Coffee Consumption and Cognitive Function among Older Adults

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This study examined the association of caffeinated and decaffeinated coffee intake with cognitive function in a community-based sample of older adults in 1988–1992. Participants were 890 women with a mean age of 72.6 years and 638 men with a mean age of 73.3 years from the Rancho Bernardo Study. Cognitive function was assessed by 12 standardized tests, and lifetime consumption and current coffee consumption were obtained by questionnaire. After adjustment for confounders, higher lifetime coffee consumption in women was associated with better (p ≤ 0.05) performance on six of 12 tests, with a trend (p ≤ 0.10) on two other cognitive function tests; current caffeinated coffee intake was associated with better performance on two tests (p < 0.05), with a trend (p < 0.10) on one other test. Among women aged 80 or more years, lifetime coffee intake was nonsignificantly associated with better performance on 11 of the 12 tests. No relation was found between coffee intake and cognitive function among men or between decaffeinated coffee intake and cognitive function in either sex. Lifetime and current exposure to caffeine may be associated with better cognitive performance among women, especially among those aged 80 or more years.

Caffeine is the most widely used psychoactive drug worldwide (1). Coffee is the main source of caffeine in the Western diet; most US adults regularly consume coffee (1, 2). As a mild stimulant, caffeine increases the activity of the central nervous system, resulting in heightened alertness and arousal (1). Results from previous studies of the effect of caffeine on cognition have been inconsistent (3–15), indicating that caffeine may have either a facilitative or a detrimental effect on cognition (16) and that the effect of caffeine may be task specific.

In some studies, caffeine has been shown to improve performance on cognitive tasks requiring speed or vigilance (3, 4). It has also been shown to improve complex, higher cognitive functions, including memory (5, 8–11). Caffeine is a methylxanthine, blocking adenosine receptors in the brain, resulting in cholinergic stimulation. It is hypothesized that cholinergic stimulation improves memory (13). In one study, caffeine reversed the memory-impairing effects of scopolamine, a drug that blocks the neurotransmitter acetylcholine (13). Performance on memory tasks improved but reaction time did not, suggesting that caffeine acted as a cognition enhancer in the presence of cholinergic dysfunction and not merely as a central nervous system stimulant.

In the only large, population-based study of the effects of habitual coffee consumption on cognition, Jarvis (17) surveyed 9,003 British adults. A significant, positive trend between coffee intake and cognitive performance was found. Additionally, an age-by-coffee interaction indicated that greater improvement in cognitive performance occurred among the oldest men and women. On the basis of the research by Jarvis (17), Reidel and Jolles (18) hypothesized that caffeine has a supplementary effect, improving memory only when cholinergic function is impaired by aging or disease.

Cognitive decline is age related. Reaction time, perceptual speed, and processing speed remain relatively stable from age 20 to age 60, while a general slowing in cognitive function occurs between the ages of 60 and 80 years (19). It is therefore plausible that caffeine intake may have a protective effect on the cognitive decline associated with aging (13, 18). The present study investigates the relation of lifetime coffee consumption and current caffeinated and current decaffeinated coffee consumption with performance on several cognitive function tests in a community-based sample of men and women aged 50 years or older.
MATERIALS AND METHODS

Participants

Between 1972 and 1974, 82 percent of the residents of Rancho Bernardo, a middle-class, predominantly Caucasian, southern California community, were enrolled in a study of heart disease risk factors. Eighty percent of the surviving men \( (n = 638) \) and women \( (n = 890) \) attended a follow-up clinic visit between 1988 and 1992, when they were interviewed, were administered tests of cognitive function, and completed the Willett Semiquantitative Food Frequency Questionnaire (20). In 1992, 69 percent of the surviving cohort men \( (n = 451) \) and women \( (n = 687) \) completed a mailed survey about their history of coffee consumption. This report includes all men and women aged 50 or more years at the 1988–1992 follow-up visit for whom interview data, measures of cognitive function, and coffee-drinking history were available. Twenty individuals with Parkinson’s disease were excluded from these analyses. All were ambulatory and gave written, informed consent. The study was approved by the Committee on Investigations Involving Human Subjects at the University of California at San Diego.

