



Published in final edited form as:

*J Alzheimers Dis.* 2018 ; 65(1): 99–105. doi:10.3233/JAD-180103.

## No effects of black tea on cognitive decline among older US men: a prospective cohort study

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### Abstract

**Background:** Accumulating evidence supports the neuroprotective effects of bioactive compounds from tea leaves. There are limited data from black tea consumption populations.

**Objective:** To determine whether black tea consumption is associated with cognitive decline among older men.

**Methods:** We chose to study the association between black tea consumption and cognition using data from the MrOS cohort, which collected information on tea consumption at baseline and has repeatedly assessed cognitive function in 3844 men aged 65+ years (mean=72.4 years). We defined tea drinkers as those who drank black tea at least once per week and further grouped them into weekly drinkers and daily drinkers. Cognitive function was assessed at baseline and approximately 7 years later using the Modified Mini Mental State Examination (3MSE). Multivariable logistic regression and linear regression models were constructed to assess the

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**Disclosure statement:** The authors report no disclosures.

association between black tea consumption and risk of fast cognitive decline as a binary variable and change in 3MSE scores as continuous variable. Fast cognitive decline was defined as decline in 3MSE >1.5 standard deviation of mean change score. Models were adjusted for age, education level and baseline cognitive scores.

**Results:** Weekly and daily black tea drinkers were 24.8% and 12.4% of the study cohort, respectively. Fast cognitive decline occurred in 243 (6.3%) participants. Tea consumption was not associated with risk of cognitive decline, nor was tea associated with cognitive decline measured by absolute change in 3MSE scores.

**Conclusions:** There was no association of black tea consumption and cognitive decline among older men in the US.

### Keywords

black tea; cognitive decline; men; aging

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## INTRODUCTION

The potential role of tea drinking in delaying age-related cognitive decline has attracted increasing attention in recent years. The biological plausibility of a neuroprotective effect of tea drinking is supported by various bioactive properties of compounds in tea leaves [1]. To date, human evidence has emerged from populations with an established tea-drinking culture such as Singapore [2-4], Japan [5-7] and China [8] where non-fermented (green) and partially fermented (oolong) tea are widely consumed.

Based on data from Singapore, Feng reported that both black /oolong tea and green tea consumption were associated with better cognitive performance in older Chinese [2]. However, a Finnish study reported no association between black tea consumption during mid-life and dementia incidence [9]. Another study from a black tea-consuming population found that tea drinking was associated with slower cognitive decline, but in women only [10]. The latter study is intriguing as there is no known biological explanation for sex differences of the hypothesized tea and cognition association.

We analyzed longitudinal data from the Osteoporotic Fractures in Men (MrOS) study cohort to examine the association between black tea consumption and cognitive decline among older US men to clarify the aforementioned issues. We aimed to examine the association of black tea consumption with fast cognitive decline and the absolute change of cognitive scores during the follow-up period.

## MATERIALS AND METHODS

### Subjects

The MrOS study population consists of community dwelling, ambulatory men aged 65 years or older [11, 12]. The cohort recruited 5994 men at baseline, among whom 4681 were assessed approximately 7 years ( $6.84 \pm 0.35$  years) later at a follow-up visit. Among the 4681 subjects, 820 had missing data on the Modified Mini-Mental State Examination (3MSE) and

17 had missing data on black tea consumption. Accordingly, the association between black tea consumption and 3MSE was analyzed using data from 3844 MrOS participants.

### **Cognitive function**

The 3MSE test was used to assess cognitive function. The 3MSE is a screening test of global cognitive function. 3MSE scores range from zero to 100, with higher scores representing better cognitive function. We defined fast cognitive decline as a decline of  $> 1.5$  SD above the mean change score from baseline to follow-up based on criteria that have been used in a prior study [13]. The cutoff value for 3MSE was determined using available data from 3861 MrOS participants.

### **Tea consumption**

Tea consumption at baseline was estimated using the MrOS Brief Food Frequency Questionnaire. Participants were asked how often, on average, did they drink black tea in the past year. Responses were coded as: (1) Never; (2) A few times per year; (3) Once per month; (4) 2-3 times per month; (5) Once per week; (6) Twice per week; (7) 3-4 times per week; (8) 5-6 times per week; and (9) Every day. We defined black tea drinkers as those who drank black tea at least once per week and further grouped black tea drinkers into weekly drinkers (1-6 times per week) and daily drinkers (drink tea every day).

### **Other variables**

Information on age, education, medical conditions was collected at baseline. Education was recoded as a binary variable (college and above vs. others) before analysis. One question in the MrOS Brief Food Frequency Questionnaire was used to collect information on average coffee consumption in the past year; the responses were coded in the same way as tea consumption.

