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Caffeine, Cognition, and Socioeconomic Status

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Abstract. There is interest in age-related cognitive decline and environmental risk factors for Alzheimer's disease (AD). This interest is focused on individual differences in exposure to agents that may harm or protect cognitive function. Caffeine is used as a short acting mental stimulant and may possess longer-term properties that protect against age-related decline and, possibly, AD. The current study aimed to: 1) examine current cognitive function in a narrow age range sample ($n = 351$) without dementia (MMSE > 25) who are, by reason of age, entering the period of increased risk of AD; and 2) link cognitive function to self-reported intake of caffeine and socioeconomic status (SES). Possible confounding by gender, childhood intelligence, education, and symptoms of anxiety and depression was introduced into the statistical model. There were significant differences between SES groups in caffeine intake ($p < 0.05$) and cognitive performance ($p < 0.001$). Higher quartiles of caffeine intake were associated with slower digit symbol speed ($F = 3.38$, $p < 0.02$) but this finding was removed after allowing for SES. The results are discussed in terms of the withdrawal effects of caffeine during cognitive testing and strong links between SES and cognitive performance. No evidence in support of cognitive enhancing effects of caffeine was found.

Keywords: Alcohol, anxiety, attention, caffeine, childhood intelligence, neuroticism, non-verbal reasoning, processing speed, smoking, socioeconomic status, spatial ability, verbal memory

INTRODUCTION

The behavioral effects of moderate short-term caffeine consumption are well-known and are subject to many psychopharmacological and pharmacokinetic investigations. Short term effects of caffeine include improved alertness, increased anxiety, better cognitive performance, and benefits in sustained, directed, and divided attention [1]. These gains may also be seen in better performance in activities of daily living among regular caffeine users, many of whom discriminate between benefits when caffeine is consumed in the morning and its disadvantages when taken in the hours before sleep. Likewise, anxiety-prone individuals may prefer to avoid caffeine altogether because they believe it can induce or prolong feelings of anxiety. There is, as might be expected for such a widely used and available drug, a good public understanding of the need to strike a balance between moderate and excessive caffeine intake and recognition that the optimum level of caffeine intake lies below a level that might cause unwanted effects. These effects may be modified by the presence of symptoms of anxiety or depression or the personality trait of neuroticism. The numerous studies on the cognitive effects of caffeine (reviewed by [2]) suggest many possible sources of experimental variation in the cognitive effects of caffeine that include the level of habitual caffeine intake and the possibility that when performance was improved, the benefits were attributable to reversal of caffeine withdrawal in some habitually dependent individuals.

Possible associations between habitual coffee and tea consumption and cognitive performance may differ between older and younger habitual users of caffeine. This question was addressed in a cross-sectional survey

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of a representative sample of 9003 British adults (the Health and Lifestyle Survey) [3]. Participants completed tests of simple reaction time, choice reaction time, incidental verbal memory, and visuo-spatial reasoning, and also provided self-reports of habitual coffee and tea consumption. After adjustment for potential confounders, a dose-response trend to improved performance with higher levels of coffee consumption was detected for all four tests ($p < 0.001$ in each case). Older participants showed greater cognitive improvement associated with caffeine than younger participants; no gender differences were found. The long-term effects of caffeine on cognition are uncertain. In some small-scale cross-sectional population studies, greater than average habitual intake of caffeine is associated with better verbal memory performance and psychomotor speed that could, potentially, reduce or postpone age-related cognitive decline. This hypothesis was tested in the large-scale Maastricht Aging Study (MAAS) among 1376 participants aged between 24 and 81 years who were followed up for 6 years [4]. Baseline intake of caffeine-containing beverages was available. After adjustment for demographic characteristics, baseline performance and health status (but not smoking or alcohol intake), significant associations between the overall estimated caffeine intake and a small 6-year change in choice reaction time. Caffeine intake and verbal memory performance were not associated. Regular caffeine intake is not associated with a substantial reduction in age-related cognitive decline in the largest study so far on this topic. A possible link between coffee intake at midlife and late onset dementia has been reported in two large studies. In the first study, Ritchie et al. [5] explored possible associations between caffeine intake, cognitive decline, and incident dementia in older adults aged 65 years and over. Their study examined 4,197 women and 2,820 men recruited from the general population of three French cities. Cognitive performance, clinical diagnosis of dementia, and caffeine consumption were recorded on recruitment and at follow-up 2 and 4 years later. As expected, caffeine consumption was associated with many socio-demographic, lifestyle, and clinical variables that could also influence cognitive decline. Multivariate mixed models and multivariate adjusted logistic regression found that women who consumed more than three cups of coffee per day (approximately 300 mg caffeine daily) exhibited less decline in verbal retrieval and in visuo-spatial memory over 4 years of follow-up than women consuming one cup or less. No link was found between caffeine intake and cognitive decline in men. Caffeine consumption did not reduce dementia risk over 4 years. The psychopharmacological effects of caffeine might, therefore, slow or even prevent cognitive decline in women without dementia. New studies are needed to support further the role of caffeine as a useful neuroprotective agent in the prevention of dementia.