Procedures

At the 1988–1992 follow-up visit, participants came into the clinic after an overnight fast of 12–16 hours. A standardized interview assessed demographic data, cigarette smoking, alcohol consumption, and history of stroke, Parkinson’s disease, heart attack, or estrogen use (in women). Medication use, including estrogen replacement therapy, was validated by examination of prescriptions or pills brought to the clinic for that purpose. Diet was assessed with a self-administered food frequency questionnaire. Finally, 12 measures of cognitive function were administered individually by trained personnel. All cognitive tests had demonstrated adequate reliability and validity (21, 22).

Cognitive tests. The Buschke-Fuld Selective Reminding Test (23) assesses short- and long-term storage and retrieval of spoken words. Ten unrelated words are read to participants at a rate of one every 2 seconds. Immediately after, the participant is asked to recall the entire list. This procedure is followed for six trials. Measures of long- and short-term memory and of total recall are obtained. Higher scores on the short-term memory test indicate poorer performance.

The Heaton Visual Reproduction Test (24), adapted from the Wechsler Memory Scale (25), assesses memory for geometric forms. Three stimuli of increasing complexity are presented one at a time, for 10 seconds each. The participant is asked to reproduce the figures immediately to assess short-term memory and after 30 minutes of unrelated testing to assess long-term memory for geometric forms. After both memory trials are completed, the participant copies the stimulus figures to account for any existing visuospatial impairments. Three scores are obtained: immediate recall, delayed recall, and copying.

The Mini-Mental State Examination (26, 27) assesses orientation, registration, attention, calculation, language, and recall. Total Mini-Mental State Examination scores range from 0 to 30. Two items were analyzed separately: counting backward from 100 by sevens (Serial 7’s), which assesses calculation, and spelling the word “world” backward (“World” Backwards), which assesses attention. For either item, the maximum possible score is 5.

Two items from the information-memory-concentration test of Blessed et al. (21) (Blessed Items) assess concentration by having the participant name the months of the year backward and assess memory by asking participants to recall a five-part name and address following a 10-minute delay. The maximum possible score across the two items is 7.

The Trail-Making Test, part B, from the Halstead-Reitan Neuropsychological Test Battery (28), tests visuomotor tracking and attention. The participant scans a page continuously to identify numbers and letters in a specified sequence while shifting from number to letter sets. A maximum of 300 seconds is given; scoring is the time taken to finish the test. A higher score indicates a poorer test performance.

Category fluency (29) is assessed by naming as many animals as possible in 1 minute. The score is the number of animals named correctly.

Coffee intake. The Willett Semiquantitative Food Frequency Questionnaire (20) is self-administered and was used to assess dietary intake. It contains two items assessing caffeinated and decaffeinated coffee intake during the past year and served as the measure of current coffee intake. A 1-cup (237-ml) quantity was specified on the questionnaire, and participants marked one of nine responses to indicate their frequency of consumption. Each of the nine responses, along with the associated cups per day, was as follows: never or less than once per month, 0; 1–3 per month, 0.08; 1 per week, 0.14; 2–4 per week, 0.43; 5 or 6 per week, 0.8; 1 per day, 1; 2 or 3 per day, 2.5; 4 or 5 per day, 4.5; and 6 or more per day, 6. Values for the cups per day were converted to cups per week by multiplying by 7 and were then divided into quintiles. Regular, current drinkers of caffeinated and decaffeinated coffee were defined as thosedrinking at least 1 cup of coffee per month. Consumptions of tea, cola, and chocolate were also queried on the questionnaire and analyzed as additional sources of caffeine for current coffee consumption. The Willett Semiquantitative Food Frequency Questionnaire has demonstrated reliability and validity (20).

The mailed survey in 1992 assessed lifetime coffee intake in terms of years of use and usual number of cups per day of caffeinated and decaffeinated coffee intake. The term, “years of use,” was used to assess the answer to the open-ended question, “How many years in total did you drink caffeinated or decaffeinated coffee daily?” The term, “usual number of cups per day,” was used to assess the answer to the open-ended question, “How many cups per day did you usually drink?” Lifetime cup-years were calculated as the usual number of cups of caffeinated coffee reported per day multiplied by the number of years of caffeinated coffee use. Cup-years were then divided into quintiles of cup-years; those who reported never drinking caffeinated coffee were included in the lowest quintile. Regular lifetime drinkers of caffeinated coffee were defined as having drunk at least 1 cup of caffeinated coffee for at least 1 year.

