Tofu Intake is Associated with Poor Cognitive Performance among Community-dwelling Elderly in China

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Abstract

Tofu is a soy product which is commonly consumed in Asian countries, such as China and Indonesia. Several studies found negative associations of high tofu consumption with cognitive function in older Asian populations. However, the effect of tofu on cognitive function remains disputed as it was not found in Western populations. In the present study, the effect of weekly tofu intake on cognitive performance was investigated in an observational cross sectional study of 517 Chinese elderly from Shanghai.

Similar to earlier studies, results showed that a higher weekly intake of tofu was associated with worse memory performance using the Hopkins Verbal Learning Test (HVLT) (β=-0.10, p=0.01) after controlling for age, gender, education, being vegetarian and weekly intake of fruit/juice, green vegetables and orange/red vegetables. Furthermore, among older elderly (≥68 years of age), high tofu intake increased the risk of cognitive impairment indicative of dementia (OR=1.27, 95% CI= 0.99-1.64, p=0.04), after adjusting for all covariates. Consumption of meat and green vegetables independently also reduced risk of dementia.

To conclude, high intake of tofu was negatively related to cognitive performance among community-dwelling elderly in China. Similar findings were reported in Indonesia and in Japanese Americans in the USA. These findings suggest that the effect of tofu on cognition in elderly should be further investigated.

Introduction

Soy products containing isoflavones, such as tofu, are common foods consumed in Asian countries. However, the effects of soy products on cognition remain debatable. Several authors suggested that higher soy consumption is associated with worse cognitive performance in Asian populations over the age of 65 years [1-3]. For instance, high tofu consumption was associated with worse memory using the Hopkins Verbal Learning Test (HVLT) [4] in a community-based study conducted in Indonesia [3]. This negative association of tofu and global cognitive function was also reported in two longitudinal studies in US among Japanese Americans [1-2]. On the other hand, a better performance on cognitive tests measuring processing speed (but worse verbal memory performance) was reported in a longitudinal study conducted in the US among Asian females during and after menopausal transition with high phytoestrogen intake [5]. Similarly, genistein, the most potent isoflavone or phytoestrogen was reported to be positively related to cognitive ability among middle-aged participants, but had negative associations in elderly subjects [6][7]. In addition, superior memory performance was associated with high consumption of another type of soy product, tempe, in several studies in Indonesia [3][8]. There are also some studies reporting no association between soy consumption and cognition, especially among older European and American people [6][8][9]. Age, gender, type of test used for assessment, level of consumption, ethnicity, being an equol producer and/or type of product consumed may explain some of the differences found.

Intervention studies also reported different results of soy isoflavones on cognitive function. Improvement of cognitive function, including attention [10-11], language [12-13], executive function [11-12] and visual memory [10][13-15] were reported after daily soy supplement interventions (ranging from (60-2000 mg/day, 1.5-6 months total duration). Yet no effect of isoflavone intake on cognitive function was reported with soy supplementation interventions ranging from 60-160 mg/day, within a total duration of intervention period from 4 to 12 months [16-20]. Noticeably, among all the reported intervention studies mentioned, only one of these was conducted in an Asian sample [18], whereas all the other studies were conducted in Western countries.

The relatively low treatment dosage here may have had no effect because the Asian participants would have already consumed more daily isofalvones [21]. Soy product intake is generally relatively higher in Asian countries which may affect isoflavone metabolism and/or their subsequent effect on the brain. Only very few studies looked into the effect of tofu on cognition among Chinese elderly people in community settings. In a recent study

no association of tofu and cognitive function was found in Chinese elderly [22]. However, this study was conducted among elderly above 90 years of age and survival bias may have played a role. Hence, the current study further explored the association between tofu intake and cognitive ability among community-dwelling elderly people in Shanghai, China. We used the same memory test earlier found to be sensitive to phytoestrogen intake and that found in saliva samples [3][7][8]. This test was also found to have very good sensitivity and specificity for dementia, in particular for its early stages [8][23][24][25]. Because inter-rater reliability for dementia is often 'moderate at best [26](Hogervorst, 2000) and many older people who were thought to have mild cognitive impairment will reverse to normal function [25], in this study we used the cut-off for that test which best indicated early dementia rather than the clinical diagnoses.

