

# Green tea and coffee consumption is inversely associated with depressive symptoms in a Japanese working population

Ngoc Minh Pham<sup>1,\*</sup>, Akiko Nanri<sup>1</sup>, Kayo Kurotani<sup>1</sup>, Keisuke Kuwahara<sup>1</sup>,  
Ayami Kume<sup>1</sup>, Masao Sato<sup>2</sup>, Hitomi Hayabuchi<sup>3</sup> and Tetsuya Mizoue<sup>1</sup>

<sup>1</sup>Department of Epidemiology and Prevention, Clinical Research Center, National Center for Global Health and Medicine, 1-21-1 Toyama, Shinjuku-ku, Tokyo 162-8655, Japan: <sup>2</sup>Department of Applied Biological Chemistry, Graduate School of Bioresource and Bioenvironmental Sciences, Kyushu University, Fukuoka, Japan: <sup>3</sup>Faculty of Human Environmental Science, Fukuoka Women's University, Fukuoka, Japan

Submitted 3 September 2012: Final revision received 30 November 2012: Accepted 23 January 2013: First published online 4 March 2013

## Abstract

**Objective:** To examine the association between the consumption of green tea, coffee and caffeine and depressive symptoms.

**Design:** Cross-sectional study. Consumption of green tea and coffee was ascertained with a validated dietary questionnaire and the amount of caffeine intake was estimated from these beverages. Depressive symptoms were measured using the Center for Epidemiologic Studies Depression Scale. Multiple logistic regression analysis was performed to compute odds ratios and 95% confidence intervals for depressive symptoms with adjustments for potential confounders.

**Setting:** Two workplaces in north-eastern Kyushu, Japan, in 2009.

**Subjects:** A total of 537 men and women aged 20–68 years.

**Results:** Higher green tea consumption was associated with a lower prevalence of depressive symptoms. Compared with participants consuming  $\leq 1$  cup/d, those consuming  $\geq 4$  cups green tea/d had a 51% significantly lower prevalence odds of having depressive symptoms after adjustment for potential confounders, with significant trend association ( $P$  for trend = 0.01). Further adjustment for serum folate slightly attenuated the association. Coffee consumption was also inversely associated with depressive symptoms ( $\geq 2$  cups/d *v.*  $< 1$  cup/d: OR = 0.61; 95% CI 0.38, 0.98). Multiple-adjusted odds for depressive symptoms comparing the highest with the lowest quartile of caffeine consumption was OR = 0.57 (95% CI 0.30, 1.05;  $P$  for trend = 0.02).

**Conclusions:** Results suggest that higher consumption of green tea, coffee and caffeine may confer protection against depression.

**Keywords**  
Green tea  
Coffee  
Caffeine  
Depression

Major depression is an important public health issue, with a lifetime prevalence rate of approximately 15% among adults in high-income countries worldwide<sup>(1)</sup> and projected to be ranked third among disorders contributing to the global burden of disease by 2030<sup>(2)</sup>. In Japan, the number of patients with depression has been increasing and the suicide rate is among the highest in the world over the past decade<sup>(3)</sup>. Accumulating epidemiological evidence supports the role of dietary factors in depression<sup>(4)</sup>. Tea and coffee are the two most-consumed beverages worldwide after water<sup>(5,6)</sup>, and green tea is a typical type in Asia. In Japan, consumption of green tea and coffee is popular, with respectively 53% and 47% of adults consuming on a daily basis<sup>(7)</sup>. Animal studies have shown that green tea catechins increase serum levels of noradrenaline and dopamine<sup>(8)</sup>, which are posited to play a major role in depression<sup>(9)</sup>. Moreover, theanine, a major amino acid in green tea, is found to exert an

antidepressant effect in human participants<sup>(10)</sup>. Coffee is a major source of caffeine, which has been suggested to modulate dopaminergic transmission and facilitate the release of serotonin<sup>(11,12)</sup>. It is thus expected that consumption of green tea, coffee and caffeine may have beneficial effects against depression.

Epidemiological data on the association between these beverages and depressive symptoms are limited and/or inconsistent. A community-based study reported that Japanese elderly who consumed higher amounts of green tea had a lower prevalence of depressive symptoms<sup>(13)</sup>. Another study among breast cancer survivors in China also showed an inverse association between tea consumption, mainly green tea, and depression<sup>(14)</sup>. In an earlier Japanese study, higher green tea consumption was associated with decreased mental ill-health, although the association was not statistically significant<sup>(15)</sup>. Studies on coffee or caffeine consumption in relation to depression

have yielded inconsistent results<sup>(13,16–18)</sup>. In Japan, no association with coffee was reported from the above-mentioned study among the elderly<sup>(13)</sup> who consumed less amount of coffee, and no data are available regarding the association with caffeine intake.

Green tea is a good source of folate<sup>(19)</sup>, which has been linked to decreased depressive symptoms<sup>(20)</sup>. It would thus be of interest to examine whether the green tea–depression association is mediated by folate. Of two previous studies that showed an inverse association between green tea consumption and depression<sup>(13,14)</sup>, only one<sup>(13)</sup> considered the influence of dietary folate intake. Thus in the present study we examined the association of consumption of green tea, coffee and caffeine with depressive symptoms in a Japanese working population, with consideration of the potential role of folate as a mediator.

