Soy-Based Foods Are Negatively Associated with Cognitive Decline in Taiwan's Elderly

Hsing-Chun Lin^{1,2}, Chiung-Huei PENG³, Chien-Ning HUANG^{4,5} and Jeng-Yuan CHIOU^{6,*}

Department of Nutrition, Chung Shan Medical University, Taichung City, Taiwan
Department of Nutrition, Chung Shan Medical University Hospital, Taichung City, Taiwan
Division of Basic Medical Science, Hungkuang University, Taichung City, Taiwan
Institute of Medicine, Chung Shan Medical University, Taichung City, Taiwan
Department of Internal Medicine, Chung Shan Medical University Hospital, Taichung City, Taiwan
The School of Health Policy and Management, Chung Shan Medical University,
110 Chien-Kuo N. Road, Section 1, Taichung City 402, Taiwan
(Received January 24, 2018)

Summary Cognitive impairment is a common neurodegenerative disease in the elderly. Dietary factors have an important role in cognitive dysfunction. Soy has many benefits, and consumption of soy-based foods is general in East Asian countries. In this study, we want to investigate the association between cognitive function decline and soy-based food intake among the elderly in Taiwan. This cross-sectional study was based on data obtained from the 2005-2008 Nutrition and Health Survey in Taiwan (NAHSIT). Subjects aged less than 65 y or with missing data were excluded. There was a total of 1,105 participants aged 65 and over who completed Short Portable Mental Status Questionnaire (SPMSQ). Eighty-fivepoint-six percent of participants consumed soy-based foods every day. After adjustment for potential variables, the logistic regression model showed significant associations for age, gender, education, soy-based foods intake and physical component summary (PCS). Age and female gender were both positively correlated with cognitive impairment (odds ratios: 1.1 and 4.43, respectively). Furthermore, there were negative correlations for education, soybased foods intake and PCS (odds ratios: 0.25, 0.45 and 0.97, respectively). In this study, we found that soy-based foods were negatively associated with cognitive function decline among Taiwanese elderly. This result may be used as a reference for dietary advice for the elderly.

Key Words cognitive impairment, cross-sectional, elderly, Short Portable Mental Status Questionnaire, soy-based foods

Due to the aging of the population, there have been increases in the prevalence and incidence of cognitive impairment. Age-related cognitive decline has various mechanisms, including oxidative stress (1), endocrine (2), and neurochemical changes (3). Each year, about 10 to 15% of elderly people with mild cognitive impairment (MCI) develop dementia, and MCI is a strong risk factor for early dementia (4). In 2015, the World Health Organization (WHO) predicted that dementia will be a major cause of disability among the elderly worldwide.

Nutritional status is strongly associated with MCI and quality of life in the elderly (5). Chen et al., found that a low dietary diversity score (DDS) leads to increases in MCI and mortality rate among Taiwanese elderly based on data collected from the National Nutrition and Health Survey in Taiwan (NAHSIT), 1999–2000 (6). Consumption of soy-based foods such as soy milk, tofu, miso, and natto is more generalized in East Asian countries than in Western countries. In addition, prevention of cardiovascular disease (7), osteoporosis (8), and

neurodegeneration (9) is powerful evidence to suggest that soy has many benefits. These effects of soy could be related to the endocrine system. In recent years, soy-derived supplements already have been widely used in menopausal women. Soy-based foods are rich in soy isoflavones, especially in genistein and daidzein (10). A meta-analysis study indicated soy isoflavones supplementation can improve cognitive function in menopausal women (11).

Moreover, the quality of life of elderly people is an important issue, and is influenced by both aging and cognitive impairment. Past research had indicated that cognitive impairment not only decreases the quality of life among the elderly, but also increases the cost of health care (12). For these reasons, we hypothesize that incrementation of soy-based food consumption may improve cognitive function in Taiwan's elderly population. Hence, we want to investigate the association of soy-based foods consumption and cognitive function via NAHSIT in this study.