**Statistical analysis**

Men and women were examined in separate analyses because they differed in both coffee consumption patterns and cognitive abilities. Analyses of current coffee consumption were based on exclusive drinkers of decaffeinated or caffeinated coffee as appropriate. All cognitive function tests were scaled so that higher scores indicated better cognitive performance. The Buschke-Fuld Selective Reminding Short-Term Recall Test and the Trail-Making Test, part B, were reverse scored. Age was categorized into four groups (ages 50–59, 60–69, 70–79, and ≥80 years) to investigate the relation between coffee intake and cognitive performance as a function of age. In these analyses, cognitive function was linearly transformed to z scores. For current coffee consumption analyses, analyses were performed by coffee intake alone and by coffee with additional sources of caffeine, including tea, cola, and chocolate.

Age-adjusted comparisons of covariates by quintiles of lifetime and current caffeinated coffee intake were performed with analysis of covariance. Because cognitive function may be positively related to intelligence (30), education (1 year of college vs. less than 1 year of college) served as an indicator of intelligence and was assessed as a potential confounder along with age in regression models. A variable was identified as a confounder if its removal from the regression model resulted in a change in the beta weight of 10 percent or greater for coffee consumption. Using this criterion, a third confounder for men was the use of antihypertensive or diuretic medications, and for women, a third confounder was ever use of estrogen replacement therapy.

Other variables were evaluated and excluded as confounders, including depression (as assessed by the Beck Depression Inventory (31)), current body mass index (weight (kg)/height (m)2), current employment (yes vs. no), most recent job status (professional vs. nonprofessional), alcohol use (at least 3–4 drinks per week vs. 1–2 drinks per week or less), use of cholesterol-lowering drugs (yes vs. no), current use of estrogen replacement therapy (yes vs. no), and history of heart attack or stroke (yes vs. no). Lifetime and current coffee consumptions were entered as continuous variables in regression analyses. It was not possible to determine whether lifetime consumption of decaffeinated coffee was associated with cognitive performance, because only 23 men and 29 women reported drinking decaffeinated coffee exclusively during their lifetime.

The Statistical Analysis System, version 6.12 for Windows, 1996 (SAS Institute, Inc., Cary, North Carolina), was used for all analyses. An alpha level of 0.05 was considered statistically significant, and all statistical tests were two tailed. Because analyses were exploratory, no adjustment was made for multiple comparisons, and p values between 0.05 and 0.10 were considered as a trend toward significance.

**RESULTS**

**Sample characteristics**

At the 1988–1992 clinic visit, men were aged 52–94 years with an average age of 73.3 (standard deviation, 9) years; women were aged 50–98 years with an average age of 72.6 (standard deviation, 9) years. Most men (82 percent) and women (65 percent) had completed at least 1 year of college. Thirty-seven percent of men reported the use of antihypertensive or diuretic medications, and 76 percent of women reported ever use of estrogen replacement therapy.

**Coffee-drinking history**

Most men (90 percent) and women (86 percent) reported regular use of caffeinated coffee at some time in their lives. The average number of cup-years of caffeinated coffee consumed by men was significantly greater than the amount consumed by women (means, 153.8 vs. 118.7 cup-years, respectively); these results were unchanged after adjustment by body mass index (adjusted means, 151.6 vs. 120.3 cup-years, respectively) (table 1). The number of years that men and women drank coffee on a regular basis increased with age and ranged from 38 to 51 years in men and from 29 to 51 years in women.

Men started drinking coffee at about 20 years of age and drank an average of 3.4 cups a day for 45 years, while women started drinking coffee at age 22 years and drank an average of 2.7 cups a day for 43 years. Differences in the pattern of coffee consumption by birth cohort were also observed in men and women. Men in the oldest birth cohort, who were born about 1900, reported drinking only 2.5 cups of coffee per day each across their lifetimes. By contrast, men aged 50–59 years, who were born about 1930, reported drinking 5.2 cups per day each across their lifetimes. This twofold decrease in lifetime cups per day by age accounted for the birth cohort on cup-years’ interaction observed in men. The difference in cups per day among women by birth cohort was less striking, and cup-years did not differ across age groups for women.

There were 180 men and 233 women who were current, exclusive drinkers of caffeinated coffee and 172 men and 253 women who were current, exclusive drinkers of decaffeinated coffee. Current consumption among exclusive drinkers of caffeinated coffee decreased as a function of age for both men and women. Women, but not men, also decreased their consumption of decaffeinated coffee with age.