## Methods

### *Study procedure and participants*

In July and November 2009, a health survey was conducted among municipal employees in two workplaces in north-eastern Kyushu, Japan. The overall objective of the survey was to examine the association of lifestyle including diet with mental and physical health. At the time of the routine health check-up, all full-time workers (*n* 605) except those who were on long-term sick or maternity leave were invited to participate. Of these, 567 (325 men and 242 women aged 20–68 years) consented (response rate 94%). Participants were asked to fill out a survey questionnaire before the health check-up. The survey questionnaire was then checked by research staff for completeness and, where necessary, clarifications were made with the participant. We also obtained data that were routinely collected during the health examination, including anthropometric measurements and biochemical data, and information about medical history, smoking and alcohol drinking. We excluded participants who were pregnant (*n* 8) and those having missing data on confounding factors under study (*n* 22). After these exclusions, 537 individuals (319 men and 218 women) remained. The study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human subjects were approved by the Ethics Committee of the National Center for Global Health and Medicine, Japan. Written informed consent was obtained from all participants prior to the survey.

### *Ascertainment of depressive symptoms*

Depressive symptoms were assessed with the Japanese version<sup>(21)</sup> of the Center for Epidemiologic Studies Depression (CES-D) scale<sup>(22)</sup>. This scale comprises twenty questions addressing six symptoms of depression experienced by participants during the past week: depressed mood, feelings of guilt or worthlessness, helplessness or hopelessness, psychomotor retardation, loss of appetite

and sleep disorders. Each question is scored on a scale of 0–3 according to the frequency of the symptom and the total score ranges from 0 to 60, with a higher score indicating worse depressive status. The criterion validity of the CES-D scale has been well established in both Western<sup>(22)</sup> and Japanese<sup>(21)</sup> subjects. The presence of depressive symptoms was defined as a CES-D score of 16 or higher. As a self-rating depression scale, CES-D was developed for epidemiological surveys among adults of all ages, whereas other instruments such as the Beck Depression Inventory, the Zung Self-Rating Depression Scale and the Geriatric Depression Scale were designed for clinical research or elderly populations<sup>(23)</sup>.

### *Dietary assessment*

Information about dietary intake during the preceding month was obtained using a validated brief self-administered diet history questionnaire (BDHQ)<sup>(24)</sup>, which ascertained consumption frequency of forty-six food and non-alcoholic beverage items, including vegetables, fruit, green tea and coffee. Consumptions of green tea and coffee were elicited by a closed-ended question, and the beverage consumption in terms of volume was estimated by assigning the following values (cups/week) to the frequency of consumption<sup>(24)</sup>: 0 = none; 0.5 = <1 cup/week; 1 = 1 cup/week; 2.5 = 2–3 cups/week; 5 = 4–6 cups/week; 7 = 1 cup/d; 17.5 = 2–3 cups/d; 28 = ≥4 cups/d. A cup size of green tea or coffee was assumed as 150 ml for women and 171 ml (150 ml × 1.14) for men<sup>(24)</sup>. Correlations between consumption of green tea and coffee according to the above-mentioned BDHQ and those from 16 d dietary records were high (Spearman's  $r = 0.74$  and  $0.73$  for green tea consumption in men and women, respectively; the corresponding data for coffee consumption were  $0.85$  in men and  $0.87$  in women)<sup>(24)</sup>. Referring to the Food Composition Table in Japan<sup>(25)</sup>, we estimated daily caffeine consumption from green tea and coffee consumption, using respectively 20 and 60 mg of caffeine per 100 ml of each beverage.

### *Laboratory measurements*

Blood samples were obtained at the time of health check-up. Venous blood (7 ml) was drawn into vacuum tubes and then transported in a cooler box to a laboratory. The blood was centrifuged for 10 min, and the separated serum was divided into a maximum of six tubes (0.5 ml each) and kept at  $-30^{\circ}\text{C}$  during the survey for each workplace. One of these tubes was sent, immediately after the survey period, to an external laboratory (Mitsubishi Chemical Medicine Corporation, Tokyo, Japan) for the measurement of high-sensitivity C-reactive protein (CRP) and folate using a latex agglutination nephelometry method and chemiluminescent immunoassay, respectively.

### *Other variables*

Marital status, job position, living status, overtime work, alcohol and tobacco use, types of occupation,

non-occupational physical activity and history of diseases (cancer, CVD, diabetes or chronic hepatitis) were elicited in the questionnaire. Occupational physical activity was classified as sedentary work (managerial and clerical jobs) and active work (childcare work, school lunch preparation and technical jobs). Questions on non-occupational physical activity ascertained the time spent (in minutes) walking or cycling to commute to/from work and on five recreational activities (walking, low-, moderate- and high-intensity activities and gardening). Non-occupational physical activity was estimated in metabolic equivalent (MET) values and expressed as the sum of MET multiplied by the time (in hours) spent performing each activity<sup>(26)</sup>. Body height was measured to the nearest 0.1 cm with the participant standing without shoes. Body weight in light clothes was measured to the nearest 0.1 kg. BMI was calculated by dividing weight by the square of height (kg/m<sup>2</sup>).

### Statistical analysis

The descriptive data are presented as means and standard deviations, medians and interquartile ranges, or percentages. Participants were divided into three groups: those consuming  $\leq 1$  cup, 2–3 cups and  $\geq 4$  cups of green tea daily; and those consuming  $< 1$  cup, 1 cup and  $\geq 2$  cups of coffee daily. Caffeine consumption was estimated from caffeine contents in green tea and coffee, and was categorized into quartiles ( $\leq 100$  mg/d, 101–165 mg/d, 166–291 mg/d and  $> 291$  mg/d). Participants' characteristics according to green tea and coffee consumption, treated as ordinal variables with ordinal values from 1 to 3 assigned to the three consumption levels, were evaluated by using linear regression analysis for continuous variables and the Mantel–Haenszel test of trend for categorical variables. Multiple logistic regression analysis was performed to calculate odds ratios and 95% confidence intervals for prevalence of depressive symptoms according to the above-described categories of green tea, coffee and caffeine consumption. The base model (model 1) included age (year, continuous), sex and workplace (survey in July or November 2009). We added covariates accumulatively to model 1 in subsequent models: history of cancer, CVD, diabetes mellitus or chronic hepatitis (yes or no), marital status (married or unmarried), living status (alone or not alone), overtime work (none,  $< 10$  or  $\geq 10$  h/month), job position (low or middle and high), occupational physical activity (active or sedentary), non-occupational physical activity ( $< 5$  or  $\geq 5$  MET-h/week), current smoking (yes or no), alcohol drinking (yes or no), BMI (kg/m<sup>2</sup>, continuous), *n*-3 PUFA intake (percentage of energy, continuous), log-transformed red meat intake (g/d, continuous), log-transformed vegetable and fruit consumption (g/d, continuous) and coffee consumption ( $< 1$ , 1 or  $\geq 2$  cups/d; when calculating the OR for consumption of green tea) or green tea ( $\leq 1$ , 2–3 or  $\geq 4$  cups/d; when calculating the ORs for consumption of coffee) for model 2; log-transformed serum CRP concentrations

