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Caffeine consumption and cognitive function at age 70: the Lothian Birth Cohort 1936 Study

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ABSTRACT

Objective: To investigate the association between caffeine consumption and cognitive outcomes in later life. **Methods:** Participants were 923 healthy adults aged about 70 years in the Lothian Birth Cohort 1936 Study, on whom there were IQ data from age 11 years. Cognitive function at age 70 was assessed using a battery of tests measuring general cognitive ability, speed of information processing, and memory. Current caffeine consumption (using multiple measures of tea, coffee and total dietary caffeine) was obtained by self-report questionnaire, and demographic and health information was collected in a standardized interview. **Results:** In age- and sex-adjusted models there were significant positive associations between total caffeine intake and general cognitive ability and memory. After additional adjustment for age 11 IQ and social class—individually and together—most of these associations became non-significant. A robust positive association, however, was found between drinking ground coffee (e.g. filter and espresso) and performance on the National Adult Reading Test (NART, $p = .007$), and the Wechsler Test of Adult Reading (WTAR, $p = .02$). No gender effects were observed, contrary to previous studies. Generally, higher cognitive scores were associated with coffee consumption, and lower cognitive scores with tea consumption, but these effects were not significant in the fully adjusted model. **Conclusions:** The present study is rare in having childhood IQ in a large sample of older people. The results suggest that the significant caffeine intake-cognitive ability associations are bidirectional—because childhood IQ and estimated prior IQ are associated with the type of caffeine intake in old age—and partly confounded by social class. **Key words:** caffeine, cognitive function, childhood IQ, aging.

BMI = Body mass index; **FFQ** = Food Frequency Questionnaire; **M** = mean; **MHT** = Moray House Test; **PCA** = Principal Components Analysis; **SD** = standard deviation; **SMS1947** = Scottish Mental Survey 1947; **LBC1936** = Lothian Birth Cohort 1936; **SES** = socio-economic status

INTRODUCTION

By late adulthood, people typically experience some deterioration in cognitive abilities as part of the normal course of aging. Abilities such as memory, reasoning, and processing speed all decline, on average, with age (1). However, there are large individual differences in age-related cognitive changes and it is a research priority to identify factors that affect the rate of age-related cognitive decline. In the setting of an increasingly aged population, such knowledge can improve the health and wellbeing of older people in the future (2).

There is growing evidence from epidemiological studies that caffeine consumption is associated with better cognitive performance in later life. Caffeine is widely consumed in Western societies, primarily in coffee and tea but also in chocolate and carbonated drinks. It acts as a psychoactive stimulant and has been shown to improve cognitive performance in the short term (3). By increasing the activity of the central nervous system, caffeine consumption can result in heightened alertness, vigilance, attention and mood as well as improved complex, higher cognitive functions, including memory (4, 5). Besides these short-term effects, there is also a growing body of evidence from studies indicating that the habitual consumption of coffee and tea has long-term beneficial effects on brain function (6). Using data from the Health and Lifestyle Survey (HALS), a large cross-sectional study of 9003 British adults, Jarvis (7) reported a dose-response trend between habitual tea and coffee consumption and cognitive performance in all four tasks measured: simple reaction times, choice reaction times, incidental verbal memory, and visuospatial reasoning. Interestingly, the oldest men and women appeared to benefit most from a higher caffeine intake.

One possible explanation, underlying the positive association between caffeine and cognitive abilities in older adults, and adopted by many researchers, is that regular caffeine consumption enhances the neuroprotective actions of adenosine. Like alcohol, caffeine readily crosses the blood-brain barrier. It is well documented that, once in the brain, caffeine acts as an antagonist on the A_{2a} adenosine receptors. By counteracting adenosine, caffeine has

a disinhibitory effect, causing the stimulation of cholinergic neurotransmitters (8). These neurotransmitters exert a protective effect against β -amyloid induced neurotoxicity, a precursor to cognitive decline in humans (9) and in mice (10). Caffeine, especially coffee, is rich in biologically active substances such as polyphenols and antioxidants and is capable of increasing plasma antioxidant capacity in humans (11). Therefore, another potential physiological mechanism by which caffeine may afford some protection against brain aging, is by counteracting the oxidative stress involved in the pathogenesis of aging related diseases. Another risk factor for cognitive decline is type II diabetes (12). A systematic review of several large scale prospective studies (13) supported the hypothesis that habitual coffee consumption is associated with a substantially lower risk of type II diabetes. Others have reported protective effects of long-term caffeine intake on the risk of developing Alzheimer's disease (14, 15). Coffee drinkers are reported to have a 30% lower risk of developing Parkinson's disease (16).

