



Vascular burden and brain aging in a senior volunteer cohort: A pilot study

Raymond Y. Lo^{a*}, Yen-Chieh Lo^b, Shu-Cin Chen^a, Yu-Ying Li^a, Ya-Ling Yang^c, Yu-Ling Chang^{d,e}, Huei-Chuan Sung^f, Tina H. T. Chiu^g, Joshua O. S. Goh^{d,e,h}

^aMemory and Aging Center, Department of Neurology, Buddhist Tzu Chi General Hospital and Tzu Chi University, Hualien, Taiwan, ^bDepartment of Journalism, Chinese Culture University, Taipei, Taiwan, ^cSociety for Comprehensive Medicine, Hualien, Taiwan, ^dDepartment of Psychology, National Taiwan University, Taipei, Taiwan, ^eNeurobiology and Cognitive Science Center, National Taiwan University, Taipei, Taiwan, ^fDepartment of Nursing, Tzu Chi University of Science and Technology, Hualien, Taiwan, ^gTzu Chi Medical Mission, Hualien, Taiwan, ^hGraduate Institute of Brain and Mind Sciences, National Taiwan University, Taipei, Taiwan

Received : 03-01-2017
Revised : 20-02-2017
Accepted : 21-02-2017

ABSTRACT

Objective: To test the feasibility of establishing a senior volunteer cohort and describe vascular risks, cognitive function, and brain aging indices in a pilot study. **Materials and Methods:** We enrolled 40 senior volunteers from the Tzu Chi Foundation and other organizations in Hualien in 2014–2015. We conducted in-person interviews to collect information on demographic features, physical fitness, dietary habits, comorbidities, and narratives of aging. Vascular risks including blood pressure, body mass index (BMI), serum glucose level, and lipid profile were examined. Each participant underwent a comprehensive battery of neuropsychological tests and structural brain magnetic resonance imaging (MRI). Descriptive statistics and tabulation were applied to characterize this pilot cohort. **Results:** There were more volunteers from the Tzu Chi Foundation ($n = 25$) than other organizations. The mean age was 66.7 years (standard deviation = 5.1) and there was a female predominance (M:F = 13:27). The mean number of comorbid chronic diseases was 2.1 and the mean BMI was 24.5. Most participants (77.5%) engaged in outdoor walking activities every week. Nutrient intake in vegetarians ($n = 18$) did not differ from nonvegetarians except for lower Vitamin B12 levels (mean = 0.9 μg). All participants but one scored 26 or above in the Mini-Mental State Examination (mean = 28.4). Among the other cognitive tests, only one task related to inhibition and switching abilities was at the low average level. The mean values of vascular risk markers were within the normal ranges. The most common genotype of apolipoprotein E was $\epsilon 3/\epsilon 3$ ($n = 32$). The quality of MRI was sufficient for volumetric analysis. **Conclusion:** It is feasible to establish a volunteer-based cohort to study brain aging in Taiwan. The senior volunteers were physically active and cognitively healthy. Vascular risks were well distributed among these participants. Future longitudinal study will allow us to observe changes in these markers over time and provide dynamic evidence about vascular health and cognitive aging.

KEYWORDS: Cognitive aging, Vascular risk, Volunteer cohort

INTRODUCTION

Alzheimer's disease (AD) is the most common neurodegenerative disease, and the incidence increases with aging [1]. As the global population ages, the number of dementia cases is estimated to grow from approximately 46.8 million in 2015 to 131 million worldwide in 2050 [2]. Although AD is considered the most common type of dementia, most elderly patients with dementia have a mixed component of both AD-type pathology and vascular lesions [3,4].

Many cerebrovascular risk factors including midlife hypertension, diabetes, dyslipidemia, and smoking are known to increase the risk of AD [5]. It remains controversial whether cerebrovascular burden leads to beta-amyloid deposition or aggravates cognitive deterioration in an additive way [6]. Vascular dementia is of particular interest in Asia. Previous

studies from Japan and China two decades ago showed that vascular dementia was more prevalent than AD in Asia [7-9]. Although the case numbers of AD are increasing and the trend is changing over time, there is still a notable predisposition to vascular dementia in Asians [10,11]. In the Honolulu Asia Aging Study Autopsy Study, microinfarct pathology significantly contributed to brain atrophy and cognitive impairment, suggesting that cerebrovascular burden plays a major role in cognitive aging in Asia [12]. However, by the time dementia is diagnosed, cognitive changes are often complicated by other degenerative processes, making vascular effects less identifiable. Moreover,

*Address for correspondence:

Dr. Raymond Y. Lo,
Memory and Aging Center, Department of Neurology, Buddhist Tzu Chi General Hospital, 707, Section 3, Chung-Yang Road, Hualien, Taiwan.
E-mail: raymondldmd@gmail.com

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

How to cite this article: Lo RY, Lo YC, Chen SC, Li YY, Yang YL, Chang YL, et al. Vascular burden and brain aging in a senior volunteer cohort: A pilot study. Tzu Chi Med J 2017;29(2):91-97.

