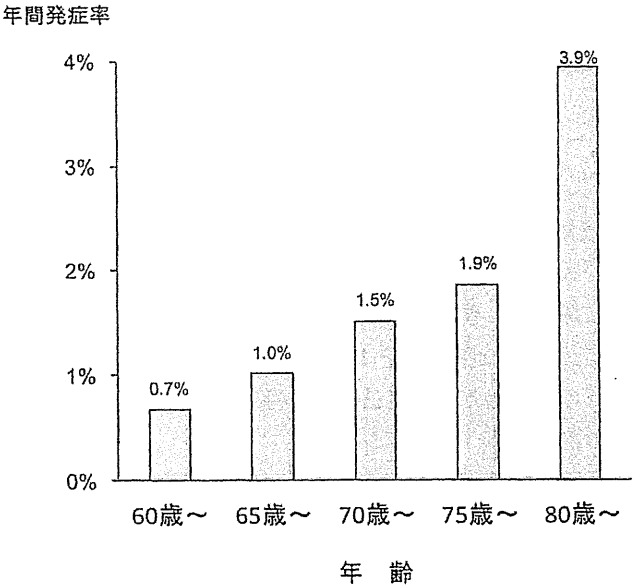


図2　認知症の年間発症率（「国立長寿医療研究センター・老化に関する長期縦断疫学研究（NILS-LSA）」の8年間の縦断的観察から）

4. 将来推計

人口の高齢化に伴う認知症患者数の将来推計を行ってみた．性別・年齢別の認知症有病率は今回の全国調査の結果を用い，人口推計は国立社会保障・人口問題研究所の平成24年度1月推計を用いた．2010年度の65歳以上の認知症推定患者数は全体として415万人で，

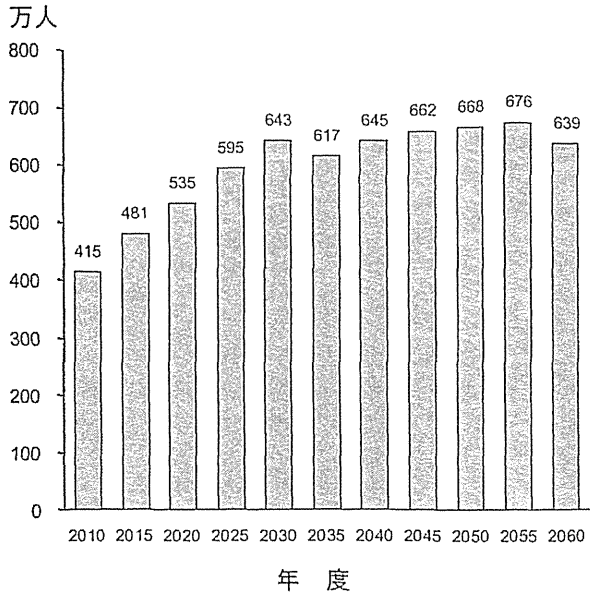


図3 認知症患者数の将来推計（人口推計は国立社会保障・人口問題研究所の平成24年度1月推計を用いた）

有病率は約14.1パーセントであると推定される．今後，高齢者人口，特に後期高齢者の人口が急増し，患者数は2020年度に535万人，2030年度には643万人と，これからの20年間にアルツハイマー病の患者数は1.5倍に大きく増加すると予測される（図3）．

5. 認知症の経過と予後に関する統計

認知症は長期にわたって慢性に進行していくことが多い．このことが社会に大きな負担となる要因のひとつである．わが国の在宅認知症患者の5年後生命予後調査では，66％～86%の生存率が報告されており[3]，認知症の発症から死亡までの全経過は現在のところ7年から10年程度だと思われる．米国での認知症患者の大規模な追跡調査では，発症からの生存年数は10.5年，診断からの生存年数は5.7年であった[8]．他の研究でも認知症患者の診断後の生存年数は5年から9年であった[9-12]．米国の国立老化研究所（NIA）からの報告では，生存期間は年齢によっても大きく異なり，75歳までに診断されたアルツハイマー病患者の生存年数は診断後7年から10年であったが，85歳以降に診断された場合は3年未満の生存期間であった[13]．しかし今後，介護技術，医療の進歩により死亡までの期間は長くなっていくと思われる．

6. 認知症予防とのその重要性

世界有数の長寿の国であるわが国は急速に高齢化が進み，それとともに認知症患者の数も増大していく．今後15年間で認知症にかかわる介護費用は大きく増加し，年間10兆円に達するとも予想される．高齢化が進む一方で，少子化も進み，介護にかかわることのできる労働人口は激減する．このままでは認知症によって日本の社会が崩壊すると言っても過言ではない．認知症を予防していくことが，今後の日本にとっては極めて重要であろう．