Methods

Participants

The present observational cross-sectional study was carried out between June 1 and August 31, 2011. All 50 to 95-year old persons born between June 1, 1916, and August 31, 1961, and registered for census purposes in Shanghai were invited to take part in the study. A total of 517 participants were recruited from urban sites in the North Xin Jing District of Shanghai, China. Ethical approval was obtained from Shanghai Mental Health Centre before the study was initiated.

Prior to the study all community elders and staff at local community health centres had been informed of the survey based study. Participants were communally talked to by the community centre supervisor and told about the study, its aims and procedures, as well as time and other commitments required for participation. Any questions were answered. The informed consent sheet was read and then signed by both participants and their caregivers when they wanted to take part (100% consented). Testing was done by the trained and supervised research assistants between 8-11 am to avoid the effects of time of day.

Assessments

The survey consisted of the following elements. General demographics covered a wide variety of information (e.g. age, gender, education, (past or present) occupation, and living arrangements). The food frequency questionnaire (FFQ) is a standardized questionnaire investigating participant’s dietary consumption habits and frequency of consumption of

particular foods [26]. Using the FFQ, consumption of foods, such as bread, rice, fruit/juice, green vegetables, orange/red vegetables, meat, tofu and tempe, were surveyed using daily, weekly and monthly frequency intakes. In the current study, food intake frequencies were calculated on a weekly basis (calculated from daily, weekly and monthly, e.g. food intake once/day, every day= 7 times/week; food intake once/month= 0.25 times/week, etc.).

The Hopkins Verbal Learning Test [4] is widely used to detect memory function. The HVLT is a word learning test consisting of 12 words from 3 low frequency categories. It has 6 parallel versions but in our study only version A was used. Words from these 3 categories ('human shelter', 'animals' and 'precious stones') were repeated 3 times for the total immediate recall (IR). Delayed Recall (DR) was not included in analyses, as earlier work found this variable to be less sensitive than the IR to associations with tofu consumption [7].

After cognitive testing, an extensive medical examination was conducted by trained and qualified medical clinicians, which led to a consensus diagnosis of dementia. Dementia and Mild Cognitive Impairment (MCI, a precursor of dementia) [27] were diagnosed according to standard clinical diagnostic criteria, the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) [28] and the revised Petersen's diagnostic algorithm for MCI [27], respectively.
Using a combination of cognitive tests and the clinical investigations, three groups were established consisting of no cognitive impairment (NCI), MCI and dementia.

Data Analysis

To establish whether the cut-off on the HVLT IR obtained in Indonesia [8], the UK [23] and the USA [4] of 18/19 also had good sensitivity and specificity for dementia in China, receiver operating characteristic (ROC) analyses was employed including MCI and dementia (possible dementia or DEM) versus controls (NCI).

Descriptive analyses were performed for frequencies and percentages for demographic, lifestyle variables and cognitive performance in the whole group and between participants who ate tofu and those who did not. The analyses were done using Chi Square tests for percentages (e.g. for gender) and independent t-tests for continuous data. The demographics variables were gender, age, education, occupation and living status (whom the participants were living with and whether this was an institution or in the community),

the sample was also described for cognitive scores on the HVLT IR. Linear regression analysis was employed to investigate the effect of tofu on HVLT performance using the HVLT IR scores (continuous data as these showed a normal distribution) as the dependent variable, adjusting for demographic and other dietary variables, including age, gender, education, being vegetarian (yes or no to eating meat), weekly intake of fruit/juice, green vegetables and orange/red vegetables.

Subsequently, having possible dementia based on the HVLT cut-off was used in logistic regression analyses as dependent variable, controlling for demographic and other dietary variables including age, gender, education, being vegetarian (yes or no), weekly intake of fruit/juice, green vegetables and orange/red vegetables. Analyses were also stratified by median age (68 years of age) to investigate previously found effects of age (Hogervorst, 2008). All data analyses were performed using SPSS 21.0., using a p value of <0.05 for significance.

Results

Table 1 shows the descriptive analyses of the cohort split into those with possible dementia (DEM) and those without (NCI). DEM was categorized using the HVLT total recall (IR) performance. The optimal cut-off score of the HVLT in discriminating between NCI and MCI and dementia cases was generated by applying the Receiver Operational Characteristics (ROC). A HVLT score of equal or less than this cut-off score (≤19 in the current study) was defined as “possible dementia (DEM) (Area Under Curve (AUC) = 0.92, 95% CI= 0.89-0.94), this rendered 90.0% sensitivity and 79.6% specificity when distinguishing DEM cases (dementia and MCI) from NCI cases. This cut-off score was further adopted in the current study to define cognitive impairment (CI). This score is similar to that found in earlier studies investigating dementia in Oxford and Indonesia and ALSO predicted diagnoses independent of education, age, gender and depression [8].