Access this article online	
Quick Response Code: 	Website: www.tcmjmed.com
	DOI: 10.4103/tcmj.tcmj_21_17

the aforementioned studies were based on aging populations decades ago. There is a need to establish a new cohort to reflect contemporary population health trends regarding cognitive aging.

Volunteering is considered an altruistic activity and also thought to have a positive impact on the well-being of older adults [13]. Senior volunteers serve as great exemplars of healthy aging. By following up senior volunteer vascular risk profiles, lifestyle practices, and cognitive performance, we can gain insight into the vascular contribution in brain aging. We thus aim to establish a cohort of senior volunteers from Hualien county to study vascular health and cognitive aging.

MATERIALS AND METHODS

Study population

Public health lectures were used to contact local volunteer groups including the Tzu Chi Foundation and other organizations in Hualien. Once contact information was obtained, we invited senior volunteers by telephone to Hualien Tzu Chi Hospital to sign an informed consent. We aimed to enroll 40 senior participants in the pilot study in 2014–2015. The eligibility criteria were as follows: active volunteers living in Hualien, between 60 and 80 (inclusive) years old; no history of traumatic brain injury, major depression, encephalitis, degenerative dementia, hospitalization for acute ischemic or hemorrhagic stroke, or contraindications to magnetic resonance imaging (MRI) scanning; no psychoactive medication; willing and able to undergo all testing procedures including blood tests, MRI scans, cognitive assessments, clinical interviews, and follow-up for up to 3 years. The study site was the Memory and Aging Center, Hualien Tzu Chi Hospital, Hualien, Taiwan.

Data collection

We collected information on demographic features, dietary habits, chronic medical diseases, serum markers for vascular risks, apolipoprotein E (APOE) alleles, physical activity and fitness, cognitive performance, and MRI scans of the brain.

Basic demographic data included birth date, age, sex, educational attainment, primary lifetime occupation, smoking, and alcohol consumption. We assessed dietary components using a 64-item quantitative food frequency questionnaire, previously validated among registered Tzu Chi volunteers [14]. We conducted in-person interviews to obtain a medical history of multiple chronic diseases. We referenced the list of multiple chronic conditions reported by the US Department of Health and Human Services Office of the Assistant Secretary of Health [15] and selected 14 chronic diseases (hypertension, diabetes mellitus, hyperlipidemia, coronary artery disease, congestive heart failure, liver cirrhosis, chronic obstructive pulmonary disease, chronic renal failure, cancer, gout, osteoarthritis, osteoporosis, depression, and stroke) based on chronicity, prevalence, and representativeness of organ systems. In addition, we used the Cumulative Illness Rating Scale for Geriatrics (CIRS-G) to assess the comorbidity burden in our study population [16]. The APOE4 genotype is associated with higher risks of AD but does not cause AD by itself. APOE genotyping was done in the Department of Laboratory Medicine at Hualien Tzu Chi Hospital. During the interview, each participant was informed that genotyping of APOE is not accurately predictive of dementia and is not recommended in clinical settings [17].

Participants were asked if they were willing to know the results given the full understanding that nothing could be done to change their genetic status or reduce the genetic risk of AD.

We performed a panel of blood tests to measure the complete blood cell count, activated partial thromboplastin time, prothrombin time, glycated hemoglobin, fasting glucose, lipid profile (total cholesterol, high-density lipoprotein, low-density lipoprotein, and triglycerides), Vitamin B₁₂, folate, thyroid function, homocysteine, uric acid, liver enzymes (serum glutamic oxaloacetic transaminase, serum glutamic-pyruvic transaminase), albumin, creatinine, fibrinogen, and C-reactive protein. Framingham cardiovascular risk scores were calculated to summarize vascular risks [18].

The physical assessment section included the Senior Fitness Test (SFT), grip strength, and Short Physical Performance Battery (SPPB). The SFT is a 6-item battery which includes measures of dynamic upper (arm curl test) and lower extremity strength (30-s chair stand test), flexibility (chair sit-and-reach test and back scratch test), aerobic endurance (2-min step test), and agility and dynamic balance (8-foot up-and-go test). The SFT measures the underlying physical parameters associated with functional ability and has demonstrated intra-rater and test-retest reliability and validity in older adults [19]. Grip strength is a reliable measurement and is known as a good predictor of unhealthy outcomes [20]. First, it was measured in kilograms using a hand-held digital dynamometer. Two measurements were done in each hand with a 15 s rest between tests, and the dominant hand was tested first. The better numerical value for each hand was used in the analysis. Like SFT, the SPPB is a group of measures that combines the results of gait speed, chair stand, and balance tests and has demonstrated predictive validity for the risks of mortality and disability [21].