(mg/l, continuous) for model 3; and log-transformed serum folate concentration (ng/ml, continuous) for model 4. Neither green tea nor coffee consumption was included in the multivariate models when examining the association between caffeine consumption and depressive symptoms. Trend tests were performed using multiple logistic regression analysis with ordinal numbers assigned to the category of green tea, coffee and caffeine consumption. We also examined effect modification by sex on the association of green tea, coffee and caffeine consumption with depressive symptoms, using the likelihood ratio test. We repeated all the above analyses after excluding participants who reported a history of psychological problems (*n* 6). Two-sided *P* values of less than 0.05 were considered statistically significant. All analyses were performed using the statistical software package STATA version 12.1.

### Results

The participants' characteristics according to green tea and coffee consumption are shown in Table 1. Participants with higher consumption of green tea were more likely to be female and less likely to be married. They were also less likely to be current smokers, alcohol drinkers and coffee drinkers. Those with higher green tea consumption tended to consume *n*-3 PUFA, vegetables and fruit more often. Green tea consumption was positively correlated with serum folate levels. Participants consuming coffee more often were older and more likely to be married. Those with a higher consumption of coffee were less likely to be engaged in sedentary work and tended to smoke cigarettes as well as consume vegetables and fruit more often.

There were significant inverse associations between consumption of green tea and coffee and likelihood of depressive symptoms (Table 2). After adjustment for demographic and lifestyle factors (model 2), compared with participants consuming  $\leq 1$  cup green tea/d, those consuming 2–3 cups/d and  $\geq 4$  cups/d had a 41% and 51% significantly lower prevalence odds of depressive symptoms, respectively (*P* for trend = 0.01). Additional adjustment for CRP (model 3) did not materially alter the results. Further adjustment for serum folate (model 4) attenuated the association by about 7% and 10% in participants who consumed 2–3 cups green tea/d and  $\geq 4$  cups green tea/d, respectively, compared with those consuming  $\leq 1$  cup/d (*P* for trend = 0.03). As regards coffee, after adjusting for demographic and lifestyle factors (model 2), compared with participants consuming  $< 1$  cup coffee/d, those consuming 1 cup/d and  $\geq 2$  cups/d had a 26% and 40% lower prevalence odds of depressive symptoms, respectively (*P* for trend = 0.03). Additional adjustment for serum CRP (model 3) and folate (model 4) did not measurably change the estimates.

**Table 1** Participants' characteristics according to green tea and coffee consumption: men and women (*n* 537) aged 20–68 years from two workplaces in north-eastern Kyushu, Japan, 2009

	Green tea consumption							Coffee consumption						
	≤1 cup/d ( <i>n</i> 269)		2–3 cups/d ( <i>n</i> 171)		≥4 cups/d ( <i>n</i> 97)		<i>P</i> *	<1 cup/d ( <i>n</i> 207)		1 cup/d ( <i>n</i> 114)		≥2 cups/d ( <i>n</i> 216)		<i>P</i> *
	Mean	SD	Mean	SD	Mean	SD		Mean	SD	Mean	SD	Mean	SD	
Age (years)	43.2	10.5	44.8	11.0	45.0	11.9	0.22	42.0	11.8	43.7	11.2	46.2	10.0	<0.001
BMI (kg/m <sup>2</sup> )	22.7	3.1	22.3	3.3	21.8	3.8	0.05	22.3	3.4	22.3	3.3	22.6	3.2	0.67
	%		%		%			%		%		%		
Women (%)	27.1		50.3		60.8		<0.001	37.2		41.2		43.5		0.19
Workplace (%)†	29.4		28.7		25.8		0.53	29.5		31.6		25.9		0.42
Married (%)	76.6		72.5		66.0		0.04	68.1		71.9		79.2		0.01
Living status (alone) (%)	10.8		11.1		6.2		0.28	11.1		10.5		8.8		0.43
Job position (low) (%)	58.4		53.8		62.9		0.71	60.4		61.4		53.2		0.14
Sedentary work (%)	83.3		78.4		82.5		0.59	89.9		79.8		74.5		<0.001
Overtime work (≥10 h/month) (%)	69.1		73.1		68.0		0.93	69.1		71.1		70.8		0.70
History of diseases (%)‡	4.1		5.3		8.3		0.13	5.8		2.6		6.0		0.91
Physical activity (≥5 MET-h/week)§ (%)	39.0		33.3		3.0		0.51	34.8		38.6		38.0		0.50
Current smoking (%)	31.2		22.8		11.3		<0.001	19.8		25.4		29.6		0.02
Current alcohol intake (%)	69.9		55.6		49.5		<0.001	62.8		57.9		62.5		0.96
Coffee consumption (≥1 cup/d) (%)	65.1		60.8		52.6		0.03	–		–		–		–
Green tea consumption (≥1 cup/d) (%)	–		–		–		–	68.1		73.7		65.3		0.52
	Median	IQR	Median	IQR	Median	IQR		Median	IQR	Median	IQR	Median	IQR	
Vegetable and fruit intake (g/d)	243	172–369	274	184–417	307	218–450	<0.001	241	172–31	261	175–354	296	200–436	0.004
Caffeine consumption (mg/d)¶	137	71–269	165	122–300	210	144–345	<0.001	86	49–126	151	120–188	300	281–362	<0.001
<i>n</i> -3 PUFA intake (% of energy)¶	1.30	0.34	1.33	0.36	1.43	0.37	0.006	1.32	0.37	1.33	0.32	1.35	0.35	0.68
Seafood intake (g/d)	54.2	36.5–80.7	53.2	35.8–80.3	58.1	35.0–95.5	0.39	53.3	35.5–81.1	55	37.9–82.7	56	36.6–85.5	0.55
Red meat intake (g/d)	37.4	20.7–47.3	37.4	25.3–45.7	39.4	23.6–52.0	0.48	38.4	26.2–47.3	38.6	20.8–47.3	36.1	20.8–47.3	0.41
Serum CRP (mg/l)	0.37	0.17–0.94	0.42	0.18–0.93	0.24	0.13–0.60	0.04	0.34	0.16–0.89	0.33	0.16–0.77	0.42	0.19–0.89	0.25
Serum folate (ng/ml)	5.4	4.3–6.9	6.2	4.9–7.8	6.4	5.0–8.4	<0.001	5.6	4.6–7.4	6.0	4.5–7.1	5.8	4.6–7.8	0.23