In a second report, the Cardiovascular Risk Factors, Aging and Dementia (CAIDE) study [6], participants who were randomly recruited from survivors of two population-based cohorts. These cohorts were previously examined in the North Karelia Project and the FINMONICA study in 1972, 1977, 1982, or 1987 (midlife visit). After an average follow-up of 21 years, 1409 individuals (71%) aged 65 to 79 were re-examined in 1998 when 61 cases of dementia [48 with Alzheimer's disease (AD)] were identified. Coffee drinkers at midlife had a lower risk of dementia at follow-up compared with those drinking no or only little coffee adjusted for possible confounders (demographic, lifestyle and vascular factors, apolipoprotein E $\varepsilon 4$ allele, and depressive symptoms). The lowest risk (65% decreased) was found in people who drank 3–5 cups per day and suggested that coffee drinking at midlife is linked to decreased dementia risk in late life. Psychopharmacological experiments on cognitive benefits of caffeine and later epidemiological studies on age-related cognitive decline and dementia support the investigation of caffeine effects in animal models of AD. Arendash and colleagues [7] examined possible long-term protective effects of caffeine intake in AD transgenic mice. Caffeine was added to the drinking water of Swedish mutation (AβPPsw) transgenic (Tg) mice between 4 and 9 months of age, with behavioral testing done during the final 6 weeks of treatment. The average daily intake of caffeine per mouse (1.5 mg) equivalent to five cups of coffee per day per human subject. Behavioral tasks of spatial learning/reference memory, working memory, and recognition/identification demonstrated that Tg mice given caffeine performed better than Tg control mice and were similar to non-Tg controls. Underlying pathophysiological mechanisms were also examined. In behaviorally-tested and aged Tg mice, long-term caffeine was linked to lower hippocampal amyloid-β (Aβ) concentrations. Expression of both presenilin 1 (PS1) and β-secretase (BACE) was lower in caffeine-treated Tg mice, suggesting decreased Aβ production to be the likely underlying mechanism. These data are consistent with human epidemiological studies showing that moderate daily intake of caffeine may delay or reduce the risk of AD. Chen et al. [8] studied rabbits

fed a cholesterol-enriched diet to test the hypothesis that chronic ingestion of caffeine protects against high cholesterol diet-induced disruptions of the blood brain barrier (BBB). Olfactory bulb histology provided the main measures of BBB leakage, BBB tight junction protein expression levels, activation of astrocytes, and microglia density. Caffeine was seen to prevent high cholesterol diet-induced increases in extravasation of IgG and fibrinogen, increases in leakage of Evan's blue dye, decreases in levels of the tight junction proteins occludin and ZO-1, increases in astrocytes activation and microglia density where IgG extravasation was present. Chronic ingestion of caffeine, therefore, was seen to protect against high cholesterol diet-induced increases in disruptions of the BBB, prompting the authors to speculate that caffeine (or drugs like caffeine) might prove useful in the treatment of AD.