In recent years, evidence has generally supported the assertion that caffeine intake (particularly from coffee) may help to maintain cognitive functions in aging. Some longitudinal studies have documented an inverse association between coffee consumption and cognitive decline. In a men-only study, Gelder et al. (17) found that, among the elderly, those who drank coffee had half the 10-year cognitive decline than non coffee drinkers. The least decline occurred for men consuming three cups of coffee per day. Others have reported gender-specific benefits of caffeine on cognitive function favoring women. In a large prospective study, women who drank more than three cups of coffee per day showed less decline in verbal cognitive functioning and visuospatial memory over a four year period than women who had low or no consumption of coffee (18). However, no effect was observed in men. Similarly, Johnson-Kozlow et al. (19) reported that lifetime and current exposure to coffee was associated with better cognitive performance among women, but not in men. Female coffee drinkers (especially those aged 80 and over) performed better on cognitive tasks of memory, attention and concentration. Although men consumed more caffeine than

women per day, they hypothesized that women are more sensitive to the pharmacological effects of caffeine than men.

However, some have investigated the relationship between caffeine and cognitive abilities with inconsistent results. Van Boxtel et al. (20) found no significant reduction in age related cognitive decline with habitual caffeine intake (from tea and coffee) after 6 years and concluded that the longitudinal effect of caffeine is limited at best. Methodological differences may, in part, account for the discrepancies between studies. Tea and coffee consumption is frequently measured as 'number of cups consumed daily', whereas others measure caffeine intake based on standard estimations of caffeine per cup of coffee or tea. However, caffeine content can vary markedly between different types of beverages. One cup of instant coffee can contain between 21mg and 120mg of caffeine, whereas the equivalent serving size of ground coffee (filter, espresso, etc.) can contain up to 254mg (21). Assuming that every cup of coffee contains an equivalent level of caffeine is unlikely to give an accurate reflection of caffeine intake. Few studies have included tea consumption in their investigations and no other study, as far as we are aware, has included the effects of overall dietary caffeine exposure on cognitive function, especially in old age.

Attempting to measure the effects of caffeine (or any variable for that matter) on cognitive abilities in old age is problematic without some measure of prior cognitive ability as a baseline comparison. If there is a significant association in a group of older people between, say, caffeine intake and cognitive ability, this does not necessarily mean that caffeine is beneficial for cognitive abilities in old age. One of the limitations of most studies in the field of cognitive aging is the possibility of reverse causation; that is, the supposed dependent (outcome) variable might be causing changes in the supposed independent (predictor) variable. It is possible that early life intelligence influences caffeine intake as well as vice versa. Indeed, it is well demonstrated in large, population-representative samples that childhood IQ influences many aspects of diet and health-related lifestyle (22). The Lothian

Birth Cohort 1936 is almost unique in terms of having a measure of IQ at both childhood (age 11) and later life (age 70) in addition to multiple cognitive domain scores and demographic and health data from late life. This dataset is in an ideal position to provide an insight into the associations, if any, between caffeine intake and cognition in older people. The aim of the present study was to examine the association between caffeine consumption (coffee, tea and additional sources) and performance on a comprehensive battery of cognitive function tests in a sample of older adults (aged about 70) from the Lothian Birth Cohort 1936 Study, whilst controlling for prior cognitive ability (age 11 IQ). Cognitive assessment at age 70 included multiple markers of memory, speed of information processing, general cognition and verbal intelligence. Focussing on these specific cognitive domains may help to untangle the effects of caffeine on cognitive performance in older adults.

METHODS

Participants and general methods

The participants were surviving participants of the Scottish Mental Survey of 1947 (SMS1947: 23). The SMS1947 tested the mental ability of almost all Scottish schoolchildren born in 1936 and attending school on June 4th 1947 (aged 11), using a well-validated test of general intelligence: a version of the Moray House Test No. 12. The 1091 surviving participants described in the present study are known as the Lothian Birth Cohort 1936 (LBC1936). Full details of the recruitment and testing of the LBC1936 are given in a free-access protocol paper (24). At the time of recruitment, LBC1936 members mostly resided in Edinburgh and its surrounding area (Lothian) in Scotland. They were relatively healthy and lived independently. Between July 2004 and May 2007, at a mean age 69.5 years, each LBC1936 participant attended the Wellcome Trust Clinical Research Facility at the Western General Hospital in Edinburgh to undergo extensive cognitive and physical testing and an interview. Cognitive assessments were conducted by trained researchers and physical testing was carried out by research nurses. The standardized interview ascertained demographic information, smoking and alcohol consumption, medical history, and medication use. As a

part of their general assessment, LBC1936 participants were asked to complete the Scottish Collaborative Group 165-item Food Frequency Questionnaire (25). Ethics permission for the Lothian Birth Cohort 1936 (LBC1936) study protocol was obtained from the Multi-Centre Research Ethics Committee for Scotland (MREC/01/0/56) and from Lothian Research Ethics Committee (LREC/2003/2/29). The research was carried out in compliance with the Helsinki Declaration. All participants gave their written, informed consent.