MET-h, metabolic equivalent hours; CRP, C-reactive protein; IQR, interquartile range.

\**P* for trend was obtained from linear regression for continuous variables by assigning ordinal numbers 1–3 to categories of green tea or coffee consumption, or from the Mantel–Haenszel test of trend for categorical variables.

†Survey conducted in July 2009.

‡Including cancer, CVD, diabetes mellitus and chronic hepatitis.

§Leisure-time physical activities and commuting to/from work.

¶Calculated from green tea and coffee.

¶Values are mean and standard deviation.

**Table 2** Odds of depressive symptoms\* according to consumption of green tea and coffee: men and women (*n* 537) aged 20–68 years from two workplaces in north-eastern Kyushu, Japan, 2009

	Green tea consumption category						<i>P</i> value†
	≤1 cup/d ( <i>n</i> 269)		2–3 cups/d ( <i>n</i> 171)		≥4 cups/d ( <i>n</i> 97)		
	OR	95% CI	OR	95% CI	OR	95% CI	
Depressed subjects	<i>n</i> 89; 33.1%		<i>n</i> 44; 25.7%		<i>n</i> 24; 24.7%		
Model 1‡	1.00	–	0.62	0.40, 0.97	0.56	0.32, 0.97	0.02
Model 2§	1.00	–	0.59	0.36, 0.94	0.49	0.27, 0.91	0.01
Model 3	1.00	–	0.59	0.36, 0.95	0.49	0.27, 0.90	0.01
Model 4¶	1.00	–	0.63	0.39, 1.02	0.54	0.29, 1.00	0.03
	Coffee consumption category						<i>P</i> value†
	<1 cup/d ( <i>n</i> 207)		1 cup/d ( <i>n</i> 114)		≥2 cups/d ( <i>n</i> 216)		
	OR	95% CI	OR	95% CI	OR	95% CI	
Depressed subjects	<i>n</i> 70; 33.8%		<i>n</i> 33; 28.9%		<i>n</i> 54; 25.0%		
Model 1‡	1.00	–	0.79	0.48, 1.31	0.63	0.41, 0.98	0.04
Model 2§	1.00	–	0.74	0.43, 1.28	0.60	0.37, 0.96	0.03
Model 3	1.00	–	0.74	0.43, 1.27	0.60	0.37, 0.96	0.03
Model 4¶	1.00	–	0.75	0.44, 1.30	0.61	0.38, 0.98	0.04

MET-h, metabolic equivalent hours; CRP, C-reactive protein.

\*Defined as a Center for Epidemiologic Studies Depression Scale score of ≥16.

†*P* for linear trend obtained from multiple logistic regression analysis with ordinal numbers 1–3 assigned to each category of green tea or coffee consumption.

‡Model 1: Adjusted for age (continuous), sex and workplace (survey in July or in November 2009).

§Model 2: Adjusted for factors in model 1 and history of cancer, CVD, diabetes mellitus or chronic hepatitis (yes or no), marital status (married or unmarried), living status (alone or not alone), overtime work (none, <10 or ≥10 h/month), job position (low or middle and high), occupational physical activity (active or sedentary), non-occupational physical activity (<5 or ≥5 MET-h/week), current smoking (yes or no), alcohol drinking (yes or no), BMI (kg/m<sup>2</sup>, continuous), *n*-3 PUFA intake (% of energy, continuous), log-transformed red meat intake (g/d, continuous), log-transformed vegetable and fruit consumption (g/d, continuous) and coffee consumption (<1 cup/d, 1 cup/d or ≥2 cups/d; when calculating the OR for green tea consumption) or green tea consumption (≤1 cup/d, 2–3 cups/d or ≥4 cups/d; when calculating the OR for coffee consumption).

||Model 3: Adjusted for factors in model 2 and log-transformed serum CRP concentrations (mg/l, continuous).

¶Model 4: Adjusted for factors in model 3 and log-transformed serum folate concentration (ng/ml, continuous).