If the benefits of caffeine intake are indeed present, these would warrant the conduct of long-term randomized clinical trials to test the value of caffeine in the slowing of age-related cognitive decline or, potentially, in the delay or prevention of progress to dementia. The analysis reported here was suggested by researchers elsewhere who wished to know if our Scottish dataset could be employed to evaluate the strength of a possible association between caffeine intake and performance on cognitive tests that measure fluid intelligence (non-verbal reasoning, spatial ability, information processing speed) and verbal memory. This is, therefore, a secondary analysis of an existing dataset that was not planned when the study began. Here, we compare lower caffeine with higher caffeine intake that we predicted would be associated with better performance on fluid intelligence tests. Further, we reasoned that introduction of confounders, including socioeconomic status (SES) into the statistical model would not remove this association.

MATERIALS AND METHODS

Sampling

From April 2000 to September 2003 we recruited, from among the local community, 506 volunteers born in 1936. All had participated in the Scottish Mental Survey of 1947 when about 95% of children born in 1936, and at school anywhere in Scotland on June 1947, had sat the Moray House Test (MHT) which is a group administered test of mental ability known as the "verbal test" (Scottish Council for Research in Education, 1947 [9]. The MHT has a maximum score of 76 points. From the population of 1823 Aberdeen city children who sat the MHT in 1947, we traced 986 to an address in North East Scotland in 1999. The 986 who were traced were linked to local general medical practices. General practitioners were selected at random to help with the study and 22 of 25 practices invited agreed to invite by post 647 local residents who could be matched exactly by birth name and date of birth with the Scottish Mental Survey (1947) archive. From these 647, 506 (75%) volunteered to participate in a long-term follow up study of brain ageing and health and among these 506, 22 did not complete their first assessment (n = 484/506). These procedures were approved by the regional Research Ethics Committee. Written informed consent was obtained to take part in a clinical study where neuropsychological, biomedical and follow-up data were required. Refusal to take part was significantly associated with lower childhood mental ability (MHT) scores ($p < 0.05$). SES was classified by usual occupation [10] before retirement. The Standard Occupational Classification consists of the following major groups: **SES Group 1** (1 – Managers and Senior Officials; 2 – Professional Occupations; 3 – Associate Professional and Technical Occupations), **SES Group 2** (4 – Administrative and Secretarial Occupations; 5 – Skilled Trades Occupations; 6 – Personal Service Occupations), **SES Group 3** (7 – Sales and Customer Service Occupations; 8 – Process, Plant and Machine Operatives; 9 – Elementary Occupations). Those who had retired and were not in paid employment were rated as undertaking no hours of work, others in part time work were rated as working less than 37.5 h per week. Some (most often self-employed) had continued to work more than 37.5 h per week.

Interview and cognitive measures

At interview (lasting one hour) with a trained research nurse, volunteers provided demographic information, detailed medical histories, accounts of current prescribed and non-prescribed medications, and completed tests of cognitive function supervised by a trained psychologist (lasting one hour). Interviews took place in a purpose built Clinical Research Centre situated in a Regional Psychiatric Hospital from either 10.00–13.00 h or 13.00 h–16.00 h. A standardized brief cognitive screening instrument, the Mini-Mental State Examination (MMSE) [11], was used as a practical method for grading cognitive ability and as a screening test for possible dementia. All volunteers completed Raven's

Table 1
Demographic and cognitive performance scores in 351 community volunteers grouped by socioeconomic status