All participants underwent a battery of internationally validated neuropsychological tests using the Taiwanese versions of the tests. The test battery broadly sampled different cognitive domains including executive function, learning and memory, psychomotor processing speed, and visuospatial ability. They were selected mainly from the Wechsler Adult Intelligence Scale III, Wechsler Memory Scale III, Mini-Mental State Exam (MMSE), and Geriatric Depression Scale (GDS). The neuropsychological battery was divided into 3 sessions for better participant tolerance. All 3 sessions were completed within 2 weeks and implemented by 2 licensed clinical psychologists and 1 intern psychologist.

Each participant had a T1-weighted MRI scan of gray and white matter structures, T2-weighted and fluid-attenuated inversion recovery (FLAIR) scans for detection of white matter hyperintensities, and diffusion tensor imaging (DTI) to assess white matter microstructure integrity. Structural scans followed the sequence protocols recommended by the AD Neuroimaging Initiative group for comparability with that dataset. Specific scan parameters were as follows – DTI: 32 3 mm axial slices, 256 × 256 matrix, 1 mm × 1 mm in-plane resolution, 30 directions; T1: 166 1 mm coronal slices, 512 × 512 matrix, 0.5 mm × 0.5 mm in-plane resolution; T2: 36 4 mm axial slices, 256 × 256 matrix, 1 mm × 1 mm in-plane resolution; and FLAIR: 30 4.4 mm axial slices, 256 × 256 matrix, 0.9 mm × 0.9 mm in-plane resolution. T1 scans afforded measures of gray matter thickness and volume,

white matter and subcortical regional volumes, using Freesurfer brain structure analysis software (<http://www.surfer.nmr.mgh.harvard.edu/>).

The neurologist (RYL) conducted a clinical interview with each participant by the time all research examinations were done. Examination findings were revealed to research participants if laboratory findings from blood tests, cognitive tests, or MRI scans were of clinical significance. An experienced journalist (Y-CL) invited 12 volunteers to have semistructured interviews on social engagement, interpersonal communication, and perspectives on aging [22]. Narratives on aging were recorded and qualitatively analyzed.

Standard protocol approvals, registrations, and patient consents

The study procedures were approved by the Research Ethics Committee of Hualien Tzu Chi Hospital (IRB102-47 and IRB102-144). Written informed consent was obtained from all research participants.

RESULTS

The public health lectures were well received by volunteers. We enrolled 25 volunteers from the Tzu Chi Foundation and 15 from other local organizations. One male participant dropped out of the study because of chest discomfort after the MRI scan. His follow-up physical examination was normal. Senior volunteers actively sought health information and their views on aging were much influenced by the aging experience of their parents or parents-in-law. At the end of interviews, all participants expressed their willingness to continue participation in our follow-up study.

Subject data are shown in Table 1. The mean age at enrollment was 66.7 years (standard deviation [SD] = 5.1; range: 59–78). The sex ratio was about 1:2 (M: F = 13:27). Most of the pilot group subjects were Taiwanese (80%). The median number of years of formal education was 12 and only one volunteer had not received any formal education. The sample included 4 smokers (10%) and 8 participants with regular alcohol consumption (20%). The mean number of comorbid chronic diseases was 2.1 (range: 0–6) and the 5 most common chronic diseases were hypertension ($n = 17$), osteoarthritis ($n = 12$), osteoporosis ($n = 11$), hyperlipidemia ($n = 11$), and diabetes mellitus ($n = 9$). The mean CIRS-G total score was 3.0 (range: 0–10) and the mean severity index was 1.52 (range: 0–2.3). The mean body mass index (BMI) was 24.5 (SD = 3.2), and about 20% were obese. The mean score on the SPPB (range 0–12) was 11 (SD = 1.36), showing that this sample had very good physical performance. These participants were highly involved in leisure activities, housework, and exercise. About 80% of the sample participated in weekly outdoor walking activities, light sports, or recreational activities. Only 30% participated in strenuous sports or recreational activities every week. Very few (5%) were engaged in muscle strength or endurance exercises every week. All participants engaged in light housework. About 47.5% participated in lawn work or yard care, but few participated in home repair (2.5%) or caregiving for other persons (10%). There were nearly equal numbers of vegetarians and nonvegetarians in the pilot

cohort. The intake of total calories, protein, fat, carbohydrate, dietary fiber, and water was comparable between the vegetarians and nonvegetarians, except for lower levels of Vitamin B12 in vegetarians [Table 2].

There were no complaints about the duration of the neuropsychological tests in participant feedback. All participants but one scored 26 or above in the MMSE (mean = 28.43), and 3 or less in the GDS (mean = 0.55). The descriptive data for all other cognitive measures are listed in Table 3. The 40 participants as a group performed within an average range for all cognitive measures, except for one task related to inhibition and switching abilities (i.e., Color-Word Interference Test), which was at the low average level. The SD was relatively large for tests related to executive function compared with tests related to other cognitive domains.