### **Statistical analyses**

We used Fisher's exact test (2-sided), Pearson chi-square test and Mann Whitney U test for the comparison of various characteristics between black tea drinkers and non-tea drinkers and between fast decliner and non-fast decliners defined by 3MSE. Multiple logistic regression models were used to analyze the association between tea consumption and the risk of fast decline. Multivariable linear regression models were used to analyze the association between tea consumption and cognitive decline measured by absolute change in 3MSE score. Models were adjusted for major determinants of cognitive decline (age, education and baseline cognitive function). Fasting glucose concentration (as a continuous variable) was further controlled for because adding sugar is a common practice among tea drinkers in the US and this may influence the results. Further analysis was conducted using linear mixed models to account for within-individual correlation of 3MSE scores. We also analyzed the associations between coffee consumption and cognitive outcomes for comparison purposes. All analyses were performed using IBM SPSS Statistics for Windows, Version 24.0 (IBM Corp, Armonk, NY, USA).

## RESULTS

There were 1430 black tea drinkers (at least once a week) in our study sample. As shown in Table 1, tea consumption was associated with a lower proportion of daily coffee drinkers but no other variables. There were 243 fast cognitive decliners. Compared with non-fast decliners, the fast decliners were older at baseline, were less likely to have a college education, had lower scores on 3MSE at baseline, and greater history of stroke and diabetes mellitus (Table 2). There was no difference in tea consumption between fast decliners and non-fast decliners. Based on results from the multivariable logistic regression, black tea consumption was not associated with fast cognitive decline (Table 3). Analyzing the data with multiple linear regressions using cognitive decline as a continuous outcome yielded similar results (Table 4). The results remained essentially the same when data were analyzed using linear mixed models. Coffee consumption was not associated with cognitive outcomes (data not shown).

## DISCUSSION:

Based on data from the MrOS cohort, we found no association of black tea consumption with cognitive decline among older men in the US. The results remained the same regardless of whether we treated cognitive decline as a binary variable or continuous score. Our findings do not support cognitive benefits of black tea consumption for older men in the US. We also did not find cognitive benefits of coffee drinking in this study population.

There are different types of tea, though all teas are produced from the same plant, *Camellia sinensis*. Due to oxidation, black tea contains more thearubigins, theaflavins and less catechins, while the amount of L-theanine is comparable with green tea and oolong tea. Since there was no association of black tea drinking with cognitive decline among MrOS participants, our findings may indirectly suggest that catechins, but not polymerized polyphenol, are responsible for any potential neuroprotective effects of tea drinking. Up to date, six studies have examined the association of tea consumption with cognitive decline or dementia prospectively (Table 5). Positive associations were reported from a population with mixed tea drinking habits (Singapore) or a population that predominantly drinks green tea (Japan) but not a population that predominantly drinks black tea (Finland and US).

The relatively small proportion of daily tea drinkers (12.4%) among MrOS participants may have biased the analysis against finding protective associations, if such associations truly exist. We analyzed tea-drinking data from two Asian cohorts from which Feng and colleagues have reported positive results previously. In the Singapore study sample [4], the proportion of daily tea drinkers was 20.2%, 21.2% and 6.7% for black tea, Chinese green and oolong tea, and green tea, respectively. In the Chinese study sample [8], there were 26.7% daily tea drinkers.

Unexpectedly, we found greater 3MSE decline among daily tea drinkers in the initial regression model. However, the association became statistically non-significant when models were adjusted for fasting glucose concentration as a continuous variable, suggesting a potential role of glucose metabolism in the tea-and-cognition associations. In the Chinese

and Japanese culture, tea is traditionally consumed without sugar, milk and creamer, while the practice of using additives is common in Western populations. A previous study showed that blood glucose concentration, regardless of a diagnosis of diabetes mellitus, is a risk factor of late life cognitive decline [14].

Our results on black tea are consistent with findings from the Cardiovascular Risk Factors, Aging, and Dementia (CAIDE) study. In this analysis, Eskelinen and colleagues reported no association between tea drinking in mid-life and risk of Alzheimer's disease or other dementia in late life. However, our results on coffee contradict the CAIDE findings of reduced risk of dementia associated with coffee consumption. We noticed that CAIDE participants drank more coffee than MrOS participants did. In the analysis by the CAIDE study team, the reference group used was those who drank less than 3 cups of coffee per day, and lowest risk of dementia was observed for those who drank 3-5 cups per day. Indeed, there is no definitive conclusion on the association between coffee consumption and late life cognitive function. In another study based on 3494 men in the Honolulu-Asia Aging Study (HAAS), Gelber and colleagues reported that midlife coffee intake was not associated with dementia and cognitive impairment in late life[15]. Many factors may affect the findings from a particular study population, and both frequency of consumption and consistency of consumption are critical. Indeed, previous studies concluded that consistent and moderate coffee consumption was associated with a reduced risk of cognitive decline and cognitive impairment [16]. An earlier study showed that adjustment for potential confounders can markedly change the main results on the relationship between coffee consumption and mortality [17]. In this study, the result of coffee consumption and cognitive decline remained statistically non-significant when we adjusted for more variables (age, education, hypertension, diabetes, heart disease, stroke) in the regression models.