MATERIALS AND METHODS

Study design and participants. This cross-sectional

^{*}To whom correspondence should be addressed. E-mail: drchiou@hotmail.com

336 Lin H-C et al.

study was based on data from 2005–2008 NAHSIT. Subjects less than 65 y or with missing data were excluded. The demographic characteristics of subjects included age, gender, education, drinking and smoking habits, and medical history. NAHSIT dietary questionnaire included questions regarding 24-h dietary recall, food frequency, dietary habits, and dietary supplements (13). Cognitive function was assessed by the Short Portable Mental Status Questionnaire (SPMSQ) (14). Quality of life was measured by the Short Form 36 Health Survey (SF-36) (15). This study was approved by the Institutional Review Board of Chung Shan Medical University Hospital (CS13071).

Dietary assessment. The dietary questionnaire included 24-h dietary recall and a simplified food frequency questionnaire (SFFQ). Daily intake and servings of six food groups (such as cereals, legumes/eggs/fish/meat, milk, vegetables, fruit, and oil) were measured, based on 24-h dietary recall. The SFFQ contained 28 items related to foods and frequencies of intake (times per day/week/month).

Cognitive status. Cognitive assessment was determined by the validated Short Portable Mental Status Questionnaire (SPMSQ) because previous research indicated that SPMSQ can be accurately applied to people without formal nervous system training (16). Furthermore, Mini-Mental State Examination (MMSE) scores are susceptible to intelligence, education, and cerebral vascular accident (CVA) even if MMSE is more sensitive and specific (17). And the SPMSQ has been established in patients with organic brain syndrome in Taiwan (18). There were ten validated questions on the SPMSQ, with score ranging from 0 to 10. Cognitive impairment was defined as a score of less than (18).

Quality of life. SF-36 is a general survey of health-related quality of life used worldwide (20), and includes questions related to physical health (Physical Component Summary, PCS) and mental health (Mental Component Summary, MCS) (21). There are 36 items for assessing physical function, vitality, and mental and general health (22).

Statistical analysis. Stata version 11.0 software was used for data analyses. Data are presented as the mean \pm standard deviation. The logistic regression model was used to evaluate the influence of cognitive impairment. A p value less than 0.05 was considered statistically significant.

RESULTS

The demographic data for the subjects are presented in Table 1. There was a total of 1,105 participants aged more than 65 y with a complete SPMSQ (73.3 \pm 6.0 y). As shown in Table 1, 85.6% of all subjects consumed soy-based foods and the average SPMSQ score was 8.9 \pm 1.6. Moreover, mean physical component summary (PCS) and mental component summary (MCS) scores were 47.0 \pm 10.7 and 55.1 \pm 8.9, respectively.

After being adjusted for all variables, the results of the logistic regression model showed significant associations between cognitive impairment and age, gender,

Table 1. Demographic data for Taiwan's elderly population (n=1,105).

tion $(n=1,105)$.			
	Unweighted sample	Weighted percentage (%)	
Age, mean±SD	73.3	3±6.0	
65–80	976	87.9	
>80	129	12.2	
Gender			
Male	563	50.6	
Female	542	49.4	
Education			
≦Elementary school	828	71.3	
>Elementary school	277	28.7	
Smoking	_,,		
Never	717	66.2	
Formerly	225	20.1	
Currently	163	13.7	
Drinking	103	13.7	
Never	736	68.9	
Moderate	254	22.1	
Heavy	115	9.0	
Betel chewing	110	3.0	
Never	986	92.5	
Formerly	64	5.5	
Currently	55	2.1	
Soybean	33	2.1	
None	190	14.4	
<1 time/d	626	57.5	
≥1 time/d	289	28.1	
Fruit	20)	20.1	
None	90	6.8	
<1 time/d	461	39.0	
≥1 time/d	554	54.2	
Coffee	331	31.2	
None	930	81.1	
<1 time/d	134	14.8	
≥1 time/d	41	4.1	
Tea	11	1.1	
None	567	49.05	
<1 time/d	235	20.28	
≥1 time/d	303	30.67	
≦1 time/u Diabetes	198	17.98	
Dyslipidemia	136	13.36	
Hypertension	512	44.15	
Heart disease	161	13.84	
Stroke	65	4.79	
PCS			
MCS	47.0±10.7 55.1±8.9		
SPMSQ, mean±SD	8 9	±1.6	
Normal (8–10)	893	84.1	
Mild (6–7)	148	10.2	
Moderate (3–5)	57	5.1	
Severe (0–2)	7	0.7	
	,	· · · · · · · · · · · · · · · · · · ·	

education, soy-based food intake and PCS (Table 2). In addition, this model was adjusted for potential variables. As shown in Table 2, our results showed that among the elderly in Taiwan, age and female gender are strongly related to cognitive impairment (odds ratio (OR): 1.1 and 4.43, respectively). Conversely, education, soy-

Table 2. Odds ratio of cognitive impairment in Taiwan's elderly population.