Major vascular risk markers are shown in Table 4. The mean values of these markers were generally within the normal limits. The mean Framingham risk score was 16.2 (range: 9–22) for men and 13.2 (range: 4–20) for women. The most common APOE allele was $\epsilon 3/\epsilon 3$ ($n = 32$), and there were 4 participants with $\epsilon 2/\epsilon 3$ and 4 with $\epsilon 3/\epsilon 4$. During the clinical interview, 29 participants were willing to have their APOE genetic information disclosed to them. The brain MRI protocol was well tolerated by all participants, and the quality of the imaging was sufficient for performing brain volumetric analysis using Freesurfer software as seen in the select regional brain volumes [Figure 1]. Target regions of interest were also developed to study specific cognitive domains in memory and executive function [Figure 2].

DISCUSSION

Our pilot study demonstrated that establishing a volunteer-based aging cohort is feasible. Most of these senior volunteers were in their mid-60s to early 70s, physically active and cognitively intact. They tolerated the fairly comprehensive set of examinations, tests, and interviews well. Their interpretations of the aging experience were diverse. They were highly motivated to participate in aging research and willing to continue follow-up in our longitudinal study.

As expected, we had more participants from the Tzu Chi Foundation than other organizations. Hualien Tzu Chi Hospital is affiliated with the Tzu Chi Foundation, which provides inherent access to its volunteers. Furthermore, the tight network within the Tzu Chi membership helped in spreading the message of our study objectives and facilitated the enrollment process. We made efforts to contact the key members of other local volunteer organizations, but individual volunteers were not necessarily bonded with other members, making the enrollment process less efficient. We meant to include equal numbers of volunteers from Tzu Chi and other organizations, but the discrepancy in recruitment efficiency made it difficult to perfectly balance the numbers. More women than men were enrolled into our study and the female predominance was likely due to the underlying distribution (63.3% of registered Tzu Chi volunteers are female) [23].

Many Tzu Chi volunteers are also Buddhists and thus vegetarians seemed to be overrepresented in the pilot cohort (45%). This unique feature can provide an advantage in studying the

Table 1: Demographic features, physical characteristics, and physical fitness (n=40)

	Mean (SD)	n (%)
Demographic features		
Age (year)	66.7 (5.1)	
Sex (male)		13 (32.5)
Education (year)	10.9 (3.5)	
Taiwanese ethnicity		32 (80)
Apolipoprotein genotype		
ε2/ε3		4 (10)
ε3/ε3		32 (80)
ε3/ε4		4 (10)
Physical characteristics		
Body weight (kg)	58.79 (8.57)	
Fat percentage	24.20 (3.12)	
Height (cm)	155.8 (8.29)	
BMI	24.45 (3.24)	
BMI <18.5		1 (2.5)
18.5 <BMI <24 (normal)		17 (42.5)
24 <BMI <27 (overweight)		14 (35)
27 <BMI <30 (slightly obesity)		5 (12.5)
30 <BMI <35 (medium obesity)		3 (7.5)
Waist line (cm)	80.39 (8.12)	
Systolic blood pressure (mmHg)	132.55 (18.88)	
Diastolic blood pressure (mmHg)	75.43 (10.92)	
Heart rate (bpm)	66.62 (9.55)	
Physical fitness		
30-s arm curl (reps)	20.75 (5.28)	90
Back scratch (cm)	5.50 (8.32)	75
Chair sit-and-reach (cm)	2.52 (6.63)	50
8-foot up-and-go (s)	3.74 (0.71)	90
Grip strength		
Right arm (kg)	25.47 (8.49)	
Left arm (kg)	24.2 (7.51)	
Short Physical Performance Battery (score)	11 (1.36)	
Outdoor walking activities		31 (77.5)
Light sport or recreational activities		34 (85)
Moderate sport or recreational activities		23 (57.5)
Strenuous sport or recreational activities		12 (30)

BMI: Body mass index, SD: Standard deviation

vegetarian effects on cognitive aging if we continue to enroll more Tzu Chi volunteers. However, our analysis did not show significant differences in intake of most types of nutrients types between vegetarians and nonvegetarians. The only difference was in Vitamin B12, although this information could be more precisely measured by blood test. Although the nutrition questionnaire has been validated and computerized, it took about 40 min to complete even with guidance from an interviewer. If our aim is to investigate the global effect of a vegetarian lifestyle rather than focus on individual nutrient types, the questionnaire would be impractical.

These senior volunteers were active in community service and fairly active in outdoor activities. Their performance in the SFT was excellent. For example, the results in both the 30 s-arm curl and 8-foot up-and-go tests were above the 90th percentile for the 65–69 years' age group. Their SPPB scores were

Table 2: Nutrient intakes (n=40)