**Table 3** Odds of depressive symptoms\* according to caffeine consumption: men and women (*n* 537) aged 20–68 years from two workplaces in north-eastern Kyushu, Japan, 2009

	Quartiles of caffeine intake								<i>P</i> value‡
	≤100 mg/d ( <i>n</i> 128)		101–165 mg/d ( <i>n</i> 148)		166–291 mg/d ( <i>n</i> 133)		>291 mg/d ( <i>n</i> 128)		
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	
Depressed subjects	<i>n</i> 46; 35.9%		<i>n</i> 50; 33.9%		<i>n</i> 30; 22.6%		<i>n</i> 31; 24.2%		
Model 1§	1.00	–	0.85	0.51, 1.41	0.54	0.31, 0.93	0.51	0.29, 0.90	0.005
Model 2	1.00	–	0.90	0.53, 1.55	0.55	0.31, 0.98	0.56	0.31, 1.04	0.02
Model 3¶	1.00	–	0.90	0.52, 1.54	0.54	0.30, 0.97	0.57	0.31, 1.05	0.02
Model 4**	1.00	–	0.92	0.53, 1.59	0.58	0.32, 1.04	0.57	0.30, 1.05	0.02

MET-h, metabolic equivalent hours; CRP, C-reactive protein.

\*Defined as a Center for Epidemiologic Studies Depression Scale score of ≥16.

†Estimated from caffeine contents in green tea and coffee (20 mg and 60 mg of caffeine per 100 ml of green tea and coffee, respectively).

‡*P* for linear trend obtained from multiple logistic regression analysis with ordinal numbers 1–4 assigned to quartiles of caffeine consumption.

§Model 1: Adjusted for age (continuous), sex and workplace (survey in July or in November 2009).

||Model 2: Adjusted for factors in model 1 and history of cancer, CVD, diabetes mellitus or chronic hepatitis (yes or no), marital status (married or unmarried), living status (alone or not alone), overtime work (none, <10 or ≥10 h/month), job position (low or middle and high), occupational physical activity (active or sedentary), non-occupational physical activity (<5 or ≥5 MET-h/week), current smoking (yes or no), alcohol drinking (yes or no), BMI (kg/m<sup>2</sup>, continuous), *n*-3 PUFA intake (% of energy, continuous), log-transformed red meat intake (g/d, continuous) and log-transformed vegetable and fruit consumption (g/d, continuous).

¶Model 3: Adjusted for factors in model 2 and log-transformed serum CRP concentrations (mg/l, continuous).

\*\*Model 4: Adjusted for factors in model 3 and log-transformed serum folate concentration (ng/ml, continuous).

Concerning caffeine consumption (Table 3), participants in the highest *v.* the lowest quartile of caffeine consumption had a 43% lower odds of having depressive symptoms in a fully adjusted model (OR = 0.57; 95% CI 0.30, 1.05; *P* for trend = 0.02).

We observed a suggestive interaction between sex and green tea consumption for depressive symptoms

(*P* for interaction = 0.09); the inverse association with green tea consumption was confined to men. The multivariate OR for depressive symptoms according to green tea consumption categories of ≤1 cup/d, 2–3 cups/d and ≥4 cups/d were 1.00 (reference), 0.53 (95% CI 0.28, 1.03) and 0.23 (95% CI 0.07, 0.73) in men (*P* for trend = 0.004), and 1.00 (reference), 0.91 (95% CI 0.41, 2.02) and

1.08 (95% CI 0.45, 2.59) in women ( $P$  for trend = 0.87). As for coffee consumption, the association was more pronounced in women than in men, although the interaction was not statistically significant ( $P$  for interaction = 0.49). The multivariate OR for depressive symptoms according to coffee consumption categories of <1 cup/d, 1 cup/d and  $\geq 2$  cups/d were 1.00 (reference), 0.48 (95% CI 0.20, 1.16) and 0.37 (95% CI 0.17, 0.81) in women ( $P$  for trend = 0.01), and 1.00 (reference), 0.84 (95% CI 0.39, 1.80) and 0.74 (95% CI 0.37, 1.42) in men ( $P$  for trend = 0.37). The association between caffeine consumption and depressive symptoms did not differ by sex ( $P$  for interaction = 0.82). The results were materially unchanged after excluding the participants with a history of psychological problems (data not shown).

## Discussion

In the present study among a Japanese working population, we found an inverse association between consumption of green tea, coffee and caffeine and prevalence of depressive symptoms. The association with green tea was only slightly attenuated after adjustment for serum folate concentration. Our study is one of the few that have investigated the association between green tea and depressive symptoms, and is the first to report a significantly decreased prevalence of depressive symptoms among those with a higher intake of coffee or caffeine among Japanese.

Our finding of an inverse association between green tea intake and depressive symptoms is closely in agreement with the results of a Japanese study among the community-dwelling elderly<sup>(13)</sup>, in which those who consumed  $\geq 4$  cups green tea/d had a 44% lower prevalence of depressive symptoms (defined as Geriatric Depression Scale score  $\geq 11$  or use of antidepressant drug) compared with those consuming  $\leq 1$  cup/d. Another population-based study including adults aged 20–69 years in Japan<sup>(15)</sup> showed a statistically non-significant reduction in odds of having mental ill-health, as assessed by the twelve-item General Health Questionnaire (score  $\geq 4$ ), in individuals with high green tea consumption; OR of having mental ill-health in those who consumed  $\geq 5$  cups/d compared with those consuming <1 cup/d was 0.78 and 0.77 for men and women, respectively. Likewise, a Chinese study among breast cancer survivors reported a 42% lower prevalence odds of depressive symptoms (CES-D score  $\geq 16$ ) in patients who consumed >100 g of dried tea leaves per month (90% of tea consumed is from green tea) compared with patients who did not drink tea regularly<sup>(14)</sup>. The present data together with these previous observations suggest that higher green tea consumption may be protective against depression.