	Crude	95% CI		Adjusted	95% CI	
	OR	Lower	Upper	OR	Lower	Upper
Age	1.10**	1.05	1.14	1.10**	1.04	1.15
Gender						
Male	1			1		
Female	5.65**	2.75	11.64	4.43**	1.75	11.26
Education						
≦Elementary school	1			1		
>Elementary school	0.11**	0.05	0.26	0.25**	0.12	0.51
Smoking						
Never	1			1		
Formerly	0.41*	0.17	0.97	1.28	0.53	3.09
Currently	0.31**	0.18	0.54	0.98	0.41	2.32
Drinking						
Never	1			1		
Moderate	0.32**	0.17	0.61	0.94	0.50	1.77
Heavy	0.46	0.16	1.30	1.43	0.40	5.04
Betel chewing						
Never	1			1		
Formerly	0.40*	0.17	0.96	0.87	0.17	4.37
Currently	1.06	0.34	3.32	2.72	0.93	7.97
Soybean				,_	0.00	
None	1			1		
<1 time/d	0.54**	0.35	0.82	0.57	0.32	1.03
≥1 time/d	0.48*	0.27	0.85	0.45**	0.25	0.81
Fruit	0.10	0.27	0.03	0.13	0.23	0.01
None	1			1		
<1 time/d	0.56*	0.33	0.95	0.58	0.32	1.04
≥1 time/d	0.33**	0.19	0.58	0.59	0.30	1.16
Coffee	0.55	0.19	0.38	0.59	0.30	1.10
None	1			1		
<1 time/d	0.43*	0.21	0.88	0.72	0.30	1.74
	0.43*	0.21 0.04		0.72	0.30	
≧1 time/d	0.20	0.04	0.98	0.50	0.11	2.39
Tea	1			1		
None	1	0.22	0.00	1	0.51	1.05
<1 time/d	0.55*	0.33	0.90	1.00	0.51	1.95
≧1 time/d	0.33**	0.19	0.57	0.58	0.29	1.17
Diabetes	0.95	0.55	1.64	0.99	0.44	2.22
Dyslipidemia	1.22	0.68	2.19	1.07	0.59	1.95
Hypertension	1.33	0.88	2.01	1.27	0.73	2.22
Heart disease	1.48	0.87	2.53	1.37	0.67	2.80
Stroke	1.21	0.53	2.74	0.99	0.36	2.73
PCS	0.95**	0.93	0.97	0.97*	0.95	0.997
MCS	1.00	0.97	1.03	1.00	0.97	1.03

Adjusted for all variables.

based food intake and PCS were negatively correlated with cognitive impairment (OR: 0.25, 0.45 and 0.97, respectively). Furthermore, elderly physical health may be less relevant to cognitive impairment.

Age, gender and educational status were important factors. Therefore, it was further confirmed whether soy-based food intake affected these factors (Table 3). The results showed that soy-based foods had different effects on cognitive risk in different age groups and educational levels. In particular, soy-based food intake significantly reduced cognitive impairment from 65 to

80 y of age and low education level (OR 0.55 and 0.56, respectively).

DISCUSSION

Among the elderly, cognitive impairment is a common neurodegenerative disorder and often affects quality of life. Age, gender, and educational level are strong risk factors for cognitive dysfunction (23). These results of our study were consistent with a previous cohort study (23).

Besides the above risk factors affecting cognitive

^{*} *p*<0.05, ** *p*<0.01.

338 Lin H-C et al.

Table 3. Subgroup analysis of odds ratio of cognitive impairment between soy-based food intake and none.