Nutrients and food groups	Mean (SD)	
	Nonvegetarians (n=22)	Vegetarians (n=18)
Energy (kcal)	1979 (873)	1974 (536)
Protein (g)	63 (28)	67 (18)
Animal protein	16 (11)	6 (6)
Plant protein	47 (22)	60 (18)
Fat (g)	71 (34)	72 (29)
Saturated fat	16 (9)	14 (5)
Monounsaturated fat	27 (15)	25 (13)
Polyunsaturated fat	20 (14)	23 (13)
Carbohydrates (g)	279 (125)	274 (74)
Dietary fiber (g)	25 (11)	28 (8)
Cholesterol (g)	158 (99)	134 (120)
Potassium (mg)	2692 (965)	2822 (848)
Calcium (mg)	588 (261)	682 (173)
Magnesium (mg)	343 (145)	399 (137)
Iron (mg)	16 (7)	20 (7)
Zinc (mg)	10 (4)	10 (3)
Thiamin (mg)	1.2 (0.5)	2.3 (1.0)
Riboflavin (mg)	1.2 (0.5)	1.0 (0.3)
Niacin (mg)	19 (9)	20 (10)
Vitamin B6 (mg)	1.3 (0.5)	1.4 (0.5)
Folate (μg)	410 (152)	503 (158)
Vitamin B12 (μg)	5.3 (14.0)	0.9 (0.6)
Vitamin C (mg)	192 (69)	209 (80)
Vitamin D (μg)	6.2 (5.7)	2.8 (2.0)
Vitamin A (μgRE)	3232 (1625)	3335 (1926)
Vitamin E (mg α-TE)	7.0 (4.6)	7.6 (3.9)
Water (mL)	2550 (693)	2526 (936)

SD: Standard deviation, TE: Tocopherol equivalents

also nearly perfect. Therefore, this cohort should be considered superior to their peers in physical fitness. However, even most of these relatively healthy and active senior adults had 2 or more chronic diseases, which is in line with a previous report that multimorbidity is a common feature in old age [24]. Cardiovascular risks remain highly prevalent among senior volunteers. Although the sample size was small, the frequency of hypertension (42.5%) was similar to the prevalence estimate for the 60–69 years' age group in Taiwan (47%) [25]. Likewise, the frequency of diabetes mellitus (22.5%) was comparable to the prevalence estimate for the 60–79 years' age group in Taiwan (men: 20% and women: 24%) [26]. These findings suggest that common chronic diseases were well distributed and the senior volunteer cohort may serve as a good basis for studying the effects of medical comorbidity on cognitive aging.

The median length of education was 12 years, which was much higher than the average level for those educated in Taiwan before 1968 when there was 6 years of compulsory education. These senior volunteers were considered highly educated. Their cognitive performance was within the normal range across different domains and their depression scores were low. We are aware of the healthy volunteer effect in research [27] and thus this cohort may not represent the underlying elderly population in the community but, instead,

may be a reference group for healthy aging. Moreover, all participants completed the 3-h long neuropsychological battery

without complaints in feedback. In fact, the entire battery was divided into 2–3 sessions to maintain adequate attention for