**Age-adjusted covariate distributions by quintile of coffee consumption**

The age-adjusted distributions of covariates by quintile of lifetime and current caffeinated coffee consumption of women and men are shown in table 2. The proportion of women who reported ever use of estrogen replacement therapy decreased with increasing lifetime coffee intake. For men, use of antihypertensive drugs decreased with increasing quintile of current coffee intake.

**Multiply adjusted cognitive function scores by quintile of coffee consumption**

For women, after adjusting for age, education, and ever use of estrogen, there were positive associations (p ≤ 0.05) between lifetime coffee consumption and better scores on...
the Buschke-Fuld Selective Reminding Total Recall, Long-Term Recall, and Short-Term Recall tests, the Heaton Visual Reproduction Delayed Recall Test, the Mini-Mental State Examination, and the Category Fluency Test (table 3). There was also a trend toward higher scores on the Heaton Visual Examination, and the Category Fluency Test (table 3). There was no association between current intake of decaffeinated coffee and any cognitive function test among women.

For men, after adjustment for age, education, and the use of antihypertensive drugs, poorer scores on “World” Backwards were associated with greater current caffeinated coffee consumption ($\beta = -0.158, p = 0.015$). The Trail-Making Test, part B, was positively associated with current decaffeinated coffee intake ($\beta = 0.131, p = 0.016$). No other tests were significantly associated with current or lifetime caffeinated or decaffeinated coffee intake among men (data not shown).

Performance on each cognitive function test, expressed as $z$ scores, by lifetime coffee quintile is shown in figure 1 for women aged 80 or more years ($n = 142$). To minimize fluctuations due to small sample sizes, only $z$ scores at the lowest and highest quintile levels are graphed, with lines interpolated between the two graphed points. On all tests but the

**TABLE 1. Mean lifetime and current caffeinated coffee-drinking behavior by age and gender among regular drinkers* of coffee, Rancho Bernardo, California, 1988–1992**

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>50–59</th>
<th>60–69</th>
<th>70–79</th>
<th>≥80</th>
<th>$p$ value†</th>
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<td><strong>Men</strong></td>
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<tr>
<td>Lifetime caffeinated coffee consumption‡‡</td>
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<tr>
<td>Years of coffee drinking</td>
<td>44.6 (17.3)$§$</td>
<td>37.7 (13.0)</td>
<td>41.1 (14.3)</td>
<td>46.0 (16.4)</td>
<td>50.9 (21.1)</td>
<td>0.001</td>
</tr>
<tr>
<td>Typical cups per day</td>
<td>3.4 (2.4)</td>
<td>5.2 (3.5)</td>
<td>3.6 (2.3)</td>
<td>3.2 (2.3)</td>
<td>2.5 (1.6)</td>
<td>0.001</td>
</tr>
<tr>
<td>Cup-years¶¶</td>
<td>153.8 (121.8)</td>
<td>209.5 (171.3)</td>
<td>153.8 (116.1)</td>
<td>147.4 (108.3)</td>
<td>136.2 (111.9)</td>
<td>0.001</td>
</tr>
<tr>
<td>Current caffeinated coffee consumption#, **</td>
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<tr>
<td>Cups per week</td>
<td>16.1 (11.1)</td>
<td>19.6 (12.1)</td>
<td>17.6 (11.7)</td>
<td>15.6 (11.0)</td>
<td>12.8 (9.2)</td>
<td>0.004</td>
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<tr>
<td>Current decaffeinated coffee consumption††, †‡</td>
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<tr>
<td>Cups per week</td>
<td>9.9 (8.6)</td>
<td>14.2 (14.7)</td>
<td>7.4 (6.6)</td>
<td>10.5 (8.6)</td>
<td>10.2 (8.7)</td>
<td>0.639</td>
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<td><strong>Women</strong></td>
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<tr>
<td>Lifetime caffeinated coffee consumption§§</td>
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<tr>
<td>Years of coffee drinking</td>
<td>42.7 (17.7)</td>
<td>29.1 (11.5)</td>
<td>39.2 (14.1)</td>
<td>45.2 (17.1)</td>
<td>51.0 (20.5)</td>
<td>0.001</td>
</tr>
<tr>
<td>Typical cups per day</td>
<td>2.7 (1.8)</td>
<td>3.5 (2.6)</td>
<td>2.9 (1.7)</td>
<td>2.5 (1.5)</td>
<td>2.5 (1.6)</td>
<td>0.001</td>
</tr>
<tr>
<td>Cup-years¶¶</td>
<td>118.7 (93.1)</td>
<td>110.0 (110.3)</td>
<td>118.9 (92.7)</td>
<td>114.3 (84.2)</td>
<td>129.9 (97.1)</td>
<td>0.227</td>
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<tr>
<td>Current caffeinated coffee consumption¶¶</td>
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<tr>
<td>Cups per week</td>
<td>13.7 (10.1)</td>
<td>16.9 (11.6)</td>
<td>15.6 (10.1)</td>
<td>12.6 (10.1)</td>
<td>11.4 (8.6)</td>
<td>0.004</td>
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<tr>
<td>Current decaffeinated coffee consumption##</td>
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<tr>
<td>Cups per week</td>
<td>11.2 (9.5)</td>
<td>16.9 (11.2)</td>
<td>12.4 (10.2)</td>
<td>11.2 (8.3)</td>
<td>8.7 (9.3)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