Participants in the DEM group were more likely to be older (74 vs. 66 years, on average) and less educated (60% vs. 23%) but had equal proportions of females as the NCI. Reflecting the cut-off score, there was a 13- point difference between DEM and NCI groups on the HVLT IR performance (12 vs. 25 word recalled) whereas an 8-point difference was observed on the HVLT DR performance between these 2 groups (1 word recalled for DEM vs. 9 for NCI, data not in table). (table 1).

Linear regression models (see table 2) demonstrated that weekly tofu intake was negatively associated with immediate recall memory on the HVLT (IR) after controlling for

demographic (age, gender and education) and other food intake variables (being vegetarian, weekly intake of fruit/juice, green vegetables and orange/red vegetables). Eating meat (not being vegetarian) was independently associated with better memory function, as was consumption of green vegetables (table 2).

A bar graph showed an overall trend for increasing weekly tofu intake to be negatively and linearly associated with subject's worse performance on the HVLT IR test (Fig 1).

A logistic regression model using DEM as a binary outcome investigated the predictive value of weekly tofu intake, controlling for demographic variables and other types of food consumed weekly. These analyses indicated that there was a trend for weekly tofu intake to increase the risk for CI by 20% (OR=1.20, p=0.08) after adjusting for age, gender, education, vegetarian habits, and weekly intake of fruit/juice, green/orange/red vegetables. In our previous study [3] tofu intake was mainly negatively associated with dementia risk and worse memory performance among 'older' elderly (>68 years of age). Therefore, in the current study stratification using a median age split (68 years of age) was applied (see table 3).

From table 3 we can see that among younger participants, there was no significant association of tofu consumption with DEM, whereas an increased risk of almost 30% was seen among older elderly (≥68 years of age) (OR=1.27, 95% CI=0.99-1.64, p=0.04) after adjusting for all the other covariates. Independently, not being vegetarian (eating meat) decreased risk for cognitive impairment almost 4-fold and eating green vegetables reduced the risk by almost 20%. Education, but not gender or age also reduced the risk independently in this older group.

Discussion

In the present study, higher intake of tofu was negatively associated with learning ability and immediate memory performance on the HVLT. Furthermore, among elderly who were 68 years of age or older, higher weekly tofu intake was a significant risk factor which increased the risk of possible dementia, independent of the other covariates, including demographic variables and other dietary habits. Similar results could be found in another earlier study conducted in Indonesia, where high tofu intake was associated with poor memory using the same test [3]. The authors also reported that in that cohort tempe intake, a fermented whole soybean food was significantly related to better memory [3][8]. However, tempe is not a popular type of food in China and only very limited number of participants reported to eat tempe (5 out of 521, less than 1% of the whole sample), hence

consumption of tempe was not included in the current analyses. Tempe, similar to green vegetables, contains folate which reduces homocysteine, a risk factor for dementia and cognitive decline [29]. Not being vegetarian, e.g. eating meat in elderly was associated with a four-fold decrease in risk of possible dementia. In contrast, one earlier study noted that meat eaters had a doubled risk of dementia [30]. This may be because meat contains saturated fats, which is a risk factors for cardiovascular disease, and risk factors for cardiovascular disease are risk factors for dementia [31]. However, meat also contains cobalamin which can further help reduce homocysteine levels [29]. This means that a well-balanced diet with little protein, such as tofu and lean meats, but plenty of vegetables are probably best suited for elderly to prevent dementia. On the other hand in Indonesia, high green vegetable consumption was associated with increased dementia risk [3], which was possibly due to pollution and heavy use of pesticides. Hence, moderation of overall food intake is probably best advised, similar to earlier advice regarding the consumption of fatty (polluted) fish.