	Soybean intake vs. none				
	OR	95% CI			
		Lower	Upper		
Age ¹					
Age=65-80	0.55*	0.32	0.97		
Age>80	0.39	0.09	1.71		
Gender ²					
Male	0.48	0.22	1.02		
Female	0.56	0.31	1.01		
Education ³					
≦Elementary school	0.56*	0.35	0.88		
>Elementary school	0.16	0.02	1.55		

- ¹ Adjusted for gender, education and PCS.
- ² Adjusted for age, education and PCS.
- $^{\rm 3}$ Adjusted for age, gender and PCS.

decline, diet also improves cognitive function in healthy elderly people (24). A Japanese study has demonstrated that the Mediterranean diet is helpful for cognitive function in Japanese elderly (25). As shown in Table 1, more than 80% of Taiwanese elderly consume soy-based foods. Dietary soy is one of the characteristics of the Mediterranean diet.

Recent study has indicated that among soy isoflavones genistein and daidzein have estrogen-like effects which can improve premenopausal symptoms, osteoporosis, cardiovascular disease, and cognitive disease (26). The major finding of the present study is that cognitive impairment is negatively associated with consumption of soy-based foods. It is confirmed that soy isoflavones could enhance cognitive function, particularly visual memory and summary cognitive function (11) via binding to an estrogen receptor. Another study indicated that soy isoflavones have a nonestrogenic effect to improve cognitive function, including antioxidation, and regulation of cerebral blood flow and the neurotransmitter system (27).

In 2010, Patisaul and Jefferson indicated that estrogen can decrease the risk of cognitive disorders, leading to increased quality of life (26). Table 2 also shows a negative correlation between PCS and cognitive impairment. Based on these beneficial effects, our study can be used as a reference for making dietary recommendations for the elderly population in Taiwan.

Data for this study was from a nationwide nutritional survey. The advantage of this study is that the results are representative of the current situation in Taiwan. However, there are some limitations in terms of research methods and diet. First of all, this was a cross-sectional study; therefore, only a general correlation between soy-based food consumption and cognitive function is presented. We were also unable to track or to quantify soy-based food consumption. Secondly, further examination

will be necessary for the verification of MCI because the SPMSQ is only for general population screening.

In summary, the major finding of the present study is that cognitive impairment is negatively associated with consumption of soy-based foods. The result of this study can be used as a reference for making dietary recommendations for the elderly population.

Acknowledgments

This study was supported by a grant from Chung Shan Medical University Hospital for research projects in 2016 (CSH-2016-A-008). All authors participated in the critical revision of the manuscript and approved the final version.

REFERENCES

- Billard JM. 2013. Serine racemase as a prime target for age-related memory deficits. Eur J Neurosci 37: 1931–1938.
- Celec P, Ostatníková D, Cagánová M, Zuchová S, Hodosy J, Putz Z, Bernadic M, Kúdela M. 2005. Endocrine and cognitive effects of short-time soybean consumption in women. Gyn Obst Invest 59: 62–66.
- Sun A, Sun G. 1979. Neurochemical aspects of the membrane hypothesis of aging. *Interdis Top Gerontol* 15: 34–53.
- 4) Albert MS, DeKosky ST, Dickson D, Dubois B, Feldman HH, Fox NC, Gamst A, Holtzman DM, Jagust WJ, Petersen RC, Snyder PJ, Carrillo MC, Thies B, Phelps CH. 2011. The diagnosis of mild cognitive impairment due to Alzheimer's disease. *Alzheimers Dement* 7: 270–279.
- 5) McMinn J, Steel C, Bowman A. 2011. Investigation and management of unintentional weight loss in older adults. *BMJ* **342**: 754–759.
- 6) Chen RCY, Chang YH, Lee MS, Wahlqvist ML. 2011. Dietary quality may enhance survival related to cognitive impairment in Taiwanese elderly. Food Nutr Res 55: 7387–7397.
- 7) Nagarajan S, Burris RL, Stewart BW, Wilkerson JE, Badger TM. 2008. Dietary soy protein isolate ameliorates atherosclerotic lesions in apolipoprotein E-deficient mice potentially by inhibiting monocyte chemoattractant protein-1 expression. *J Nutr* 138: 332–337.
- 8) Christianson MS, Shen W. 2013. Osteoporosis prevention and management: nonpharmacologic and lifestyle options. *Clin Obst Gyn* **56**: 703–710.
- 9) Kim H, Xia H, Li L, Gewin J. 2000. Attenuation of neurodegeneration-relevant modifications of brain proteins by dietary soy. *Biofactors* **12**: 243–250.
- 10) Umphress ST, Murphy SP, Franke AA, Custer LJ, Blitz CL. 2005. Isoflavone content of foods with soy additives. J Food Compos Ana 18: 533–550.
- 11) Cheng PF, Chen JJ, Zhou XY, Ren YF, Huang W, Zhou JJ, Xie P. 2015. Do soy isoflavones improve cognitive function in postmenopausal women? A meta-analysis. *Meno*pause 22: 198–206.
- 12) Xiang X, An R. 2015. Body weight status and onset of cognitive impairment among U.S. middle-aged and older adults. Arch Gerontol Geriatr 60: 394–400.
- 13) Tu SH, Chen C, Hsieh YT, Chang HY, Yeh CJ, Lin YC, Pan WH. 2011. Design and sample characteristics of the 2005–2008 Nutrition and Health Survey in Taiwan. Asia Pac J Clin Nutr 20: 225–237.
- 14) Pfeiffer E. 1975. A short portable mental status ques-