* Regular lifetime drinkers of caffeinated coffee are defined as having ever drunk 1 cup of coffee daily for 1 year. Regular current drinkers of coffee are defined as those drinking 1 or more cups per month. (One cup = 237 ml.)
† Linear trend across four age groups.
‡ Total ($n = 367$); 50–59 years ($n = 42$); 60–69 years ($n = 122$); 70–79 years ($n = 111$); ≥80 years ($n = 92$).
§ Numbers in parentheses, standard deviation.
¶ Cup-years = (years of coffee drinking × typical cups per day).
# Drinkers of decaffeinated coffee exclusively.
** Total ($n = 180$); 50–59 years ($n = 27$); 60–69 years ($n = 60$); 70–79 years ($n = 44$); ≥80 years ($n = 49$).
†† Drinkers of decaffeinated coffee exclusively.
‡‡ Total ($n = 172$); 50–59 years ($n = 7$); 60–69 years ($n = 34$); 70–79 years ($n = 61$); ≥80 years ($n = 70$).
§§ Total ($n = 516$); 50–59 years ($n = 60$); 60–69 years ($n = 165$); 70–79 years ($n = 177$); ≥80 years ($n = 114$).
¶¶ Total ($n = 233$); 50–59 years ($n = 30$); 60–69 years ($n = 62$); 70–79 years ($n = 94$); ≥80 years ($n = 47$).
## Total ($n = 253$); 50–59 years ($n = 21$); 60–69 years ($n = 61$); 70–79 years ($n = 95$); ≥80 years ($n = 76$).
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### TABLE 2. Age-adjusted distribution of covariates by quintile of lifetime and current caffeinated coffee intake by gender, Rancho Bernardo, California, 1988–1992