	Socioeconomic status				
	Professional -administrative $n = 94$	Skilled manual $n = 180$	Unskilled Manual $n = 77$	Total $n = 351$	
Caffeine [mg/day]	623.2 (188.2)	635.0 (188.2)	661.1 (207.0)	637.6 (186.0)	$F = 0.91, p = 0.403$
men:women	48:46	90:90	38:39	176:175	$\chi^2 = 0.97, p = 0.540$
Age [years]	64.3 (0.7)	64.6 (0.7)	64.1 (0.8)	64.4 (0.8)	$F = 6.28, p = 0.002$
Education [years]	13.6 (2.8)	10.4 (0.8)	10.2 (0.8)	11.2 (2.1)	$F = 137.3, p < 0.001$
Hours at work					
none	73	132	49	234	$\chi^2 = 17.97,$
0–20 h	8	19	4	31	$p = 0.006$
20–37.5 h	5	20	9	34	
$>$ 37.5 h	8	9	15	32	
Childhood mental ability	52.0 (8.9)	42.2 (11.6)	34.1 (14.0)	43.0 (13.1)	$F = 51.5, p < 0.001$
HADS-anxiety	4.9 (2.7)	5.8 (3.2)	6.9 (3.1)	5.8 (3.1)	$F = 7.8, p < 0.001$
HADS-depression	2.2 (1.6)	3.0 (2.5)	3.2 (2.3)	2.8 (2.3)	$F = 4.84, p < 0.01$
Raven's Progressive Matrices	41.9 (6.8)	35.0 (7.8)	31.3 (7.9)	36.1 (8.5)	$F = 42.9, p < 0.001$
Digit Symbol	49.6 (10.8)	43.1 (11.1)	38.7 (10.4)	44.1 (11.5)	$F = 20.1, p < 0.001$
Block Design	29.3 (8.9)	23.7 (7.7)	21.2 (7.6)	24.8 (8.6)	$F = 22.5, p < 0.001$
Auditory verbal learning	63.0 (12.0)	58.0 (12.4)	55.4 (10.6)	58.8 (12.2)	$F = 9.12, p < 0.001$
Mini-Mental State Exam	29.3 (1.1)	29.1 (1.3)	28.9 (1.4)	29.1 (1.2)	$F = 1.83, p = 0.162$

*Mean (standard deviation).

Standardized Progressive Matrices [12], Digit Symbol (DS), and Block Design (BD) subtests of the Wechsler Adult Intelligence Scale-revised WAIS-R [13] were used respectively to measure non-verbal reasoning ability, mental speed, and constructional ability. The Rey Auditory Verbal Learning Test (AVLT) [14] was used as a measure of verbal memory.

Emotional symptoms and neuroticism

The Hospital Anxiety and Depression Scale (HADS) was used by participants to self-rate symptoms of anxiety and depression [15]. The personality trait of neuroticism was self-rated using the Five Factor Inventory [16].

Caffeine intake

The MONICA food frequency questionnaire [17] was completed satisfactorily by 346 participants whose MMSE scores were $>$ 25 and these are the subjects of this study. MONICA was completed at home and returned by post to the Research Centre. This questionnaire was used to estimate the intake of caffeine containing drinks (mostly coffee, tea, and carbonated drinks) and foodstuffs (mostly chocolate). Contemporary food composition tables [18–23] were used to determine the daily amounts of caffeine as mg caffeine/day.

Statistical methods

Statistical analyses were conducted using SPSS (version 17). All p-values are two-sided and subject to a significance level of 0.05. After removal of outliers, all data met criteria for normality. Correlations between caffeine (mg/day) and all other variables were estimated using parametric or non-parametric methods as appropriate. Analyses of variance were used to compare by subgroups of occupation and by quartiles ranked by caffeine intakes. The associations between specific cognitive domains and caffeine intake were examined using multiple linear regression analyses for each cognitive domain with gender, SES, childhood intelligence, education, neuroticism, HADS-anxiety, and HADS-depression as plausible possible predictors.

RESULTS

The characteristics of the study sample are summarized by occupational group in Table 1. There were no significant differences in mean caffeine intake between occupational groups, but there were small but significant differences in age between skilled and unskilled manual workers. There were significant differences in hours spent in paid work each week between occupational groups such that the unskilled manual workers remained in paid work more often than other groups ($p =$

0.006). On all cognitive tests, professional and administrative workers performed better than either skilled or unskilled manual workers ($p < 0.001$) and had spent longer in full time education ($p < 0.001$).

There were significant correlations between caffeine intake (mg/day) and childhood mental ability so that those subjects with higher childhood mental ability had lower daily caffeine intake ($r = -0.115$, $p = 0.031$) and had spent longer in full time education ($r = 0.122$, $p = 0.022$). Higher caffeine consumption was associated with lower performance on the digit symbol test ($r = -126$, $p = 0.024$) and on the MMSE ($\rho = -0.107, p = 0.046$). After splitting the sample by gender, there were no significant differences between correlations estimated for men and women separately.