Because green tea contains folate, which has been suggested to confer protection against depression<sup>(20,27)</sup>, the green tea–depression association may be mediated by

folate status. In fact, participants with higher green tea consumption had a higher concentration of serum folate. However, adjustment for serum folate concentration attenuated the results only slightly, suggesting that the association observed between green tea and depressive symptoms may largely be attributed to green tea constituents other than folate.

The present study found a significantly lower prevalence of depressive symptoms among participants with higher consumption of coffee and caffeine. Our result aligns with a US study that reported a lower risk of depression among women who consumed higher amounts of caffeinated coffee and caffeine<sup>(17)</sup>. Similarly, a Finnish study showed a decreased risk of severe depression among light and heavy coffee drinkers as compared with coffee non-drinkers<sup>(16)</sup>, although no significant risk reduction was observed among individuals with high caffeine consumption. Moreover, consumption of coffee and caffeine was inversely associated with risk of suicide<sup>(28)</sup>, for which depression is an important predictor<sup>(29)</sup>. Conversely, a Japanese study<sup>(13)</sup> found no association between coffee consumption and depressive symptoms. The lack of an association in the Japanese study may be partly ascribed to infrequent consumption of coffee among the elderly, with only 13.2% of the study participants consuming  $\geq 2$  cups coffee/d, as reported in an earlier study that included the same participants<sup>(30)</sup>. A null finding has also been reported from a Finnish study<sup>(18)</sup>. In that study, coffee consumption was evaluated as a dichotomous variable, which may not be suitable to detect an association at a moderate coffee consumption. Our data corroborated previous observations suggesting that the consumption of coffee<sup>(16,17,28)</sup> and caffeine<sup>(17,28)</sup> may have beneficial effects against depression. Further studies are needed to confirm the antidepressant effect of higher doses of caffeine.

We found an inverse association between green tea consumption and depressive symptoms in men but not in women, although the interaction by sex was not statistically significant. The null finding in women is inconsistent with previous data among Asians showing a protective association between green tea consumption and depression in elderly women<sup>(13)</sup> or in breast cancer survivors (mean age 53.7 years)<sup>(14)</sup>. The discrepancy between our finding and prior ones may be ascribed to chance, but it could be related to the difference in age among studies; women in the present study were younger (mean age 42.7 years) than those in the previous ones<sup>(13,14)</sup>. It has been suggested that circulating oestrogen may increase vulnerability to depression in susceptible women<sup>(31)</sup>. Besides, habitual green tea consumption is associated with increased blood oestradiol concentrations, the predominant oestrogen during the reproductive age, in premenopausal women<sup>(32)</sup>. If so, green tea consumption may not afford protection against depression in premenopausal women. Further research is required to clarify

whether the effect of green tea consumption on depression differs according to menopausal status.

The mechanisms underlying the favourable associations between consumption of green tea, coffee and caffeine and depression remain to be determined, but there are possible biological explanations. Green tea is rich in polyphenols, mainly catechins<sup>(33)</sup>, which have recently been shown to exert antidepressant-like effects in mouse models of depression and to decrease corticosterone (cortisol in man) and adrenocorticotropic hormone (corticotropin) in mice<sup>(34)</sup>. Considerable evidence suggests that cortisol and corticotropin are involved in depression<sup>(9)</sup>. In rats, oral administration of epigallocatechin-3-gallate, one of the major green tea catechins, has been shown to prevent a reduction of brain dopamine concentration<sup>(35)</sup>, which plays a major role in the pathogenesis of depression<sup>(9)</sup>. Green tea is also rich in theanine, which accounts for about 50% of the amino acid content in green tea<sup>(33)</sup>, and animal studies have shown that theanine administration increases brain dopamine<sup>(36)</sup> and serotonin<sup>(37)</sup>. Moreover, green tea has potent antioxidant activities *in vivo*<sup>(38)</sup> and thus may confer protection against depression by decreasing oxidative stress, which is increased in depressed patients<sup>(39,40)</sup>. Likewise, coffee is a rich source of phenolic compounds including chlorogenic acid and caffeic acid<sup>(41)</sup>, which were found to exert antioxidant effects both *in vitro*<sup>(42)</sup> and *in vivo*<sup>(43)</sup>. Finally, caffeine can increase excitatory neurotransmitters through modulating dopaminergic transmission<sup>(11)</sup> and facilitate the release of acetylcholine and serotonin<sup>(12)</sup>.

Major strengths of the present study include a high response rate (94%), the use of a validated dietary questionnaire, and adjustment for known and putative risk factors for depressive symptoms. Several limitations need consideration. First, cross-sectional data do not allow us to conclude whether or not consumption of green tea or coffee decreases depressive symptoms. Participants with depressive symptoms may have refrained from drinking these beverages due to concerns about side-effects of caffeine. Nevertheless, prospective studies have shown a decreased risk of depression among individuals with higher consumption of coffee<sup>(16,17)</sup> or caffeine<sup>(17)</sup>. Second, the assessment of coffee and green tea consumption was based on a self-administered questionnaire. However, data on green tea and coffee obtained from the self-administered questionnaire and those from 16 d dietary records were shown to be highly correlated<sup>(24)</sup>. Moreover, intakes of specific foods or beverages that contain caffeine (except coffee and green tea) were not specifically asked in this dietary questionnaire. Nevertheless, in Japan, coffee and green tea are major contributors to caffeine consumption, with an estimated proportion of 47% and 38%, respectively<sup>(44)</sup>. Further, the questionnaire did not include questions about types, strengths or preparation methods of green tea and coffee, which might have resulted in imprecise

estimates of caffeine consumption. A better method of corroborating beverage consumption could be the use of relevant biomarkers including caffeine and its metabolites<sup>(45)</sup>, coffee-derived chlorogenic acid and caffeic acid metabolites<sup>(45,46)</sup> and green tea catechins<sup>(47)</sup> in blood as well as coffee-derived chlorogenic acid metabolites<sup>(46)</sup> and green tea catechins<sup>(47)</sup> in urine. Third, because of the limited number of individuals consuming large amounts of coffee in our study population, we were unable to address the association of high consumption of coffee or caffeine with depressive symptoms. Fourth, we could not fully allow for a detailed history of depressive episodes and use of antidepressants because these data were not specifically inquired. However, given the nature of the study population (working population), the prevalence of these factors would be low and thus their impact, if present, on study results would be minimal. Fifth, despite adjustment for main potential confounders, the possibility of residual confounding cannot be ruled out. Finally, the present findings among a selected, working population might not represent non-working or elderly populations, which may include a higher proportion of patients with severe depression.