^{*}*p*<0.05.

- tionnaire for the assessment of organic brain deficit in elderly patients. *J Amer Geriat Soc* **23**: 433–441.
- 15) Garratt AM, Ruta DA, Abdalla MI, Buckingham JK, Russell IT. 1993. The SF36 health survey questionnaire: an outcome measure suitable for routine use within the NHS? BMJ 306: 440–444.
- 16) Welch DC, West RL. 1999. The Short Portable Mental Status Questionnaire: assessing cognitive ability in nursing home residents. *Nurs Res* **48**: 329–332.
- 17) MacKenzie DM, Copp P, Shaw RJ, Goodwin GMA. 1996. Comparison of the Mini-Mental State Examination (MMSE), Abbreviated Mental Test (AMT) and Mental Status Questionnaire (MSQ). Psychol Med 26: 427–430.
- 18) Lee MB, Lee YJ. 1990. A cross-sectional epidemiological study of psychiatric comorbidity in hospitalized medically ill. *Chinese Psychi* 4: 10–26.
- 19) Xiu LL, Wahlqvist ML, Lee MS, Chen RCY. 2013. Cognitive impairment and limited dietary diversity or physical inactivity are conjoint precursors of incident diabetes more so in elderly women than men. Asia Pac J Clin Nutr 22: 635–645.
- 20) Meijer CJ, Schene AH, Koeter MWJ. 2002. Quality of life in schizophrenia measured by the MOS SF-36 and the Lancashire Quality of Life Profile: a comparison. *Acta Psych Scand* 105: 293–300.
- 21) Harvey PD, Bertisch H, Friedman JI, Marcus S, Parrella

- M, White L, Davis KL. 2003. The course of functional decline in geriatric patients with schizophrenia: cognitive functional and clinical symptoms as determinants of change. *Am J Geriatr Psychiatry* **11**: 610–619.
- 22) Lee MS, Chen RCY, Chang YH, Huang YC, Wahlqvist ML. 2012. Physical function mitigates the adverse effects of being thin on mortality in a free-living older Taiwanese cohort. J Nutr Health Aging 16: 766–783.
- 23) Yen CH, Yeh CJ, Wang CC, Liao WC, Chen SC, Chen CC, Liang J, Lai TJ, Lin HS, Lee SH, Lee MC. 2010. Determinants of cognitive impairment over time among the elderly in Taiwan: Results of the national longitudinal study. *Arch Gerontol Geriatr* **50**: 53–57.
- 24) Nolan KA, Blass JP. 1992. Preventing cognitive decline. *Clin Geriatr Med* **8**: 19–34.
- Okubo H, Inagaki H, Gondo Y, Kamide K, Ikebe K, Masui Y, Arai Y, Ishizaki T, Sasaki S, Nakagawa T, Kabayama M, Sugimoto K, Rakugi H, Maeda Y. 2017. Association between dietary patterns and cognitive function among 70-year-old Japanese elderly: a cross-sectional analysis of the SONIC study. Nutr J 16: 56–67.
- 26) Patisaul HB, Jefferson W. 2010. The pros and cons of phytoestrogens. Front Neuroendocrinol 31: 400–419.
- 27) Lee YB, Lee HJ, Sohn HS. 2005. Soy isoflavones and cognitive function. *J Nutr Biochem* **16**: 641–649.