Table 2 shows summary data that are comparable to Table 1. In Table 2, the data are grouped by quartile of caffeine consumption which fell in the range 226–1134 mg/day. Higher caffeine intake was associated with unskilled manual work group ($p = 0.037$). With the single exception of lower performance on the Digit Symbol test ($p = 0.02$), cognitive test scores did not distinguish between quartiles based on caffeine intake.

Table 3 presents regression coefficients from multiple regression analyses in which performance on individual cognitive tests was predicted by a combination of childhood mental ability, education, socio-economic status, neuroticism, and caffeine intake. After inclusion of all these terms in the regression models, caffeine intake did not contribute to prediction of current performance on any of the cognitive tests (Raven's Progressive Matrices, Auditory verbal learning test, Digit Symbol or Block Design).

DISCUSSION

These data were obtained from a volunteer sample aged about 64 years. All were without dementia and living independently in the community. There were significant differences ($p = 0.006$) within the sample between those whose usual occupation had been professional or administrative and manual workers in the extent to which they had remained in paid employment at the age of examination (about 64 years). Univariate analyses demonstrated one significant difference between groups ranked by quartiles of caffeine intake and showed that performance on the Digit Symbol test was lowest among those with the highest caffeine intake. After adjustment for the contribution of socioeconomic status, this difference was removed. The results of multivariate linear regression supported this finding; caffeine intake did not contribute to performance on any of the cognitive domains in any of the analyses.

These data were analyzed with the aim of contributing to current understanding of the possible role of caffeine intake to protection against dementia and/or cognitive aging. The study sample excluded subjects whose MMSE score fell below 25 points and, therefore, did not contain those subjects who may have met criteria for mild cognitive impairment. It is possible that these selection criteria (when applied to a narrow age range (63–65 years) of the general population living independently in the community) yielded a sample that was not yet at risk of age-related cognitive impairment and in whom the putative benefits of caffeine intake would not be detected. Other studies using a predictive longitudinal design indicate a protective role of caffeine detected on follow-up from middle age to late life (e.g. [6]). The data reported here are not comparable with these follow up studies but can be compared to other cross-sectional studies. These studies have yielded inconsistent results possibly because sampling procedures differed to an extent sufficient to produce subjects at varied points on the trajectory from preclinical AD to the late stage of deterioration found in clinical dementia [24–27]. Comparisons between this and other studies on caffeine intake and cognitive decline are not straightforward. Subjects reported here were relatively high caffeine consumers although this difference may be partly attributable to inclusion of all caffeine containing foodstuffs when estimating caffeine intake and using coffee intake alone. This difference may be an important limitation of the study design or, from the standpoint of nutritional epidemiology, provide a better guide to caffeine consumption.

Previously, we have shown that childhood mental ability scores account for about 50% of the variance in scores on cognitive tests completed in late adulthood [28]. The data reported here are consistent with this earlier finding. Table 3 shows how childhood mental ability was the single strongest predictor of cognitive performance in this sample (aged about 64 years). There are also strong links between childhood mental ability, duration of education, and socioeconomic status. When these three linked variables were entered into the multiple regression analyses, no effect of caffeine intake remained.

Satisfactory measurement of habitual daily caffeine intake depends on reliable reporting of caffeine consumption. Reporting and recording of food and drink