Procedure

Measurement of caffeine intake

Caffeine intake was assessed using the Scottish Collaborative Group Food Frequency Questionnaire (FFQ) version 7.0. (26). The FFQ has been found to have good repeatability (dietary intake in later life is reasonably stable in the short term) and good validity for most nutrients in community dwelling older populations (27, 28). This self-report questionnaire comprises questions about dietary intake over the previous 2-3 month period and is designed to estimate daily intake of a wide range of nutrients. The FFQ measures intake of caffeine from the main dietary sources, namely: 'instant coffee' (freeze-dried), 'filter, espresso or cappuccino coffee' (hereby collectively referred to as 'ground coffee'), 'decaffeinated coffee', 'tea (regular)', 'herbal, fruit or decaffeinated tea', 'diet fizzy drinks (cola, lemonade etc)', 'regular fizzy drinks', 'hot chocolate', 'Horlicks or Ovaltine', 'mousse, blancmange, trifle, meringue', 'chocolate bars (e.g. Mars, Dairy Milk)', 'chocolate sweets, toffees or fudge', 'chocolate coated biscuits', 'peanut butter or chocolate spread'. Each item on the questionnaire refers to a standard measure, e.g., 1 cup or mug (hot drinks), 1 biscuit, 1 can (fizzy drinks). Participants mark one of nine responses to indicate frequency of consumption of the measure: rarely or never; 1-3 per month; 1 per week; 2-3 per week; 4-6 per week; 1 per day; 2-3 per day; 4-6 per day; 7+ per day.

The FFQ was given at the clinic visit and returned in a stamped addressed envelope. In the event of any missing responses, a letter was sent requesting the information. If there were

more than 10 missing items (even after a letter had been sent) the FFQ was labelled 'incomplete' and excluded from the analyses. 929 participants (85%) returned completed (<10 missing items) questionnaires (51.6% by women). 97 were not returned, 26 were returned blank, 39 were incomplete. One 'completed' questionnaire had several missing caffeine containing items and was excluded. Five further individuals were excluded because they were identified as having potential dementia based on a score of <24 on the Mini-Mental State Examination (29). Therefore, the final sample for analysis in the present study comprised 923 relatively healthy participants (446 men, 477 women) aged about 70 (m = 69.5, sd = 0.8) years at time of testing.

The amount of caffeine (coded as milligrams daily) estimated to be present in each item was calculated using a caffeine composition database compiled from British beverage and food caffeine surveys, where caffeine levels were obtained using validated analytical techniques (30, 21, 31, 32, 33, 34, 35). Estimated average caffeine values were assigned to each food or drink including (per 1 cup or mug serving): tea (34.2mg), instant coffee (43.7 mg) and ground coffee (93.1mg). A measure of 'total caffeine' consumption was derived from all 14 caffeine containing items in the FFQ. In order to investigate the effect of overall coffee intake, because this is often used in the previous literature, an additional measure of 'total caffeine from coffee' was derived by combining consumption of both instant coffee and ground coffee.

Measurement of cognitive performance at age 70

A full description of the cognitive tests and administration procedures used can be found in the free-access LBC1936 protocol article (24). Cognitive testing was carried out by a trained researcher. Brief descriptions of the tests follow.

The *Mini-Mental State Examination* (MMSE) was used as a screening measure for cognitive pathology (29). Scores range from 0-30, with a score of less than 24 indicating possible dementia.

From the Wechsler Adult Intelligence Scale-III^{UK} (WAIS-III: 36) we included: *Digit Symbol Coding* (speed of information processing); *Block Design* (constructional ability); *Matrix reasoning* (non-verbal reasoning); *Digit Span backwards* (working memory); *Symbol Search* (speed of information processing); *Letter-number sequencing* (working memory).

From the Wechsler Memory Scale-III^{UK} (WMS-III: 37) we used: *Logical Memory I and II* (verbal declarative memory, immediate and delayed recall); *Verbal Paired Associates I and II* (verbal learning and memory, immediate and delayed recall); *Spatial Span* (non-verbal spatial learning and memory).

Verbal Fluency (phonemic) provides a measure of executive function (38). *National Adult Reading Test* (NART: 39) and *Wechsler Test of Adult Reading* (WTAR: 40) are widely used to estimate prior cognitive ability and they require the pronunciation of irregular words. *Simple and Four-choice reaction time* measure speed and variability of simple information processing, using a purpose built portable machine (41, 42). *Inspection time* is a computer-based task used to assess speed of elementary visual processing (43).

Demographic and control variables, including childhood IQ

Demographic and medical information was obtained at the clinic assessment. During the standardized interview, participants were asked questions relating to their marital status, education (number of years of full time [F/T] education), current alcohol consumption (type and frequency, from which units per week were calculated), and smoking status (current, ex or never smoker). Social class was derived from participants' highest reported occupation (44) and consisted of 6 categories ranging from I (professional occupations) to V (unskilled occupations), with III (skilled occupations) divided into IIIN (non-manual) and IIIM (manual). The women in the cohort were asked for their husband's occupation as well as their own, and assigned a social class based on the highest occupation of the household. This was derived from their own occupation for about half of the women, and from their husband's occupation for the remainder. Social class is here represented in a numeric fashion with classes IIIN and IIIM expressed as 3 and 3.5 respectively to reflect their relative status. A

detailed medical history was taken (including diagnoses of diabetes, high blood pressure, and high cholesterol). Anxiety and depression symptoms were assessed using the Hospital Anxiety and Depression Scale (HADS). This is a short self-assessment scale consisting of 7 items for anxiety and 7 for depression. A physical examination was performed by a nurse including measurements of height and weight, from which body mass index (BMI) was calculated. Participants completed a 20-page questionnaire booklet containing various social and lifestyle questionnaires and measures of physical activity (including number of days per month of exercise).