Data from the Cardiovascular Health Study have shown that cognitive benefits of black tea drinking were evident at relatively low levels of intake. In this analysis, Arab and colleagues revealed reduced rates of cognitive decline for various levels of tea consumption lower than at least once a day among women, with no such effect for men [10]. Our negative findings in men are consistent with their findings. However, there is no good biological explanation for such a sex difference on cognitive benefits of tea drinking. Social-demographic and related lifestyle factors may play a role and should be examined in future studies that include both men and women.

A recent systematic review of selected longitudinal population-based studies suggests that tea is associated with a reduction in cognitive decline but there is a lack of a linear dose-response relationship, and the effect is stronger among women than men [18]. The authors proposed that the lack of a linear dose-response relationship suggests that some other factor or factors associated with consumption and nonconsumption of the beverage may explain the associations found [18]. Our study showed that black tea consumption has no effects on cognitive decline in men, regardless of the frequency of intake (weekly or daily). Without a distinct dose-response relationship and consistent benefits observed in both women and men, the underlying causes (true biological effects vs. lifestyles associated with tea consumption vs. other uncontrolled characteristics of tea consumers) of previous reported associations between tea and lowered cognitive decline remain to be answered. A randomized controlled

trial with both genders, multiple intervention arms (low dose vs. high dose) and sensitive outcome measures may be the best research study design to answer those questions, and potentially end the ongoing controversies.

The strengths of our study included the prospective study design and repeated assessment of cognitive function using standardized cognitive test. However, we only used 3MSE to define cognitive decline. Several cross-sectional and longitudinal population-based studies suggested a protective effect of coffee, tea, and caffeine against late life cognitive impairment and cognitive decline, although the association was not found in all cognitive domains investigated [19]. Also, we did not collect detailed information on duration of tea consumption and the possible changing of tea drinking habits. Another limitation of our study and all previous cohort studies that have examined the association between tea consumption and cognition is the lack of objective biomarkers for tea intake. Self-reporting is prone to bias and measurement errors, and does not reflect the absorption of bioactive compounds by the digestive system. Objective markers of tea bioactive compounds in the blood and urine should be measured in future studies. Such biomarkers may include catechins, theaflavins, thearubigins, L-theanine and their metabolites. The addition of tea biomarkers may help to reduce measurement errors and also provide clues on what are the compounds that contribute to observed cognitive benefits, if any. Biomarkers of brain pathology such as Magnetic Resonance Imaging (MRI), Positron Emission Tomography (PET) and cerebrospinal fluid based biomarkers of tau and amyloid can be monitored [20] because such biomarkers are more sensitive than cognitive tests in detecting smaller effects.

In summary, we found that black tea consumption was not associated with cognitive decline among older men in the US. The role of tea consumption as a protective factor for cognitive decline should be further clarified; special attention should be paid to types of tea consumed. For definitive conclusions, a randomized controlled trial with tea consumption or tea bioactive compounds as the intervention should be conducted.

## Acknowledgements:

The Osteoporotic Fractures in Men (MrOS) Study is supported by National Institutes of Health funding. The following institutes provide support: the National Institute on Aging (NIA), the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), the National Center for Advancing Translational Sciences (NCATS), and NIH Roadmap for Medical Research under the following grant numbers: U01 AG027810, U01 AG042124, U01 AG042139, U01 AG042140, U01 AG042143, U01 AG042145, U01 AG042168, U01 AR066160, and UL1 TR000128. Dr. Feng is supported in part by the National Medical Research Council of Singapore [grant number NMRC/TA/0053/2016].

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**Table 1.**

Description of the study population based on tea drinking status at baseline

Variable	Tea drinkers (N=1430)	Non-tea drinkers N=2414)	p value
<b>Baseline variables</b>			
Age in years, mean (SD)	72.6 (5.2)	72.3 (5.2)	0.14
Education: college and above, N (%)	818 (57.2)	1356 (56.2)	0.55
Hypertension, N (%)	600 (42.0)	952 (39.4)	0.13
Diabetes mellitus, N (%)	140 (9.8)	205 (8.5)	0.18
Heart diseases <sup>*</sup> , N (%)	289 (20.2)	471 (19.5)	0.62
Stroke, N (%)	55 (3.9)	104 (4.3)	0.50
Fasting glucose (mg/dL), mean (SD)	105.5 (23.7)	104.4 (22.5)	0.18
Weekly coffee drinker, N (%)	353 (24.7)	404 (16.8)	<0.001
Daily coffee drinker, N (%)	757 (53.0)	1561 (64.7)	
3MSE, mean (SD)	94.3 (4.7)	94.3 (4.7)	0.86
<b>Follow-up variable</b>			
3MSE, mean (SD)	91.7 (7.5)	92.0 (7.3)	0.10

Tea drinkers were defined as those who drink tea at least once per week.