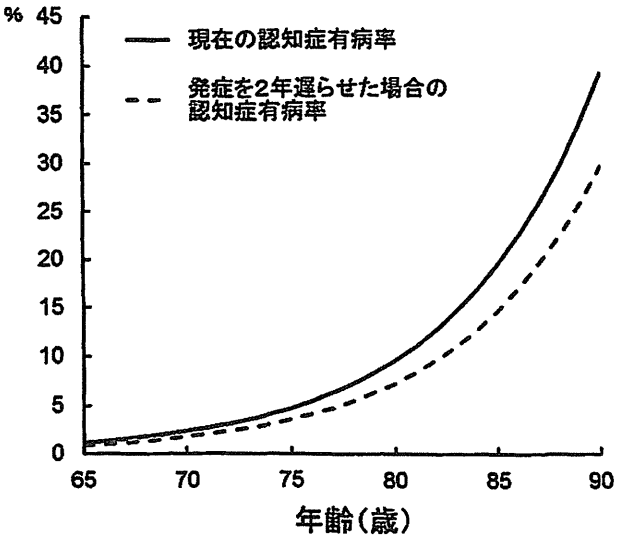
アルツハイマー病予防の切り札としてワクチンの開発が進められている．ワクチンはアルツハイマー病を引き起こすアミロイドβ蛋白の蓄積を予防するような作用を持つとされるが，脳炎などの重篤な副作用も報告されている[14]．また中年以降ではすでにアミロイドβ蛋白は蓄積されてしまっており，ワクチンは30歳以前に使用しなければ効果はないという．たとえワクチンが開発されたとしても，50年後の認知症発症を予防するために，有効性が不明でしかも脳炎などの副作用のリスクがあるワクチンを若者が使用するかどうかは疑問である．

認知症は生活習慣病でもあり，生活習慣の改善である程度の予防が可能である．生活習慣は血管性認知症だけでなくアルツハイマー病の発症と関連している可能性がある．特に食事は毎日の生活の中で繰り返され，影響が大きい．認知症の予防にはビタミンE，ビタミンC，カロテノイドのような抗酸化ビタミンが有用であり，中でも抗酸化作用を持つビタミンEが期待される[15,16]．葉酸やビタミンDの認知症予防作用も明らかにされてきている[17,18]．多価不飽和脂肪酸，特にn-3系のドコサヘキサエン酸（DHA），エイコサペンタエン酸（EPA）は認知症の予防に有用であり[19,20]，またアラキドン酸についても有用性の研究が進んでいる[21]．食事のパターンとしては野菜や魚類をバランス良く摂ることが重要である．適度な飲酒，特にワインが認知症の予防に有用であり[22]，喫煙は多くの研究で認知症の危険因子となることが報告されている[23]．運動によって認知症やアルツハイマー病のリスクを下げることは多くの論文で報告されている[24]．運動が糖尿病，脂質異常症，高血圧症を

予防し，その結果，動脈硬化の進行を遅らせて認知症の発症リスクを下げると考えられるが，運動自体が脳神経のネットワーク機能を強化し，認知症の発症を防ぐという直接的な効果も推測されている．

認知症の素因としての遺伝子多型の研究も進み始めている．しかし危険因子間の相互作用，特に遺伝子と生活習慣との相互作用についてはほとんど研究が進んでいない．例えば食塩の摂取により血圧が高くなる遺伝子多型は，塩分感受性遺伝子多型として知られている．特定の遺伝子多型を持つ人は塩分を多く摂ると高血圧症になりやすく，それが認知症のリスクとなる．このような遺伝子多型とライフスタイル，環境因子との相互作用は数多い．認知症に関連する遺伝子多型は直接に認知症を引き起こすわけではなく，むしろライフスタイルや環境因子の影響を修飾することで認知症の発症に関与するものと考えられる．特定の遺伝子多型の認知症発症寄与率は集団全体の生活習慣などによって異なると考えられ，このために集団が異なれば結果も異なることになり，遺伝子多型の影響について一定の結果が得られにくい．こうした，危険因子相互の作用について明らかにしていくには，大規模な一般住民で追跡を行い，生活習慣や認知機能の変化を継続的に観察する縦断的研究が必要である[25]．

医薬品の開発などで認知症の発症を完全に予防できなくても，仮に2年間だけでも遅らせるようなことが出来れば，各年齢の認知症の有病率は，2歳若い年齢に相当する有病率になると期待できる（図4）．65歳以上の全人口に対して，実際の年齢よりも2歳若い年齢の有病率を使って患者数を計算すると期待患者減少数は33万人，医療費削減効果は2,000億円，介護費用削減効果は7,700億円となる．さらに，家族が介護のために職につけなかったり，本人が病気のため社会参加が出来なかったりした損失も加えると合計の費用削減効果は，年間約2兆円にも達する．こうした経済的な効果を考えると，認知症性疾患の基礎研究，臨床研究へのわが国における研究費の支出は驚くほど少ない．



■図4　年齢別にみた認知症の有病率と認知症の発症を2年遅らせた場合の有病率
期待患者減少数は33万人，医療費削減効果は2,000億円，介護費用削減効果は7,700億円と推定される．

7. 最後に

世界でも類をみない速度で高齢化が進んでいるわが国にとって，認知症患者の増加は大きな社会問題である．今後15年間で認知症にかかわる介護費用は倍増し，年間10兆円に達するとも予想される[5]．高齢化が進む一方で，少子化も進み，介護にかかわることのできる労働人口は激減する．このままでは認知症によって日本の社会が崩壊すると言っても過言ではないかも知れない．一方で，認知症の発症を2年遅らせることができれば，それだけで年間2兆円もの費用が削減できる可能性がある．

日本人で比較的多いと言われる血管性認知症は，喫煙や高脂血症，高血圧，糖尿病などが要因となっており，禁煙や減塩，身体活動，食生活の改善などである程度予防することが可能である．最近ではアルツハイマー病も生活習慣病であると言われ始めており，生活習慣の改善である程度の予防が可能であろう．認知症の素因としての遺伝子多型の研究も進み始めている．こうした研究の推進により高齢者の知的機能を守り，高齢者の社会参画を可能にしていくことが是非とも必要であろう．

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