There were several limitations to the current study. Firstly, the results from the current study may have limited representativeness. The socioeconomic status (SES) was not different for those with possible dementia and those without. However, overall SES of the cohort investigated was quite low (the current sample was drawn from a relatively underdeveloped area in Shanghai, China). Because the present study was conducted in a cross-sectional community setting, it is not possible to examine whether elderly who eat more tofu actually also deteriorated cognitively. A follow-up study thus needs to be performed. In addition, the current sample was constituted of Chinese elderly only. Therefore results might not apply to Western countries as several earlier studies did not find these types of associations in non-Asian populations. Lastly, it may well be that lower quantities of tofu consumption do not lead to cognitive impairment and an optimal dosage needs to be investigated to maintain optimal health and cognitive function in the elderly. Our graphs in China and Indonesia did not suggest optimal intakes of tofu for elderly, although for those of middle-age optimal levels of genistein associated with better cognitive function were detected in Indonesia [7]. This may be associated with its estrogenic effects on brain function, which may be positive in middle-aged people but which may worsen pathology in the old [7]. In sum, further research needs to investigate whether tofu really is associated with worse cognitive function and increased risk for dementia in those over 68 years of age and whether a balanced diet and exercise particularly in midlife can affect this risk in later life [32].

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Conflict of Interest

None.

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Table 1. Descriptives of demographic and lifestyle variables and HVLT performance in DEM and NCI groups

	DEM Group 115 (22.1%)	NCI Group 406 (77.9%)	p Value
Demographic Variables			
Age	73.8 ± 9.9	65.7 ± 9.6	<0.001
Gender (Female %)	69 (60.0%)	215 (53.0%)	NS
Education			
No education or only primary level	69 (60.0%)	93 (22.9%)	<0.001
Secondary and above level	46 (40.0%)	313 (77.1%)	
Profession			
No Job or Manual	81 (70.4%)	267 (65.8%)	NS
Non Manual	34 (29.6%)	139 (34.2%)	
Dietary Habit Variables			
Vegetarian (Yes % , not eating meat)	74 (64.3%)	202 (49.8%)	0.006
Type of food (times/week)			
Tofu (mean weekly intake)	1.6 ± 1.5	1.8 ± 1.6	NS
Fruit/juice (mean weekly intake)	2.7 ± 1.9	2.7 ± 1.9	NS
Vegetables (mean weekly intake)	8.7 ± 4.4	9.9 ± 3.4	0.007
HVLT Performance			
HVLT IR	11.8 ± 6.6	25.4 ± 7.1	<0.001

[a]= trend level significance

Table 2. Linear regression analyses in 2 steps: step1, entering weekly tofu consumption (times per day/month x 7) controlled for age, gender and education; step 2, also controlled for other dietary intake

	HVLT (IR)			
	Step 1		Step 2	
	β	p Value	β	p Value
Tofu (weekly)	-0.11	0.009	-0.10	0.01
Age	-0.34	<0.001	-0.31	<0.001
Gender	-0.05	NS	-0.03	NS
Education	0.27	<0.001	0.3	<0.001
Not being vegetarian	-	-	0.16	<0.001
Fruit/Juice (weekly)	-	-	0.06	NS
Green Vegetables (weekly)	-	-	0.17	<0.001
Orange/Red Vegetables (weekly)	-	-	0.004	NS

NS= Not Significant

Table 3. Logistic regression analyses stratified for age using the median split (68 years of age), controlled for age, gender and education in step 1, and dietary habits in step 2

	<68 years of age		≥68 years of age	
	Step 1	Step 2	Step 1	Step 2
	Odd Ratio (95% CI), p value			
Weekly Tofu intake	NS	NS	1.24 (0.97-1.57), p=0.08[a]	1.27 (0.99-1.64), p=0.04
Age	NS	NS	1.10 (1.01-1.18), p=0.02	NS
Education	0.90 (0.84-0.96), p=0.002	0.87 (0.81-0.94), p<0.001	0.85 (0.76-0.94), p=0.001	0.83 (0.74-0.93), p=0.001
Gender (Male)	NS	NS	0.49 (0.27-0.90), p=0.02	0.54 (0.28-1.04), p=0.06[a]
Not being Vegetarian	-	NS	-	3.80 (1.87-7.70), p<0.001
Weekly fruit/juice intake	-	NS	-	NS
Weekly green vegetables intake	-	0.83 (0.75-0.92), p<0.001	-	0.81 (0.73-0.89), p<0.001
Weekly orange/red vegetables intake	-	NS	-	NS

NS= Not Significant; [a]= trend for significance

Fig 1. Relationship between mean HVLT IR score and weekly Tofu intake