Age 11 scores were obtained, in collaboration with the Scottish Council for Research in Education (SCRE) and with the permission of LBC1936 participants, from the original Scottish Mental Survey of 1947 (SMS1947) records. The Moray House Test (MHT) No.12 was taken by participants in the SMS1947 at age 11 (45) and repeated at their clinic visit aged about 70. MHT scores were corrected for age in days at time of testing and converted to standard IQ type scores where mean = 100 and sd = 15. This is a well-validated general mental test comprising 71 items (mostly verbal reasoning, but also some numerical, spatial and other items) with a maximum score of 76 and a 45-minute time limit.

Statistical analyses

Demographic and health differences between tertiles of caffeine intake groups were examined using ANOVA, Chi-Square and t-tests as appropriate. Tertiles of consumption were used for illustration purposes only; the main analyses were conducted using caffeine as a continuous variable. Associations between caffeine consumption (derived from total caffeine, tea, instant coffee, ground coffee and total coffee) and cognitive function were examined using univariate general linear models. Four models were fitted to the data, each including adjustment for potential confounding factors. The base model included age (in days at time of testing) and sex. The second model included age, sex, and occupational social class. A third model included age, sex, and age 11 IQ to control for early life cognitive ability. In the fourth and

final model, all four control variables were included. A general cognitive ability component score (*g* factor) was derived from principal components analysis (PCA) of six WAIS-III subtests (Letter-number sequencing, Matrix reasoning, Block design, Digit symbol, Digit Span backwards, Symbol search). A general processing speed component score (*speed*) was similarly derived from a PCA of the set of speed measures (Symbol search, Digit symbol, Simple RT mean, Choice RT mean, Inspection time). The extraction of these factors by PCA has been described elsewhere (46). Using the same method, a general memory factor (*memory*) was extracted from the WMS-III subtests (Logical memory I immediate and II delayed recall, Spatial span forwards, Spatial span backwards, Verbal paired associates I immediate and II delayed recall) and two WAIS-III subtests (Letter-number sequencing, Digit Span backwards). The fourth cognitive outcome variable used in the present study is age 70 IQ (Moray House Test score at age 70 corrected for age in days at time of testing and converted to an IQ scale where mean = 100 and sd = 15). Additional analyses were performed with NART and WTAR scores (measures of verbal IQ) as cognitive outcomes. We present estimates of effect size as well as *p* values.

RESULTS

The characteristics of study participants are presented in Table 1 by tertile of total caffeine consumption; low caffeine (1.2 – 131.0 mg/day); medium caffeine (131.0 – 211.0 mg/day); high caffeine (211.0mg – 701.1 mg/day). Of the 923 participants who provided caffeine data, data from 16 cells were incomplete (no more than 1 incomplete caffeine item per person). Analyses were conducted on caffeine data from all 923 FFQs; however, total caffeine was calculated only where data were complete (*n* = 907). High caffeine consumers were significantly less likely to have had a diagnosis of high blood pressure (*p* < .001), diabetes (*p* = .005) or cholesterol (*p* = .008) than low caffeine consumers. Medium caffeine consumers were significantly less likely to have had a diagnosis of high blood pressure (*p* = .04) or diabetes (*p* = .03) than low caffeine consumers. Level of caffeine consumption was not significantly associated with any other demographic variable. Non-responders to the FFQ

(where questionnaires were not returned or returned blank, n = 123) were significantly more likely to be men than women (n = 74 vs. 49, $\chi^2(1) = 5.47$, p = .02), have less years of full time education (m = 10.52 vs. 10.77, p = .02) and lower MMSE scores (m = 28.3 vs. 28.9, p < .001) than responders. Responders and non-responders differed significantly in their smoking status ($\chi^2(2) = 6.192$, p = .04).

[TABLE 1 about here]

Total caffeine: Mean total caffeine intake (per day) from all dietary sources was 182.5mg, and ranged from 1.2mg to 701.1mg (see table 2). Caffeine intake (mean) was slightly higher in women (187.9mg) than men (176.8mg) although this difference was non-significant.

[TABLE 2 about here]

Caffeinated tea/coffee: Coffee and tea consumption in this Scottish cohort was widespread. 97.7% of participants reported consuming caffeinated tea or coffee in the last 2-3 months. 21 participants (2.3%) reported that they 'rarely or never' drank caffeinated tea or coffee. Of the total sample, 85.5% consumed tea, 72.0% consumed instant coffee and 49.0% consumed ground coffee (see table 2 for a breakdown by gender). Women consumed significantly more ground coffee than men; otherwise, there were no statistical differences between the consumption of different types of caffeinated tea or coffee by gender. Beverage preference did not appear to be exclusive; 84% of the sample drank both tea and coffee. However, as expected, there was a significant negative correlation between tea and coffee consumption (-.28, p < .001) suggesting that heavy consumers of tea tend to drink little coffee and vice versa.