<table>
<thead>
<tr>
<th>Quintiles of coffee consumption</th>
<th>Lowest quintile</th>
<th>Quintile 2</th>
<th>Quintile 3</th>
<th>Quintile 4</th>
<th>Highest quintile</th>
<th>p value*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Men</strong></td>
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</tr>
<tr>
<td><strong>Lifetime caffeinated coffee consumption†</strong></td>
<td>9.5 (0–39)</td>
<td>60.1 (40–82)</td>
<td>112.0 (83–138)</td>
<td>169.6 (139–209)</td>
<td>329.7 (210–720)</td>
<td>0.001</td>
</tr>
<tr>
<td>Cup-years (mean (range))</td>
<td>2.6 (0–19)</td>
<td>37.7 (20–59)</td>
<td>77.0 (60–99)</td>
<td>123.7 (100–161)</td>
<td>254.0 (162–684)</td>
<td>0.001</td>
</tr>
<tr>
<td>Age (years) (mean (standard error))</td>
<td>72.2 (1.08)</td>
<td>72.6 (0.99)</td>
<td>70.6 (0.93)</td>
<td>72.3 (1.03)</td>
<td>69.7 (0.93)</td>
<td>0.045</td>
</tr>
<tr>
<td>Education‡ (%)</td>
<td>81.6</td>
<td>82.1</td>
<td>85.9</td>
<td>81.9</td>
<td>79.0</td>
<td>0.590</td>
</tr>
<tr>
<td>Hypertension drugs (yes/no) (%)</td>
<td>30.6</td>
<td>37.2</td>
<td>37.3</td>
<td>33.0</td>
<td>44.1</td>
<td>0.192</td>
</tr>
<tr>
<td><strong>Current caffeinated coffee consumption§</strong></td>
<td>0 (0)</td>
<td>3.2 (0.6–5.6)</td>
<td>7 (7)</td>
<td>17.5 (17.5)</td>
<td>33.9 (31.5–42)</td>
<td>0.001</td>
</tr>
<tr>
<td>Cups per week (mean (range))</td>
<td>73.5 (1.17)</td>
<td>75.0 (1.55)</td>
<td>71.1 (1.40)</td>
<td>72.2 (1.23)</td>
<td>66.6 (1.32)</td>
<td>0.001</td>
</tr>
<tr>
<td>Education (%)</td>
<td>64.8</td>
<td>73.0</td>
<td>66.8</td>
<td>76.7</td>
<td>76.4</td>
<td>0.301</td>
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<tr>
<td>Hypertension drugs (yes/no) (%)</td>
<td>39.1</td>
<td>39.5</td>
<td>36.8</td>
<td>24.5</td>
<td>22.6</td>
<td>0.037</td>
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<tr>
<td><strong>Women</strong></td>
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<tr>
<td><strong>Lifetime caffeinated coffee consumption¶</strong></td>
<td>2.6 (0–19)</td>
<td>37.7 (20–59)</td>
<td>77.0 (60–99)</td>
<td>123.7 (100–161)</td>
<td>254.0 (162–684)</td>
<td>0.001</td>
</tr>
<tr>
<td>Cup-years (mean (range))</td>
<td>72.4 (0.97)</td>
<td>72.1 (1.36)</td>
<td>74.3 (1.02)</td>
<td>70.0 (0.95)</td>
<td>68.8 (1.72)</td>
<td>0.044</td>
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<tr>
<td>Age (years) (mean (standard error))</td>
<td>63.0</td>
<td>65.4</td>
<td>64.3</td>
<td>56.4</td>
<td>49.3</td>
<td>0.343</td>
</tr>
<tr>
<td>Education (yes/no) (%)</td>
<td>73.6</td>
<td>66.6</td>
<td>69.2</td>
<td>71.3</td>
<td>65.1</td>
<td>0.597</td>
</tr>
</tbody>
</table>

* Linear trend across five coffee consumption groups. (One cup = 237 ml.)
† Total (n = 408); lowest quintile (n = 78); quintile 2 (n = 85); quintile 3 (n = 82); quintile 4 (n = 77); highest quintile (n = 86).
‡ Education is dichotomized as at least 1 year of college versus less than 1 year of college.
§ Total (n = 249); lowest quintile (n = 69); quintile 2 (n = 73); quintile 3 (n = 40); highest quintile (n = 39).
¶ Total (n = 589); lowest quintile (n = 107); quintile 2 (n = 118); quintile 3 (n = 115); quintile 4 (n = 137); highest quintile (n = 121).
# Total (n = 345); lowest quintile (n = 73); quintile 2 (n = 45); quintile 3 (n = 82); quintile 4 (n = 84); highest quintile (n = 31).

Heaton Visual Reproduction Copying Test, there was a nonsignificant increase in cognitive function among the eldest members of the cohort as a function of lifetime coffee intake.

**DISCUSSION**

In this community-based sample, men drank more coffee across their lifetimes than did women, based on all the indices: years of coffee drinking, cups per day, and cups-years. Nevertheless, higher levels of lifetime and current caffeinated coffee intake were associated with better scores on several tests of cognitive performance in women but not in men. The trend was strongest for lifetime, as compared with current, coffee intake and among women aged 80 or more years. This observed coffee-cognitive function association was not explained by age, education, or estrogen replacement therapy in women. No effect for decaffeinated coffee intake was found. These findings are partially consistent with those of the population-based study of 9,003 British adults aged 18 years or more, conducted by Jarvis (17), which found a positive effect of caffeine on cognitive performance in both women and men. In the present study, caffeine was positively associated with cognitive performance in the oldest women. These results are consistent with those of the Jarvis study (17); when participants were stratified into three age groups (16–34, 35–54, and 55 or more years), the association of coffee intake with verbal memory, visuospatial reasoning, and reaction time increased with age.