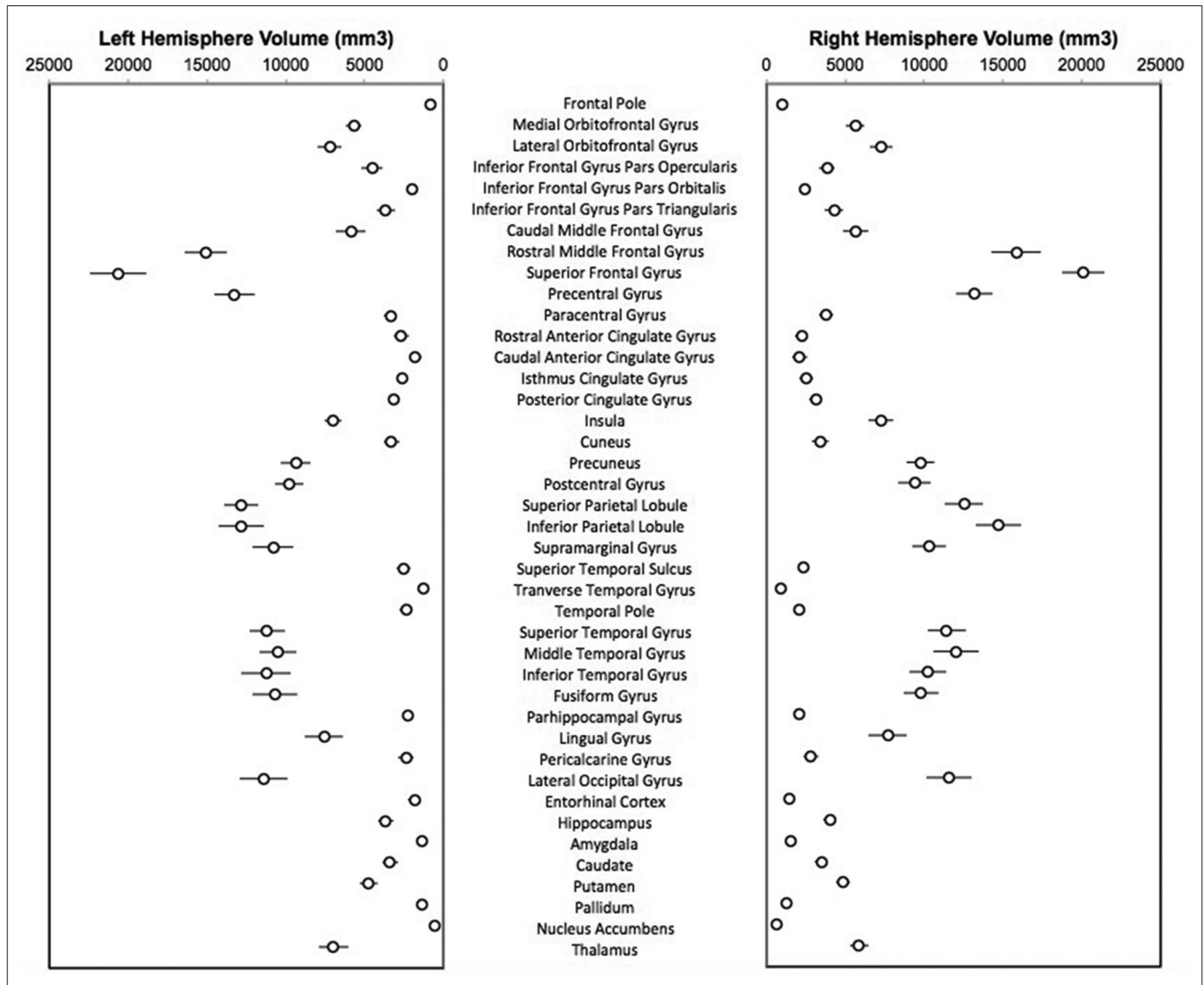


Figure 1: Graphic summary of gray matter volume in selected brain regions

Table 3: Neuropsychological batteries (n=40)

Measurement	Mean (SD)	Range
Mini-Mental State Examination	28.43 (1.52)	22-30
Geriatric Depression Scale	0.55 (0.75)	0-3
Digit Span of WAIS-3 (scaled score)	11.65 (2.78)	6-19
Spatial Span of WMS-3 (scaled score)	11.68 (2.67)	7-18
Letter-Number Sequencing of WAIS-3 (scaled score)	10.68 (2.80)	2-15
Digit symbol of WAI-3 (scaled score)	10.17 (2.51)	5-15
Verbal paired associated-immediate recall (scaled score)	10.51 (2.43)	6-15
Verbal paired associated- delayed recall (scaled score)	10.85 (3.07)	5-18
Category fluency (animal, words generated)	16.08 (4.10)	10-25
Color Trails Test part 1 (time in s)	53.37 (30.60)	4-94
Color Trails Test part 2 (time in s)	62.47 (24.53)	9-98
Design fluency-switching condition (scaled score)	11.02 (2.99)	3-17
Color-Word Interference Test: The inhibition condition (scaled score)	10.00 (3.06)	1-16
Color-Word Interference Test: The switching/inhibition condition (scaled score)	6.98 (3.67)	1-14

SD: Standard deviation, WAIS: Wechsler Adult Intelligence Scale, WMS: Wechsler Memory Scale

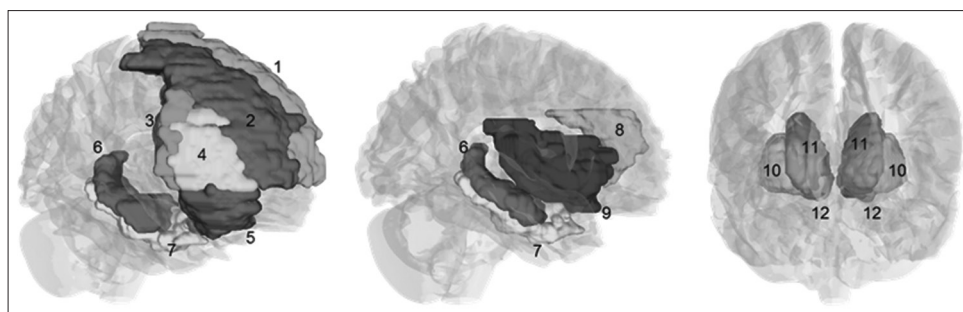


Figure 2: Target regions-of-interest used for studying memory and executive function. (1) Superior frontal gyrus, (2) middle frontal gyrus, (3) inferior frontal gyrus (Oper), (4) inferior frontal gyrus (Tri), (5) inferior frontal gyrus (Orb), (6) parahippocampal gyrus, (7) hippocampal gyrus, (8) anterior cingulate gyrus, (9) insula, (10) putamen, (11) caudate, (12) nucleus accumbens

Table 4: The blood test profile including vascular risk markers (n=40)