Decaffeinated tea/coffee: Men and women differed significantly in their consumption of decaffeinated tea and coffee. Compared to men, women had a significantly higher mean intake of decaffeinated tea (p < .001) and decaffeinated coffee (p = .001) (data not presented). In this older cohort, consumption of decaffeinated coffee and herbal tea was insufficient to warrant inclusion in the analyses as separate measures of caffeine consumption. Although

they contribute relatively small amounts of caffeine to the diet and are consumed by less than a quarter of our sample, they are included in the ‘total caffeine’ measure (see table 2).

Caffeine consumption, age 11 IQ and social class

Age 11 IQ and social class were identified as potential confounding variables of an association between caffeine intake and cognitive ability at age 70. There were significant positive correlations between age 11 IQ score and caffeine from ground coffee and total coffee, and a significant negative correlation with tea (see table 2). There were significant negative correlations between social class group (where a lower number indicates a more professional occupation) and total caffeine, caffeine from ground coffee, total coffee, decaffeinated coffee and herbal/other tea and a significant positive correlation with tea. There was a general trend for increasing (caffeinated) tea consumption in the lower social class groups and those with lower age 11 IQ scores; and there was generally higher coffee consumption in higher social class groups and those with higher age 11 age scores.

Caffeine consumption and cognitive performance at age 70

Table 3 displays the results of four univariate general linear models for each cognitive outcome variable. Examination of models including appropriate interaction terms revealed no significant effects of caffeine by gender. Results are therefore not differentiated by gender below, and interactions were not included in the final models.

[TABLE 3]

The overall caffeine measure ‘total caffeine’ was significantly and positively associated with memory (in the base model only) and with age 70 IQ, NART and WTAR in the base model and model 3 (with age 11 IQ) but not after social class adjustment or in the fully adjusted model. Caffeine from tea had a significant, inverse association with age 70 IQ, *g* factor, processing speed, NART and WTAR scores in model 1 (sex and age adjusted, $p < .01$) and model 2 (sex, age and social class adjusted, $p < .05$). However, when age 11 IQ was added (as

in models 3 and 4) all significant associations fell to non-significant levels. The memory factor was not found to be associated with this caffeine measure. Results indicated no relationship between caffeine from instant coffee and cognitive test scores at age 70 at any stage in the analyses. Caffeine from ground coffee was significantly associated with better performance on all age 70 cognitive measures (age 70 IQ, *g* factor, processing speed, memory, NART and WTAR, $p < .001$) but this was found in the baseline model only, with the exception of processing speed, NART and WTAR. The association with processing speed was attenuated with the addition of age 11 IQ then declined to non-significant levels when social class was included (models 2 and 4). The association with NART and WTAR scores, however, not only retained significance when controlling for age 11 IQ but survived full adjustment for all covariates ($p = .007$ and $p = .02$, respectively). Additional adjustment for years of full-time education further attenuated this association but did not remove it ($p = .02$, $\eta_p^2 = .006$; $p = .04$, $\eta_p^2 = .005$, respectively). Education correlates strongly with age 11 IQ in this sample (.382, $p < .001$) and explains less of the variance in age 70 IQ than age 11 IQ. For this reason, we do not present the results using education as a confounder. Caffeine from total coffee (a measure often used in the literature) had a significant, positive association with all age 70 cognitive measures using the base model ($p < .001$). Unlike caffeine derived from ground coffee only, the associations between this combination coffee measure and all five cognitive outcome variables, remained significant when controlling for social class. However, these associations were either attenuated (processing speed, NART) or declined to non-significance once age 11 IQ scores are included in the model. None of the associations survive the fully adjusted model.

DISCUSSION

The results provide limited support for a positive effect of caffeine consumption on cognition in later life. There are three main results of interest. First, after adjustment for childhood IQ, most of the ‘protective’ effects of caffeine on cognition are removed. Previous studies reporting beneficial effects of caffeine (or coffee) consumption on cognitive function in old

age have been unable to control for prior ability. IQ is relatively stable over time (47, 48). In this sample, the correlation between age 11 and age 70 IQ is .66 ($p < .001$), supporting the assertion that childhood IQ accounts for the majority of variance in later life cognition. The remaining variance is accounted for by factors other than caffeine intake. With full adjustments for age, sex, social class and age 11 IQ, we found no protective effects of caffeine consumption on performance on memory, speed of information processing or general cognition component scores and on the MHT (a general intelligence test) at age 70.

Second, the only indication that caffeine consumption exerts a protective influence on cognitive performance was that drinkers of ground (filter and espresso type-) coffee performed better on tests of verbal intelligence (NART and WTAR) than non drinkers of ground coffee even when controlling for age 11 IQ and social class. Performance on these tests is widely assumed to reflect prior cognitive ability and level of education. Indeed, highly significant, positive correlations exist between age 11 IQ and NART and WTAR scores (.66, $p < .001$; .64, $p < .001$ respectively) in this population. For this reason, it was initially surprising that there remained a beneficial effect of ground coffee intake on performance on these tests, once age 11 IQ has been controlled for. However, NART and WTAR are thought to capture peak prior adult cognitive ability. Perhaps the association between ground/espresso coffee drinking and NART and WTAR is still significant after adjusting for age 11 IQ because they capture variance related to intellectual development and its associated education and lifestyle choices between childhood and adulthood.