Table 2

Demographic and cognitive performance data by quartiles of self reported daily caffeine intake in 351 volunteers without dementia. Values are means and (standard deviations) unless otherwise specified. SES – Socioeconomic status; K-Wallis, Kruskal – Wallis non-parametric analysis by ran

variable	Quartiles of caffeine consumption					Univariate ANOVA	Multivariate ANCOVA	
	(1) Lowest $n = 89$	(2) $n = 88$	(3) $n = 89$	(4) Highest $n = 85$	Total $n = 351$		By quartile of caffeine intake	By quartile of caffeine intake with SES
Caffeine (mg/day)	407.9 (74.0)	572.9 (37.5)	692.0 (33.2)	887.9 (95.0)	637.6 (66.8)			
range	226–504	505–634	635–751	743–1134	226–1134			
Socioeconomic status						K-Wallis		
Professional/administrative	22	26	32	14	94	$\chi^2 = 8.49$,		
Skilled manual	47	46	40	47	180	$p = 0.037$		
Unskilled manual	20	16	17	24	77			
men/women	42/47	44/44	49/40	41/44	176/175	$X^2 = 1.3$, $p = 0.73$		
Education (yrs)	11.5 (2.3)	11.3 (2.2)	11.3 (2.3)	10.7 (1.7)	11.2 (2.1)	$F = 1.90$, $p = 0.12$		
Childhood mental ability	44.3 (12.0)	45.3 (13.0)	41.4 (14.6)	41.2 (12.3)	43.1 (13.1)	$F = 2.20$, $p = 0.09$		
HADS-anxiety	5.7 (3.0)	5.7 (3.0)	5.9 (3.6)	5.9 (3.6)	43.1 (13.1)	$F = 0.09$, $p = 0.97$		
HADS-depression	2.9 (2.2)	2.7 (1.8)	2.8 (2.5)	3.3 (2.5)	2.8 (2.3)	$F = 1.96$, $p = 0.12$		
Raven's Progressive Matrices	36.8 (8.6)	36.9 (9.2)	36.1 (8.3)	34.5 (7.7)	36.1 (8.5)	$F = 1.57$, $p = 0.20$	$F = 1.64$, $p = 0.18$	$F = 0.91$, $p = 0.44$
Digit symbol	45.6 (10.8)	45.6 (11.6)	44.1 (12.0)	40.6 (11.1)	44.1 (11.5)	$F = 3.34$, $p = 0.02$	$F = 2.76$, $p = 0.04$	$F = 1.71$, $p = 0.17$
Block design	24.0 (8.0)	25.9 (10.2)	25.5 (8.2)	23.8 (7.7)	24.8 (8.6)	$F = 1.17$, $p = 0.323$	$F = 2.33$, $p = 0.08$	$F = 1.67$, $p = 0.17$
Auditory verbal learning	59.4 (12.9)	58.9 (12.9)	58.3 (11.9)	58.6 (11.3)	58.6 (12.2)	$F = 0.128$, $p = 0.128$	$F = 0.16$, $p = 0.92$	$F = 0.39$, $p = 0.76$
Mini-Mental State Exam	29.2 (1.2)	29.2 (1.2)	28.8 (1.4)	29.0 (1.2)	29.1 (1.2)	$F = 2.08$, $p = 0.103$		

Table 3
Linear regression models examining the relation of childhood mental ability, duration of education (years), Socioeconomic status, neuroticism and daily caffeine intake (mg/day) to specific domains of cognitive function. Initially, anxiety and depression scores, gender, smoking, alcohol intake and Mini-Mental State scores were included in the models but here only significant scores and caffeine intake are shown. Negative β represents an inverse interaction between predictor and cognitive performance and a positive β represents a positive interaction. Socioeconomic status (SES) was scored inversely so that the highest SES was scored low and lowest scored high

	Auditory verbal learning			Progressive matrices			Digit symbol			Block design		
Model terms	β	SE	p	β	SE	p	β	SE	p	β	SE	p
Childhood mental ability	0.334	0.059	< 0.001	0.272	0.035	< 0.001	0.342	0.053	< 0.001	0.215	0.041	< 0.001
Education (years)	0.733	0.353	$= 0.038$	0.508	0.200	$= 0.012$	0.272	0.308	$= 0.377$	0.453	0.238	$= 0.058$
Socioeconomic status	0.80	0.355	$= 0.822$	-0.635	0.204	$= 0.002$	-0.706	0.319	$= 0.028$	-0.430	0.248	$= 0.084$
Neuroticism	0.031	0.083	$= 0.705$	-0.145	0.048	$= 0.003$	-0.143	0.074	$= 0.054$	0.162	0.057	$= 0.005$
Caffeine (mg/day)	0.001	0.003	$= 0.793$	0.000	0.002	$= 0.864$	-0.005	0.003	$= 0.117$	0.003	0.002	$= 0.058$

