

Depression and Cognitive Impairment Are Associated with Low Education and Literacy Status and Smoking but Not Caffeine Consumption in Urban African Americans and White Adults

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Background: Recent research has linked caffeine consumption with a lower risk for depression and cognitive decline. However, no studies have examined the relationship in an African American compared to a white, socioeconomically diverse representative urban sample.

Methods: Data from a cross-sectional study were used to determine the associations of caffeine use with depressive symptomatology and cognition in a sample of 1,724 participants in the Healthy Aging in Neighborhoods of Diversity across the Life Span (HANDLS) study. The United States Department of Agriculture's Automated Multiple Pass Method was used by trained interviewers to collect two, in-person 24-hour dietary recalls. Depressive symptoms and global cognition were assessed using two well-validated measures: the Center for Epidemiologic Studies Depressive Scale (CES-D) and Mini Mental State Examination (MMSE), respectively. Usual caffeine intake was based on both recalls. Data were analyzed with *t*- and chi-square tests, correlation analysis, and ordinal logistic regression.

Results: African Americans consumed significantly less caffeine than did whites (89.0 ± 3.2 and 244.0 ± 8.7 mg respectively). Caffeine consumption was not associated with depressive symptomatology or global cognition. Age, less than 5th grade literacy, and less than high school education were significantly associated with both depressive symptoms and cognitive function. Smokers had a 43% greater risk for depression but only a 3% higher risk for cognitive impairment.

Conclusion: The low level of dietary caffeine intake in combination with smoking among HANDLS study participants may have influenced the lack of association with depressive symptomatology or global cognition. For this sample, low literacy and education appear more highly associated with depressive symptoms and cognitive function than caffeine intake.

Introduction

CAFFEINE IS THE MOST WIDELY consumed psychoactive drug worldwide. It can cross the blood-brain barrier, affecting cognition, mood, and alertness.¹⁻³ Cognition is the mental process crucial for conducting activities of daily living, including memory, judgment, verbal expression, and manipulating information. Symptoms of

depression, a mood disorder, include persistent feelings of guilt, worthlessness, helplessness, and hopelessness; appetite loss; sleep disturbance; and low energy levels.

According to the Centers for Disease Control and Prevention, 1 in 10 U.S. adults in the Behavioral Risk Factor Surveillance Survey reported depression assessed by the Patient Health Questionnaire 8.⁴ Studies such as the Nurse's Health Study (United States), Kuopio Ischemic

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Heart Disease Risk Factor Study (Finland), Bristol Stress and Health at Work Study (the United Kingdom), Cardiff Health and Safety at Work Study (the United Kingdom), and Cardiovascular Health Study (United States) have provided insight into the effects of caffeine on depression risk and cognitive function, two measures of mental health status.^{5–8} Among many variables studied, caffeine intake has been found to be associated with depressive symptomatology. These studies found a decreased risk of depression with increased caffeine intake among study participants.^{5,6} Despite these suggestive findings, Lucas *et al.*⁷ noted that the effect of caffeine on depression is poorly understood and understudied. Other investigators have reported that higher educational status may be associated with reduced risk for depression and cognitive decline,^{9–11} although the role of caffeine across the educational continuum remains unclear, particularly in urban populations.

An inverse and J-shaped curve has been reported between the number of cups of coffee consumed and cognition, specifically cognitive impairment over time.^{5,6,8,12} Multiple studies have reported little or no effect of caffeine if the dose is < 100–150 mg.^{5,8} In a study of people aged ≥ 65 years conducted by Arab *et al.*,⁸ the least cognitive decline, over a median of 7.9 years, was found in those who drank three cups of coffee daily. However, Lucas *et al.*⁵ showed that when caffeine is consumed in excessive amounts, effects can be detrimental. When more than eight cups of coffee were consumed by the study sample (females aged 54–70 years), an increased risk for suicide was observed.⁵ A challenge in comparing the findings of studies is variability in the amounts of caffeine reported in beverages and in the number of fluid ounces (fl. oz.) to define a cup of beverage containing caffeine. In the United States, brewed coffee is estimated to contain 85 mg of caffeine per 5 fl. oz. cup, while in Europe, brewed coffee is estimated to contain 100 mg of caffeine per 150 cc. cup.¹³ Mitchell *et al.*¹⁴ report that caffeine content of coffee and tea can vary widely due to the origin of the crop, processing, and preparation.