Third, even before controlling for age 11 IQ, no gender effects were found, contrary to previous studies. Many have reported effects of caffeine on cognition in women, but not men. However, patterns of consumption differ widely as a result of cultural habits. Much of the caffeine research reporting gender effects comes from cohorts in the Netherlands and Finland which are known for being heavy caffeine (predominantly coffee) consumers with an average daily caffeine intake of 400mg per day in both men and women (49). The results of these

studies may not be generalisable to the UK where survey data reveals average consumption to be a more moderate 240mg a day. The Bristol Dietary Caffeine and Health Study surveyed 5870 British adults and found that caffeine intakes were significantly higher in men (263mg/day) than in women (226mg/day) (50). However, in the present study, the average age was older at 70. Mean daily caffeine intake was lower (182mg per day) than the UK average and comparable in men and women. This is not surprising given that caffeine (especially coffee) intake decreases with age, especially after about 65. Coffee has significantly higher concentrations of caffeine and more stimulating effects than tea. Since there is a greater sensitivity to the effects of caffeine in older people, tea may become the beverage of choice. Perhaps any prior difference in caffeine consumption (and its effects) by gender disappears with increasing age. It is nevertheless surprising that, given the very narrow age range in this cohort (all born in 1936), there was a (non-significant) trend for the high caffeine consumers to be younger than both medium and low caffeine consumers.

Throughout the models, there was a general trend for individuals who drink more coffee and less tea to have better cognitive health at age 70, but these effects were not borne out statistically by our analyses. Previous studies have attributed the opposing effects of tea and coffee on health outcomes, either to differing ‘pharmacological’ effects of tea and coffee or to lifestyle or socio-economic differences between the consumers of these beverages (51, 52). In Scotland, research suggests that coffee drinking is associated with higher socio-economic status (SES) and good health whereas drinking tea is associated with lower SES and poorer health outcomes (53). The present study supports (in part) these research findings; in the LBC1936, tea consumption was higher in the ‘lower’ social classes whereas those who drink coffee were more likely to belong to the ‘higher’ social classes. However, the more important confounder in this study was age 11 IQ (with some contribution from social class). The results of the general linear models suggest that it is age 11 IQ which is driving most of the associations with performance on cognitive tasks at age 70. Individuals with a high childhood IQ at age 11 were more likely to continue to perform better into adulthood than those with a

lower age 11 IQ irrespective of their caffeine intake. Age 11 IQ was also predictive of tea or total coffee intake in late life; higher IQ children were more likely to drink coffee, while poorer performance on the age 11 test was linked with a preference for tea some 60 years later. These findings suggest a bidirectional relationship between type of caffeine intake and IQ.

We conducted a post-hoc mediational analysis (Sobel test), in order to examine the extent to which the age 11 IQ and coffee intake at age 70 association is mediated by social class. The standardized beta of the direct path (age 11 IQ-ground coffee consumption) was 0.132, and 0.054 after social class was introduced as a mediator. The amount of the relationship between age 11 IQ and ground coffee consumption, accounted for by social class as a mediator, was .08; this represents 59.1% of the direct effect ($z = 5.27, p < .001$). Rather than suggesting a causal link between early life ability and adult tea or coffee preference, the results may reflect the fact that those individuals with a higher childhood IQ are more likely to achieve a higher SES and may, therefore, be more represented in social groups that choose to follow a lifestyle which is more 'cosmopolitan'. This would be reflected in social and dietary preferences. Coffee drinking, in the UK, is associated with an urban lifestyle among both young and older educated individuals. Therefore, the association between adult cognitive ability and tea and coffee consumption may simply be reflecting lifestyle preferences which vary with IQ/SES.

Further support for this alternative explanation may arise from the finding that caffeine consumption in our cohort was associated with a range of health outcomes also associated with cognitive decline. We found less evidence of markers of ill health in the high caffeine group than the low caffeine group. Men and women with the highest consumption of caffeine were less likely to have ever had diabetes, high blood pressure and high cholesterol than those drinking less caffeine. This contradicts prevailing medical opinion that caffeine has adverse effects on health but supports, to a certain extent, the findings of the Scottish Heart Health

Study (53); they reported that in Scotland, coffee drinking was associated with a reduction in coronary risk factors, coronary risk and mortality and the converse was true of tea.

One of the advantages of this study is that we have used a uniformly older cohort who share the same year of birth. We were able to control for a range of demographic variables which have previously been related to caffeine intake. Second, we were able to investigate the effects of drinking different types of coffees as well as measuring total caffeine consumption from a wide variety of dietary sources, not just tea and coffee. Third, using general cognitive factors (extracted from the large cognitive test battery), we were able to investigate the effects of caffeine on different aspects of cognitive function. Fourth, we had a measure of childhood IQ. There will be opportunities for follow-ups of this cohort offering the potential to investigate caffeine's effects on cognitive decline.