## Conclusion

We found that higher consumption of green tea, coffee and caffeine was each associated with a lower prevalence of depressive symptoms in a Japanese working population. These findings add support for a protective role of green tea, coffee and caffeine against depression. Longitudinal studies including persons with a high intake of coffee and caffeine are required to confirm the present cross-sectional association.

## Acknowledgements

*Sources of funding:* This study was supported by a Grant-in-Aid for Scientific Research (B) (21390213) from the Japan Society for the Promotion of Science; a Grant-in-Aid for Young Scientists (B) (21790598) from the Ministry of Education, Culture, Sports, Science and Technology; and a Grant of the National Center for Global Health and Medicine. *Conflicts of interest:* The authors declare no conflict of interest. *Authors' contributions:* N.M.P. analysed the data and wrote the manuscript. A.N. planned and coordinated the field survey and contributed to the discussion. K. Kurotani contributed to data interpretation and discussion. K. Kuwahara contributed to data interpretation and discussion. A.K. contributed to data interpretation and discussion. M.S. planned and coordinated the field survey and contributed to the discussion. H.H. planned and coordinated the field survey and contributed to the discussion. T.M. edited the manuscript and is the Principal Investigator of the present study. *Acknowledgment:* The authors are

grateful to the study participants for their cooperation and participation. They also thank Seiko Miyazaki and Yasutaka Horiuchi (Kyushu University); Emi Tanaka, Youko Tsuruda, Misaki Hirose, Meishu Sai, Miho Isayama, Midori Sasaki, Mie Shimomura and Azumi Uehara (Fukuoka Women's University); Yaeko Nagano (retired nurse); and Yumi Matsushita, Akiko Hayashi, Yu Teruyama, Kae Saito, Kayoko Washizuka and Yuho Mizoue (National Center for Global Health and Medicine) for their help in data collection.