The results of this study indicate that lifetime coffee intake among women may have differential effects, depending on the type of cognitive process involved. The majority of the cognitive function tests positively associated with coffee intake involved a verbal component (22). Although the cognitive function tests were interrelated, the tests shared less than 30 percent of their variance. Correlations between the tests, not including between subtests, ranged between 0.11 and 0.54. Additionally, differential effects of coffee on various cognitive tests may be due at least in part to differences in the psychometric properties of the tests. In the
present study, the “World” Backwards and Serial 7’s tests had a marked ceiling effect, and no significant association with coffee intake was found for these tests. Ninety-four percent of the women scored 5 of 5 points on “World” Backwards, and 75 percent of the women obtained one of the top two scores on the 6-point Serial 7’s test. The limited score variance decreased the likelihood of observing a coffee-cognition association. The remaining tests with adequate test score variance demonstrated at least marginally significant positive associations with lifetime coffee intake among women. The two tests (Heaton Visual Reproduction Copying Test and Trail-Making Test, part B) not significantly associated with lifetime caffeinated coffee intake involve, at least in part, visuomotor tracking (22).

It is biologically plausible that caffeine lessens age-related cognitive decline, in that a stronger effect of caffeine among older adults as compared with younger adults has been demonstrated previously (17, 32, 33). Alzheimer’s disease, a progressive disease associated with aging, involves deterioration of cholinergic neurons, resulting in decreasing levels of the neurotransmitter acetylcholine (34). Molchan et al. (35) demonstrated that older adults with an average age of 66 years were more susceptible to the memory-impairing effects of the anticholinergic drug scopolamine, as compared with younger adults with an average age of 27 years. Riedel et al. (13) reversed the effects of scopolamine through the administration of 250 mg of caffeine and concluded that caffeine has specific memory-enhancing properties, acts through cholinergic pathways, and may be a protective factor against age-associated memory deficits as well as dementia. Riedel and Jolles (18) suggested that caffeine may have a supplementary effect on cholinergic stimulation: Caffeine does not affect memory in younger adults when cholinergic function is optimal, but it may exert a positive effect on memory when cholinergic dysfunction is induced experimentally or occurs naturally because of aging.

The present study found stronger effects for lifetime as compared with current coffee intake. The pharmacologic effects of caffeine in the body are complex (36). Caffeine is a nonselective A1 and A2A adenosine receptor antagonist (36). While adenosine has sedative effects within the body, the antagonist properties of caffeine result in central nervous stimulation, and an effect of adenosine on memory and learning has been demonstrated (37). The chronic effects of caffeine, however, often differ markedly from its acute effects (36), although much of the cognitive-based research on the effect of caffeine has been oriented toward acute administration. Although many of the physiologic effects of acute caffeine administration are detrimental, chronic administration of caffeine is often protective (36). For example, chronic treatment with caffeine decreased susceptibility to ischemic brain damage in gerbils, while acute administration increased damage (38). Similar findings for the positive effect of chronic versus the negative effect of acute administration of caffeine on spatial memory and seizures in mice have also been demonstrated (36). Therefore, although caffeine ingested as coffee is readily and essentially completely absorbed from the gastrointestinal tract and peak levels of caffeine in body fluids are reached about an hour after ingestion, long-term intake of caffeine may result in significant adaptive changes in the brain (36).

Adenosinergic therapy has been proposed in the treatment of various neurodegenerative disorders, including Alzheimer’s (39) and Parkinson’s (40) diseases. A recent 30-year follow-up study of 8,000 Japanese-American men participating in the Honolulu Heart Program (41) suggests that cumu-
Relative coffee intake protects against Parkinson’s disease. Both Alzheimer’s and Parkinson’s diseases are neurodegenerative, and approximately 30 percent of Parkinson’s disease patients develop an Alzheimer’s-like dementia and 30 percent of Alzheimer’s patients develop Parkinson’s-like changes (42). That lifetime coffee intake was more strongly associated with cognitive function than was current coffee intake in the present study may also suggest that it is the cumulative exposure to caffeine that is protective against losses in cognitive function.