Selective attrition could have contributed to a healthy survivor effect. One potential limitation of the study is that the sample represents a healthy and high functioning sub-group of the Scottish Mental Survey 1947 cohort. Our sample achieved higher mean age 11 IQ scores ($m = 50.02$, $sd = 11.04$) than the original cohort ($m = 36.74$, $sd = 16.10$) and this may have restricted the range of cognitive outcome scores. That said, the range of age 11 IQ scores in the sample was large. The most likely result of this is some small underestimation of effects sizes of the associations. Further limitations of the study concern the measurement of caffeine. FFQ responses reflect the previous 2-3 month period only. Current intake was assumed to be representative of habitual intake as diet (including tea and coffee consumption) is likely to remain stable over time (barring illness, of course). Even so, we cannot exclude the possibility that some people may have significantly altered their caffeine intake following a diagnosis or period of bad health. Medical advice often dictates that coffee intake should be kept to a minimum, especially in the presence of high blood pressure and vascular problems.

Caffeine levels in this study are estimations only, based on the best available government survey data and are not comparable to the experimental caffeine studies which are laboratory based. Using estimated measures of caffeine content in drinks is problematic. Caffeine intake estimates may be limited by the high variability in caffeine composition of foods and beverages. In theory, ground coffee has a higher caffeine content than instant coffee and making this distinction during data collection is important. However, a weak ground coffee may be equivalent in caffeine strength to a strong instant coffee. The effects found in this Scottish sample may not be generalizable to other populations. Tea drinking is the norm in the UK where there is a higher annual per capita tea consumption than any other country. Even by today's standards, drinking filter and espresso coffee is associated with an educated, middle class lifestyle. In many other countries, consumption of strong, ground coffee is ubiquitous and independent of social position. Although coffee drinking in the UK is associated with SES, the mediation analysis, which found that childhood IQ explains more of the variance in adult cognitive ability than social class, provides a clear locus in the present study's findings where there are implications beyond the UK setting.

CONCLUSIONS

The present study provides little evidence that caffeine consumption has protective effects on cognitive function at age 70. It would appear that childhood IQ and other factors including social class, rather than caffeine intake, are driving the association with later life cognition. This study places childhood IQ and social class firmly within the framework of the diet-cognition relationship and raises doubts about the hypothesized causal effects of long-term caffeine consumption as a protective factor against cognitive decline in later life. However, there may be some residual benefit of drinking ground coffee (typically the stronger types of coffee often consumed in cafes and restaurants) on verbal IQ, irrespective of prior ability. While these associations are interesting, the contribution of caffeine is very small in relation to other intervening factors. Before advocating the benefits of coffee on cognitive health and

general well-being, further research is needed to fully understand the nature of these associations and rule out chance confounding by other factors.

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TABLE 1. Characteristics of the study population by category of daily caffeine consumption (mean values and % prevalence)

	Total sample		Low caffeine		Medium caffeine		High caffeine		
	N = 923*		N = 302		N = 303		N = 302		
	Mean	sd	Mean	sd	Mean	sd	Mean	sd	<i>p</i>
Caffeine (mg/day)	182.5	97.8	85.5	34.3	175.0	22.8	287.2	81.1	
Age (in years)	69.5	0.84	69.6	0.83	69.5	0.85	69.4	0.84	.30
Sex									.24
Male (%)	48.3		51.0		50.2		44.7		
Female (%)	51.7		49.0		49.8		55.3		
Marital status									.10
Married (%)	72.4		67.9		72.3		77.2		
Widowed (%)	13.3		14.9		14.1		10.9		
Unmarried/divorced (%)	14.2		16.9		13.5		11.8		
Education (yrs f/t)	10.8	1.2	10.7	1.1	10.8	1.1	10.9	1.3	.10
MMSE	28.9	1.2	28.8	1.3	29	1.2	29	1.2	.18
Alcohol consumption (units/wk)	10.6	14.3	11.6	18.2	9.9	12.2	10.1	11.4	.27
Body Mass Index (kg/m ²)	27.6	4.3	28.1	4.1	27.4	4.1	27.4	4.5	.08
Physical activity (days/mth)	7.5	8.0	7.0	7.6	8.0	8.2	7.7	8.3	.33
Smoking status									.29
Non-smokers (%)	44.4		43.0		47.5		42.1		
Ex-smokers (%)	43.2		47.0		40.6		43.0		
Current smokers (%)	12.4		9.9		11.9		14.9		
Hypertension, yes (%)	39.5		47.0		38.6		33.1		.002
Diabetes, yes (%)	7.5		11.3		6.3		5.0		.008
Cholesterol, yes (%)	35.1		39.7		35.8		29.5		.03

*Full study sample comprises 923 men and women. Due to some missing caffeine data, 16 subjects have no total caffeine measure and therefore not included in the tertiles of consumption