## References

- Bromet E, Andrade LH, Hwang I *et al.* (2011) Cross-national epidemiology of DSM-IV major depressive episode. *BMC Med* **9**, 90.
- Mathers CD & Loncar D (2006) Projections of global mortality and burden of disease from 2002 to 2030. *PLoS Med* **3**, e442.
- Ministry of Health, Labour and Welfare (2008) *Vital Statistics of Japan*. Tokyo: Health and Welfare Statistics Association.
- Murakami K & Sasaki S (2010) Dietary intake and depressive symptoms: a systematic review of observational studies. *Mol Nutr Food Res* **54**, 471–488.
- McKay DL & Blumberg JB (2002) The role of tea in human health: an update. *J Am Coll Nutr* **21**, 1–13.
- Butt MS & Sultan MT (2011) Coffee and its consumption: benefits and risks. *Crit Rev Food Sci Nutr* **51**, 363–373.
- Iso H, Date C, Wakai K *et al.* (2006) The relationship between green tea and total caffeine intake and risk for self-reported type 2 diabetes among Japanese adults. *Ann Intern Med* **144**, 554–562.
- Chen WQ, Zhao XL, Hou Y *et al.* (2009) Protective effects of green tea polyphenols on cognitive impairments induced by psychological stress in rats. *Behav Brain Res* **202**, 71–76.
- Belmaker RH & Agam G (2008) Major depressive disorder. *N Engl J Med* **358**, 55–68.
- Kimura K, Ozeki M, Juneja LR *et al.* (2007) L-Theanine reduces psychological and physiological stress responses. *Biol Psychol* **74**, 39–45.
- Ferré S (2008) An update on the mechanisms of the psychostimulant effects of caffeine. *J Neurochem* **105**, 1067–1079.
- Ferré S, Ciruela F, Borycz J *et al.* (2008) Adenosine A1–A2A receptor heteromers: new targets for caffeine in the brain. *Front Biosci* **13**, 2391–2399.
- Niu K, Hozawa A, Kuriyama S *et al.* (2009) Green tea consumption is associated with depressive symptoms in the elderly. *Am J Clin Nutr* **90**, 1615–1622.
- Chen X, Lu W, Zheng Y *et al.* (2010) Exercise, tea consumption, and depression among breast cancer survivors. *J Clin Oncol* **28**, 991–998.
- Shimbo M, Nakamura K, Shi HJ *et al.* (2005) Green tea consumption in everyday life and mental health. *Public Health Nutr* **8**, 1300–1306.
- Ruusunen A, Lehto SM, Tolmunen T *et al.* (2010) Coffee, tea and caffeine intake and the risk of severe depression in middle-aged Finnish men: the Kuopio Ischaemic Heart Disease Risk Factor Study. *Public Health Nutr* **13**, 1215–1220.
- Lucas M, Mirzaei F, Pan A *et al.* (2011) Coffee, caffeine, and risk of depression among women. *Arch Intern Med* **171**, 1571–1578.
- Hintikka J, Tolmunen T, Honkalampi K *et al.* (2005) Daily tea drinking is associated with a low level of depressive symptoms in the Finnish general population. *Eur J Epidemiol* **20**, 359–363.
- Chen TS, Lui CK & Smith CH (1983) Folic acid content of tea. *J Am Diet Assoc* **82**, 627–632.
- Nanri A, Hayabuchi H, Ohta M *et al.* (2012) Serum folate and depressive symptoms among Japanese men and women: a cross-sectional and prospective study. *Psychiatry Res* **200**, 349–353.
- Shima S, Shikano T, Kitamura T *et al.* (1985) New self-rating scale for depression. *Jpn J Clin Psychiatry* **27**, 717–723.
- Radloff LS (1977) A self-report depression scale for research in the general population. *Appl Psychol Meas* **1**, 250–267.
- McDowell I (2006) Depression. In *Measuring Health: A Guide to Rating Scales and Questionnaires*, 3rd ed., pp. 329–393. New York: Oxford University Press.
- Kobayashi S, Murakami K, Sasaki S *et al.* (2011) Comparison of relative validity of food group intakes estimated by comprehensive and brief-type self-administered diet history questionnaires against 16-d dietary records in Japanese adults. *Public Health Nutr* **14**, 1200–1211.
- Science and Technology Agency (2005) *Standard Tables of Food Composition in Japan*, 5th revised and enlarged ed. Tokyo: Printing Bureau of the Ministry of Finance.
- Ainsworth BE, Haskell WL, Whitt MC *et al.* (2000) Compendium of physical activities: an update of activity codes and MET intensities. *Med Sci Sports Exerc* **32**, 9 Suppl., S498–S516.
- Gilbody S, Lightfoot T & Sheldon T (2007) Is low folate a risk factor for depression? A meta-analysis and exploration of heterogeneity. *J Epidemiol Community Health* **61**, 631–637.
- Kawachi I, Willett WC, Colditz GA *et al.* (1996) A prospective study of coffee drinking and suicide in women. *Arch Intern Med* **156**, 521–525.
- Hawton K & van Heeringen K (2009) Suicide. *Lancet* **373**, 1372–1381.
- Kuriyama S, Hozawa A, Ohmori K *et al.* (2006) Green tea consumption and cognitive function: a cross-sectional study from the Tsurugaya Project. *Am J Clin Nutr* **83**, 355–361.
- Llaneza P, García-Portilla MP, Llaneza-Suárez D *et al.* (2012) Depressive disorders and the menopause transition. *Maturitas* **71**, 120–130.
- Schliep KC, Schisterman EF, Mumford SL *et al.* (2012) Caffeinated beverage intake and reproductive hormones among premenopausal women in the BioCycle Study. *Am J Clin Nutr* **95**, 488–497.
- Liao S, Kao YH & Hiipakka RA (2001) Green tea: biochemical and biological basis for health benefits. *Vitam Horm* **62**, 1–94.
- Zhu WL, Shi HS, Wei YM *et al.* (2012) Green tea polyphenols produce antidepressant-like effects in adult mice. *Pharmacol Res* **65**, 74–80.
- Levites Y, Weinreb O, Maor G *et al.* (2001) Green tea polyphenol (–)-epigallocatechin-3-gallate prevents N-methyl-4-phenyl-1,2,3,6-tetrahydropyridine-induced dopaminergic neurodegeneration. *J Neurochem* **78**, 1073–1082.
- Yokogoshi H, Kobayashi M, Mochizuki M *et al.* (1998) Effect of theanine, R-glutamylethylamide, on brain monoamines and striatal dopamine release in conscious rats. *Neurochem Res* **23**, 667–673.
- Nathan PJ, Lu K, Gray M *et al.* (2006) The neuropharmacology of L-theanine (N-ethyl-L-glutamine): a possible neuroprotective and cognitive enhancing agent. *J Herb Pharmacother* **6**, 21–30.
- Crespy V & Williamson G (2004) A review of the health effects of green tea catechins in *in vivo* animal models. *J Nutr* **134**, 12 Suppl., 3431S–3440S.

39. Stefanescu C & Ciobica A (2012) The relevance of oxidative stress status in first episode and recurrent depression. *J Affect Disord* **143**, 34–38.
40. Sarandol A, Sarandol E, Eker SS *et al.* (2007) Major depressive disorder is accompanied with oxidative stress: short-term antidepressant treatment does not alter oxidative–antioxidative systems. *Hum Psychopharmacol* **22**, 67–73.
41. Higdon JV & Frei B (2006) Coffee and health: a review of recent human research. *Crit Rev Food Sci Nutr* **46**, 101–123.
42. Scalbert A & Williamson G (2000) Dietary intake and bioavailability of polyphenols. *J Nutr* **130**, 8S Suppl., 2073S–2085S.
43. Natella F, Nardini M, Giannetti I *et al.* (2002) Coffee drinking influences plasma antioxidant capacity in humans. *J Agric Food Chem* **50**, 6211–6216.
44. Yamada M, Sasaki S, Murakami K *et al.* (2010) Estimation of caffeine intake in Japanese adults using 16 d weighed diet records based on a food composition database newly developed for Japanese populations. *Public Health Nutr* **13**, 663–672.
45. Kempf K, Herder C, Erlund I *et al.* (2010) Effects of coffee consumption on subclinical inflammation and other risk factors for type 2 diabetes: a clinical trial. *Am J Clin Nutr* **91**, 950–957.
46. Farah A, Monteiro M, Donangelo CM *et al.* (2008) Chlorogenic acids from green coffee extract are highly bioavailable in humans. *J Nutr* **138**, 2309–2315.
47. Lee MJ, Wang ZY, Li H *et al.* (1995) Analysis of plasma and urinary tea polyphenols in human subjects. *Cancer Epidemiol Biomarkers Prev* **4**, 393–399.