P values were calculated using Fisher's exact test (2-sided) for binary variables, Pearson chi-square test for categorical variables and Mann Whitney U test for continuous variables.

\* Heart attack, angina or heart failure.



**Table 2.**

Description of the study population based on cognitive decline (3MSE) status

Variable	Fast decliner (N=243)	Non-fast decliner N=3601)	p value
<b>Baseline variables</b>			
Age in years, mean (SD)	75.3 (5.4)	72.2 (5.1)	<0.001
Education: college and above, N (%)	120 (49.4)	2054 (57.0)	0.023
Hypertension, N (%)	108 (44.4)	1444 (40.1)	0.20
Diabetes mellitus, N (%)	37 (15.2)	308 (8.6)	0.001
Heart diseases <sup>*</sup> , N (%)	58 (23.9)	702 (19.5)	0.11
Stroke, N (%)	16 (6.6)	143 (4.0)	0.06
Fasting glucose (mg/dL), mean (SD)	107.3 (25.6)	104.6 (22.7)	0.13
Baseline 3MSE, mean (SD)	92.8 (5.4)	94.4 (4.6)	<0.001
Weekly tea drinker, N (%)	65 (26.7)	887 (24.6)	0.39
Daily tea drinker, N (%)	35 (14.4)	443 (12.3)	
Weekly coffee drinker, N (%)	50 (20.6)	707 (19.6)	0.11
Daily coffee drinker, N (%)	133 (54.7)	2185 (60.7)	
<b>Follow-up variable</b>			
3MSE, mean (SD)	73.5 (11.7)	93.1 (5.0)	<0.001

Fast cognitive decline was defined as decline of 3MSE score 12 points.

P values were calculated using Fisher's exact test (2-sided) for binary variables, Pearson chi-square test for categorical variables and Mann Whitney U test for continuous variables.

\* Heart attack, angina or heart failure.

**Table 3.**

Association between tea consumption and fast cognitive decline: binary logistic regression

Tea consumption	Total N	Cognitive decline N (%)	Odds Ratio (95% CI)	P value
Non-tea drinkers	2414	143 (5.9%)	Reference	
Weekly tea drinkers	952	65 (6.8%)	1.16 (0.85, 1.58)	0.34
Daily tea drinkers	478	35 (7.3%)	1.19 (0.81, 1.75)	0.38

Fast cognitive decline was defined as decline of 3MSE score  $\geq$  12 points.

Adjusted for age, education and baseline 3MSE scores

**Table 4.**

Association between tea consumption and cognitive decline: linear regression

Tea consumption	Change in 3MSE score	
	Coefficient (95% CI)	p value
Non-tea drinkers	Reference	
<b>Model 1</b> *		
Weekly tea drinkers	0.08 (-0.38, 0.55)	0.72
Daily tea drinkers	0.66 (0.05, 1.27)	0.03
<b>Model 2</b> **		
Weekly tea drinkers	0.06 (-0.43, 0.54)	0.82
Daily tea drinkers	0.60 (-0.03, 1.24)	0.06

Dependent variable was the change score of 3MSE from baseline to follow-up: 3MSE change score= baseline 3MSE – follow-up 3MSE score; greater change score indicates greater cognitive decline.

\* Adjusted for age, education and baseline 3MSE.

\*\* Further adjusted for fasting glucose.

**Table 5.**

Summary of major prospective cohort studies on tea consumption and late life cognition

<b>Cohort</b>	<b>Country</b>	<b>Tea consumed</b>	<b>key findings</b>
SLAS	Singapore	Mixed: green, oolong and black tea	Tea consumption was associated with lower risk of cognitive decline
CAIDE	Finland	Black tea	Tea consumption was not associated with the incidence of dementia and Alzheimer's disease.
CHS	US	Black tea	Tea consumption was associated with slower cognitive decline among women but not men.
Nakajima	Japan	Green tea	Green tea consumption was associated with lower risk cognitive decline.
SLAS	Singapore	Mixed: green, oolong and black tea	Tea consumption was associated with lower risk of incident neurocognitive disorders.
Ohsaki	Japan	Green tea	Green tea consumption was associated with lower risk of incident dementia.