Abbreviations: sd, standard deviation; MMSE, Mini-Mental State Examination

p values are from t-tests, ANOVA and chi-square tests as appropriate

TABLE 2. Caffeine consumption in men and women (median values, ranges and p values) and correlations with age 11 IQ and social class

	Total sample		Men		Women		Age 11 IQ		Social class			
	N = 923		N = 446		N = 477							
							Mann-Whitney	Spearman rho	Spearman rho			
							U					
Caffeine (mg per day)	Median (range)	%	Median (range)	%	Median (range)	%	<i>U</i>	(<i>p</i>)	<i>r_s</i>	(<i>p</i>)	<i>r_s</i>	(<i>p</i>)
		reporting		reporting		reporting						
Total caffeine (all sources)*	177.5 (0-701.1)		175.7 (1.2-563.2)		178.1 (7.0-701.1)		97406.5	(.18)	.053	(.12)	-.098	(.003)
Caffeine from tea (regular)	85.5 (0-256.5)	85.5	85.5 (0-256.5)	87.6	85.5 (0-256.5)	83.4	103064.5	(.47)	-.113	(.001)	.067	(.04)
Caffeine from instant coffee	43.7 (0-327.8)	72.0	43.7 (0-327.8)	75.2	31.0 (0-327.8)	68.8	98315.5	(.08)	.034	(.32)	.042	(.21)
Caffeine from ground coffee	0 (0-698.3)	49.0	0 (0-465.5)	44.6	6.5 (0-698.3)	52.6	97022.0	(.01)	.236	(<.001)	-.277	(<.001)
Total caffeine from coffee	50.2 (0-698.3)		50.2 (0-465.5)		50.2 (0-698.3)		104849.0	(.92)	.159	(<.001)	-.154	(<.001)

* Due to some missing caffeine data, 16 subjects have no total caffeine measure

TABLE 3. Associations between caffeine intake and cognitive outcomes. General linear models, p values and associated partial eta squared values

Model 1: sex + age; Model 2: sex + age + social class; Model 3: sex + age + age 11 IQ; Model 4: sex + age + age 11 IQ + social class

Predictor		*Age 70 IQ		g factor		processing speed		memory		NART		WTAR	
		N = 919		N = 909		N = 887		N = 893		N = 923		N = 923	
mg per day	Model	<i>p</i>	η_p^2	<i>p</i>	η_p^2	<i>p</i>	η_p^2	<i>p</i>	η_p^2	<i>p</i>	η_p^2	<i>p</i>	η_p^2
Total caffeine	1	.03^a	.005	.05	.004	.27	.001	.02^a	.007	.01^a	.007	.02^a	.006
(all sources)	2	.35	.001	.47	.000	.93	.000	.13	.003	.29	.001	.33	.001
	3	.04^a	.005	.14	.003	.36	.001	.05	.004	.02^a	.007	.02^a	.006
	4	.12	.003	.44	.000	.90	.000	.11	.003	.14	.003	.16	.002
Caffeine from	1	<.001^b	.012	<.001^b	.014	.001^b	.013	.20	.002	.002^b	.011	.007^b	.008
tea	2	.006^b	.008	.003^b	.010	.002^b	.011	.39	.000	.01^b	.007	.03^b	.005
	3	.62	.000	.26	.001	.08	.004	.37	.000	.68	.000	.97	.000
	4	.74	.000	.30	.001	.06	.004	.38	.000	.70	.000	.99	.000
Caffeine from	1	.07	.004	.30	.001	.16	.002	.29	.001	.94	.000	.98	.000
instant coffee	2	.06	.004	.25	.002	.21	.002	.28	.001	.80	.000	.93	.000

	3	.19	.002	.78	.000	.34	.001	.75	.000	.31	.001	.25	.002
	4	.21	.002	.72	.000	.39	.001	.73	.000	.42	.000	.29	.001
<hr/>													
Caffeine from	1	<.001^a	.014	<.001^a	.017	<.001^a	.001	<.001^a	.014	<.001^a	.033	<.001^a	.028
ground coffee	2	.15	.002	.08	.003	.06	.004	.05	.004	.002^a	.011	.005^a	.009
	3	.20	.002	.05	.004	.03^a	.006	.11	.003	<.001^a	.018	<.001^a	.014
	4	.49	.000	.38	.000	.16	.002	.25	.002	.007^a	.008	.02^a	.007
<hr/>													
Total caffeine	1	<.001^a	.018	<.001^a	.016	<.001^a	.015	<.001^a	.014	<.001^a	.021	<.001^a	.017
from coffee	2	.01^a	.007	.03^a	.005	.02^a	.006	.02^a	.006	.008^a	.008	.02^a	.006
	3	.05	.004	.08	.003	.02^a	.007	.14	.003	.01^a	.007	.05	.004
	4	.15	.002	.34	.001	.09	.004	.24	.002	.12	.003	.26	.002

*Age 70 IQ is already age-adjusted (age not included in the models for this outcome variable)

^a denotes a positive model correlation coefficient

^b denotes a negative model correlation coefficient