The differences found between men and women may be due to unmeasured confounding or the somewhat smaller sample size of men, or they may be real. Unmeasured confounding may mask a true effect among men or create an illusory finding among women. If the effect of chronic administration of caffeine on cognitive function is weak or if measurement of caffeine intake is poor, then the smaller sample size among men may result in nonsignificant findings. A real finding may indicate that women are more vulnerable to the effects of chronic administration of caffeine than are men. The elimination half-life of caffeine ranges between 3 and 7 hours; however, among women, elimination is 20–30 percent shorter because of more rapid biotransformation (1). Despite the differences in clearance, the levels of metabolites among men and women do not differ, however (1). Research by Carrillo and Benitez (43) indicates that, in healthy participants, women were more likely than men to experience acute toxic reactions, such as restlessness, palpitation, muscle tremor, and dizziness, after administration of high doses of caffeine compared with men. Thus, gender differences may be due to pharmacodynamic differences in sensitivity to caffeine effects between men and women. In another study, Relling et al. (44) found that healthy women had higher levels of xanthine oxidase activity as compared with men, after ingestion of equal amounts of caffeine (<23 mg), indicating that men and women metabolize caffeine differently. That coffee-cognition effects were found for women but not for men in the present study may also suggest that women are more susceptible to the

FIGURE 1. Cognitive function scores by quintile of lifetime coffee consumption for women aged 80 or more years (n = 142), Rancho Bernardo, California, 1988–1992. Quintiles are defined as Q1 = 0–19, Q2 = 20–59, Q3 = 60–99, Q4 = 100–161, and Q5 = 162–684 cup-years of lifetime coffee consumption.
cholinergic properties of caffeine than men are in older populations. A meta-analysis indicated that women are at 1.6 times higher risk of developing Alzheimer’s disease than men are (45). Another meta-analysis (46) suggested that women are more susceptible to Alzheimer’s disease regardless of their apolipoprotein genotype.

Several limitations of the present study were considered. This study is an observational field study; therefore, conclusions about the causal effect of caffeine on cognitive function are limited. Self-reported lifetime coffee intake may be inaccurate, and the resulting nondifferential misclassification bias (1) would obscure a true association. Because current coffee drinkers may have better cognitive function, they may have better recall on retrospective recalls, thus strengthening the results for current coffee intake. Lifetime assessment of coffee intake has unknown reliability and validity. However, self-reported habitual coffee intake has previously been shown to be reliable (47), and dietary assessment data have been found to be accurate to within 10–15 percent after 10–15 years (48). Although lifetime coffee intake was measured 1–4 years after cognitive testing, if caffeine has a cumulative effect, the hypothesized effect of caffeine on cognition would still be valid. If caffeine intake is associated with mortality, survival bias could eliminate from the sample those with the highest levels of coffee consumption. However, vital status did not differ by mean caffeine consumption (based on the Willett Semiquantitative Food Frequency Questionnaire (20)) after adjustment for age and cigarette smoking. Information bias may occur if those who responded to the mailed coffee survey differed from the total cohort. Post hoc, sex-specific comparisons among those who attended the 1988–1992 follow-up visit indicated that nonresponders of the coffee survey were on average 3–4 years older (p < 0.001) than the responders but did not differ in any other health or behavioral characteristics. The Rancho Bernardo cohort is relatively well educated; results of the present study of cognitive function may not generalize to less-educated populations. It was not possible to study the isolated effects of decaffeinated coffee, and no distinction between lifetime caffeinated coffee intake and overall caffeine consumption was made. However, Stavric (49) reports that the physiologic effects of caffeine are very closely associated with drinking coffee. Similarly, in the present study, intake of coffee had greater correlation (r = 0.96) with an overall measure of caffeine intake as assessed by the Willett Semiquantitative Food Frequency Questionnaire (20) than did other caffeine-containing food items such as tea, cola, and chocolate (r = 0.18, 0.08, and 0.02, respectively).

The results of this study suggest that coffee intake may be positively associated with cognitive performance among elderly women. This study also suggests that long-term follow-up studies should be conducted to examine the relation between cumulative and short-term coffee intakes and development of Alzheimer’s disease. The results of the present study should not, however, be used to promote increased coffee consumption, as some research indicates that coffee intake may be associated with increased risk of cardiovascular disease and other chronic diseases (48). Long-term studies using population-based samples are needed to further elucidate the effects of caffeine on cognitive performance among the elderly.

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REFERENCES