Serum markers	Mean (SD)	Range
HbA1c (%)	5.9 (0.8)	4.9-9.0
AC glucose (mg/dL)	104.3 (23.8)	79-182
Total cholesterol (mg/dL)	178.6 (34.4)	112-265
LDL (mg/dL)	110.7 (31.5)	60-193
HDL (mg/dL)	53.7 (12.5)	31-80
Triglyceride (mg/dL)	104.7 (61.3)	42-380
Uric acid (mg/dL)	4.9 (1.3)	2.2-9.0
Creatinine (mg/dL)	0.8 (0.2)	0.4-1.5
Homocysteine (μ mol/L)	11.4 (5.2)	4.9-31.7
Hemoglobin (g/dL)	13.4 (1.2)	11.3-15.8
C-reactive protein (mg/dL)	0.29 (0.49)	0.06-2.98
TSH (μ IU/mL)	1.97 (1.18)	0.007-5.20
Vitamin B12 (pg/mL)	499.5 (256.0)	152-1295
Folate (ng/mL)	15.4 (7.9)	4.6-35.4

SD: Standard deviation, HbA1c: Glycated hemoglobin, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, TSH: Thyroid-stimulating hormone, AC: Ante cibum

each participant. This created challenges because of conflicts with the outside work schedules of the neuropsychologists and research participants. In order to make the data collection process more efficient, we plan to shorten the battery by focusing on memory and executive function, as they are the two domains mostly affected in vascular cognitive impairment.

In addition to individual vascular risk measurements, such as BMI, blood pressure, glucose level, lipid profile, smoking, and drinking habits, we used the Framingham risk score to summarize the vascular burden. The Framingham risk scoring system has been validated as predictive of cardiovascular diseases including ischemic stroke. The risk scores in our pilot study corresponded to 10-year cardiovascular disease risks of 25.3% for men and 10.0% for women, showing a gender discrepancy in vascular burden. Nevertheless, the actual range of their risk scores was wide, and the heterogeneity will allow us to examine the differential effects of vascular risks on cognitive aging.

The frequency of three APOE forms ($\epsilon 2/\epsilon 3$, $\epsilon 3/\epsilon 3$, and $\epsilon 3/\epsilon 4$) in this small sample was comparable to and did not deviate much from that in the general population [28]. If the prevalence of AD or vascular dementia in Asia is different from other areas, the allele frequency of APOE may be informative. The

implication of APOE genotyping was made clear during the final clinical interview, and the majority of the pilot cohort (72.5%) were willing to have their APOE genetic information disclosed and explained to them. No short-term psychological risks have been associated with disclosure of APOE information to first-degree relatives of AD patients [29]. A 1-year follow-up study also showed that the test recipients felt the pros of disclosure outweighed the cons [30]. The concept of precision medicine or genetic medicine is gaining more acceptance from the public. Since there is no curative medicine or effective prevention for AD, we will continue to ensure our participants fully understand before disclosing APOE information and we will obtain their feedback in subsequent years.

The MRI protocol was well tolerated by all participants and the quality of the imaging was satisfactory. Brain volumetric analysis using Freesurfer software yielded reasonable indices of regional brain volumes. However, the current dataset is still too small to run meaningful analyses. An expanded sample size of MRI scans is warranted to more reliably assess different brain structural indices and their associations with age-related effects on cognition and vascular health.

CONCLUSION

Establishing a senior volunteer cohort is feasible. The aging cohort can serve as a basis for studying the vascular contribution to brain aging at the population level. We plan to expand the cohort size and repeatedly measure vascular, cognitive, and imaging markers together with the narrative approach to obtain both subjective and objective views of aging. Our hypothesis is that through vegetarian practice, regular exercise, and vascular risk control, cognitive health can be well maintained and evidenced by MRI indices. The study results will contribute to the development of health policies for dementia prevention.

Financial support and sponsorship

This study was supported by the Ministry of Science and Technology (MOST103-2314-B-303-008) and the National Science Council (NSC 102-2410-H-034-019-MY2).

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Mayeux R. Epidemiology of neurodegeneration. *Annu Rev Neurosci* 2003;26:81-104.