data may be subject to error. At the simplest level, where variation in cognitive performance is the outcome variable of interest, it seems reasonable to suspect that differences in cognitive ability might affect not only cognitive test scores but reliability of self-reports of food and drink intakes. This influence on self reported caffeine consumption might be greatest at lower levels of cognitive performance especially if affected by age or dementia. This limitation is an important methodological concern in studies of age-related cognitive impairment and extends beyond the reports of coffee consumption into related areas of those foods and beverages that contain caffeine. In addition, the preparation and brewing of caffeine-containing beverages varies greatly in practice and duration, and may also be compounded by differences between standard food composition tables and foodstuffs available in local outlets. The MONICA self-report food frequency questionnaire is typical of the many methods of self-reporting food intakes. In the present study, no methods were introduced to determine systematically the reliability and validity of MONICA ratings. However, comparisons between low and high cognitive performers did not suggest greater variation in caffeine intake in low cognitive scorers as might be predicted if low cognitive function was associated with less reliability of self reported caffeine intake.

The division of caffeine intake into quartiles, while useful for analysis of the study sample, may not be helpful when seeking to compare these data with other studies. Division of caffeine intake into "low" and "high" consumers is difficult in the absence of agreed boundaries between caffeine consumers. Multiple regression analyses reported here entered caffeine intake on an interval scale and retained the main findings of the preceding categorical analyses. Studies of the validity of self-reported caffeine intake suggest that in the normal range of caffeine intake (< 1200 mg/daily), these questionnaire methods are valid, but when higher intakes are reported, other supportive measures are required to corroborate this estimation [29].

Performance on cognitive tests may be impaired by caffeine withdrawal in habitual high caffeine users [2]. We did not introduce methods to detect caffeine dependency nor did we direct volunteers to modify their caffeine consumption in the period immediately before testing. It is, therefore, possible that withdrawal from caffeine impaired performance on cognitive tests in some high caffeine users. Such an effect may have been sufficient to impair performance on the Digit Symbol Test, a measure of information processing speed.

It is relevant to consider how certain predispositional traits may have associated caffeine use with work task efficiency and how this may have affected results reported here. In one model of habitual caffeine use, some individuals who are innately susceptible to caffeine (because caffeine induces unpleasant feelings) remain long term low users of caffeine. By extension, some high users of caffeine associate caffeine intake with meeting occupational demands, especially when these require maintained vigilance. This putative association may underlie the link observed here between lower socio-economic status and higher caffeine intake. This line of reasoning can be extended to consideration of the usual cognitive demands encountered in occupations where high average cognitive ability was an important part of requirements to enter these occupations. It could, therefore, be envisaged that greater caffeine consumption could be a consequence of occupational demands which would be more frequently faced in those of higher original mental ability. Work elsewhere [30,31] suggests that dementia risk is lower in those of higher childhood mental ability. If higher dementia risk could be equated with greater than expected age-related cognitive decline, then it would seem plausible to argue that lower childhood mental ability would be linked to lower caffeine intake and, therefore, to greater cognitive decline. Data reported here do not

support this line of reasoning: higher childhood mental ability was associated with lower caffeine intake and longer durations of full-time education.

In this study, self-reported caffeine intake appeared to have little or no effect on cognitive performance. It is possible that the slight effects observed reflected impaired cognitive performance related to caffeine withdrawal. The extent to which habitual caffeine intake may ameliorate cognitive decline in an ageing population was not explored in these largely cross-sectional data and this may yet prove to be the cognitive benefit of caffeine most relevant to dementia [5]. The introduction of multiple predictors into statistical models of the cognitive effects of habitual caffeine intake removed evidence of slight impairments in digit symbol performance (mental speed). Putative associations between caffeine use and occupational demands or work patterns merit further study.

DISCLOSURE STATEMENT

Authors' disclosures available online (http://www.j-alz.com/disclosures/view.php?id=277).

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