2. World Alzheimer's Report 2015. London: Alzheimer's Disease International; 2015.
3. Schneider JA, Arvanitakis Z, Bang W, Bennett DA. Mixed brain pathologies account for most dementia cases in community-dwelling older persons. *Neurology* 2007;69:2197-204.
4. Fernando MS, Ince PG; MRC Cognitive Function and Ageing Neuropathology Study Group. Vascular pathologies and cognition in a population-based cohort of elderly people. *J Neurol Sci* 2004;226:13-7.
5. Purnell C, Gao S, Callahan CM, Hendrie HC. Cardiovascular risk factors and incident Alzheimer disease: A systematic review of the literature. *Alzheimer Dis Assoc Disord* 2009;23:1-10.
6. Lo RY, Jagust WJ; Alzheimer's Disease Neuroimaging Initiative. Vascular burden and Alzheimer disease pathologic progression. *Neurology* 2012;79:1349-55.
7. Li G, Shen YC, Chen CH, Zhau YW, Li SR, Lu M. A three-year follow-up study of age-related dementia in an urban area of Beijing. *Acta Psychiatr Scand* 1991;83:99-104.
8. Yoshitake T, Kiyohara Y, Kato I, Ohmura T, Iwamoto H, Nakayama K, et al. Incidence and risk factors of vascular dementia and Alzheimer's disease in a defined elderly Japanese population: The Hisayama Study. *Neurology* 1995;45:1161-8.
9. Ikeda M, Hokoishi K, Maki N, Nebu A, Tachibana N, Komori K, et al. Increased prevalence of vascular dementia in Japan: A community-based epidemiological study. *Neurology* 2001;57:839-44.
10. Dodge HH, Buracchio TJ, Fisher GG, Kiyohara Y, Meguro K, Tanizaki Y, et al. Trends in the prevalence of dementia in Japan. *Int J Alzheimers Dis* 2012;2012:956354.
11. Jia J, Wang F, Wei C, Zhou A, Jia X, Li F, et al. The prevalence of dementia in urban and rural areas of China. *Alzheimers Dement* 2014;10:1-9.
12. Launer LJ, Hughes TM, White LR. Microinfarcts, brain atrophy, and cognitive function: The Honolulu Asia Aging Study Autopsy Study. *Ann Neurol* 2011;70:774-80.
13. Morrow-Howell N, Hinterlong J, Rozario PA, Tang F. Effects of volunteering on the well-being of older adults. *J Gerontol B Psychol Sci Soc Sci* 2003;58:S137-45.
14. Chiu TH, Huang HY, Chen KJ, Wu YR, Chiu JP, Li YH, et al. Relative validity and reproducibility of a quantitative FFQ for assessing nutrient intakes of vegetarians in Taiwan. *Public Health Nutr* 2014;17:1459-66.
15. Goodman RA, Posner SF, Huang ES, Parekh AK, Koh HK. Defining and measuring chronic conditions: Imperatives for research, policy, program, and practice. *Prev Chronic Dis* 2013;10:E66.
16. Miller MD, Paradis CF, Houck PR, Mazumdar S, Stack JA, Rifai AH, et al. Rating chronic medical illness burden in geropsychiatric practice and research: Application of the Cumulative Illness Rating Scale. *Psychiatry Res* 1992;41:237-48.
17. Knopman DS, DeKosky ST, Cummings JL, Chui H, Corey-Bloom J, Relkin N, et al. Practice parameter: Diagnosis of dementia (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology* 2001;56:1143-53.
18. D'Agostino RB Sr., Vasan RS, Pencina MJ, Wolf PA, Cobain M, Massaro JM, et al. General cardiovascular risk profile for use in primary care: The Framingham Heart Study. *Circulation* 2008;117:743-53.
19. Rikli RE, Jones CJ. Development and validation of criterion-referenced clinically relevant fitness standards for maintaining physical independence in later years. *Gerontologist* 2013;53:255-67.
20. Rantanen T, Guralnik JM, Foley D, Masaki K, Leveille S, Curb JD, et al. Midlife hand grip strength as a predictor of old age disability. *JAMA* 1999;281:558-60.
21. Guralnik JM, Ferrucci L, Pieper CF, Leveille SG, Markides KS, Ostir GV, 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:M221-31.
22. Kvale S. *Interviews: An Introduction to Qualitative Research Interviewing*. Thousand Oaks, Calif.: Sage Publications; 1996.
23. Tzu Chi Foundation. *Tzu Chi Almanac: Charity, Medicine, Education, Humanity*. Hualien, Taiwan: Tzu Chi Foundation; 2011.
24. Barnett K, Mercer SW, Norbury M, Watt G, Wyke S, Guthrie B. Epidemiology of multimorbidity and implications for health care, research, and medical education: A cross-sectional study. *Lancet* 2012;380:37-43.
25. Su TC, Bai CH, Chang HY, You SL, Chien KL, Chen MF, et al. Evidence for improved control of hypertension in Taiwan: 1993-2002. *J Hypertens* 2008;26:600-6.
26. Jiang YD, Chang CH, Tai TY, Chen JF, Chuang LM. Incidence and prevalence rates of diabetes mellitus in Taiwan: Analysis of the 2000-2009 Nationwide Health Insurance database. *J Formos Med Assoc* 2012;111:599-604.
27. Lindsted KD, Fraser GE, Steinkohl M, Beeson WL. Healthy volunteer effect in a cohort study: Temporal resolution in the Adventist Health Study. *J Clin Epidemiol* 1996;49:783-90.
28. Raber J, Huang Y, Ashford JW. ApoE genotype accounts for the vast majority of AD risk and AD pathology. *Neurobiol Aging* 2004;25:641-50.
29. Green RC, Roberts JS, Cupples LA, Relkin NR, Whitehouse PJ, Brown T, et al. Disclosure of APOE genotype for risk of Alzheimer's disease. *N Engl J Med* 2009;361:245-54.
30. Christensen KD, Roberts JS, Uhlmann WR, Green RC. Changes to perceptions of the pros and cons of genetic susceptibility testing after APOE genotyping for Alzheimer disease risk. *Genet Med* 2011;13:409-14.