Other modifiable lifestyle factors such as smoking, sleep, and diet may alter the effects of caffeine on depression and cognitive function.^{15–17} For example, the byproducts of tobacco smoking, particularly the polycyclic aromatic hydrocarbons, are metabolic inducers of CYP1A2 enzyme. Caffeine is more than 90% dependent on CYP1A2 for its metabolism.¹⁷ Thus, because smoking is associated with increased caffeine metabolism, smokers may need to ingest more caffeine than nonsmokers to achieve the same plasma caffeine levels and mental health effects.¹⁷ Smith⁷ reported that caffeine has no benefit when people are sleep deprived. Morris *et al.*¹⁸ noted that low red blood cell folate and serum folate levels were linked to depressive episodes, suggesting folate may mediate or moderate the effects of caffeine. Higher caffeine intake along with higher diet quality as indicated by the nutrient adequacy score was found to be associ-

ated with better global cognition in older participants examined in the Baltimore Longitudinal Aging Study.¹⁶

Few studies have examined the source of caffeine associated with measures of depression or cognitive function.^{5–8} In the United States, the major contributor of dietary caffeine among adults is coffee, whereas soft drinks are the main source among teenagers.¹⁹ Other sources of caffeine include tea, energy drinks, and chocolate as well as selected medications. The source of caffeine may be important because caffeine-containing food and beverages are also sources of phytochemicals that may impact health. For example, cocoa or chocolate, which are rich in flavanols, have been associated with cognitive function.^{20,21} Similar to the xanthine structure of caffeine, theobromine, which is found in cocoa and tea, has been reported to be beneficial to health.²²

The assessment of depression varies among studies, posing an additional challenge to compare results. Ruusunen *et al.*⁶ found that coffee but not tea or caffeine consumption in Finnish men may be associated with lower risk for severe depression, as determined by the Human Population Laboratory depression scale. Furthermore, Lucas *et al.*⁵ reported no association between tea, sugared soft drink, or chocolate and risk for depression using a Mental Health Inventory-5. However, using longitudinal data, Lucas *et al.*⁵ found that risk for depression decreased with increased caffeinated coffee consumption. To our knowledge, no study has examined the association between caffeine consumption or the sources of caffeine and risk for depression using the Center for Epidemiologic Studies Depression (CES-D) scale, the best validated scale.²³ Many epidemiological studies use the CES-D scale to measure depressive symptomatology.^{24,25} Although the CES-D is not a diagnostic instrument, scores are highly correlated with clinical symptoms, and a standard cutoff identifies individuals at risk for clinical diagnoses.

The current study examined associations between caffeine intake, cognitive function, and depressive symptomatology among African American compared to white males and females who participated in the baseline wave of the Healthy Aging in Neighborhoods of Diversity across the Life Span (HANDLS) study. The specific objectives were to determine the relationship between caffeine intake and risk for depression, and between caffeine intake and global cognition, controlling for selected demographic factors and smoking. Theobromine, present in foods and beverages containing caffeine, exerts a similar effect as caffeine and was also examined. In this paper, the terms depressive symptomatology and risk for depression are used interchangeably.

Methods

Study background

The HANDLS study was a prospective 20-year longitudinal study. Participants were from a fixed cohort

drawn from 13 predetermined neighborhoods in Baltimore City, yielding representative distributions of individuals between 30 and 64 years old who were African American and white, male and female, and lower (<125% Poverty Income Ratio [PIR]) and higher (>125%PIR) socioeconomic status (SES).²⁶ The heuristic study design is a factorial cross of four factors—age, sex, race, and SES—with approximately equal numbers of subjects per factorial cell. A flow diagram of the household sampling to eligible participants for this study is presented in the CONSORT figure (Fig. 1).

There were two phases in the baseline HANDLS study. The first phase of data collection was done in the participants' homes, and consisted of interviews that included questionnaires about the participants' health status, health service utilization, dietary recall, discrimination, religiosity, active coping, household composition, neighborhood characteristics, and demographics. The second phase was completed 4–10 days later on mobile Medical Research Vehicles (MRVs) located in the participants' neighborhoods. MRV assessments included a medical

history and physical examination, dietary recall, cognitive evaluation, physiological assessments including heart rate variability, carotid Doppler, bone density, physical performance including strength and functioning to complete daily activities such as carry 10 pounds or walking up a flight of stairs, and laboratory measures.

The study protocol was approved by the human investigation review boards at the National Institutes of Environmental Health Science, National Institutes of Health, and the University of Delaware. All HANDLS participants provided written informed consent and received monetary remuneration.

Sample

The present sample consisted of 1,744 individuals who completed 2 days of 24-hour dietary recalls, 4–10 days apart. Participants who completed only the phase 1 recall ($n = 1,544$) were excluded, since physical examinations, literacy testing, medical history, and the second dietary recall were performed during phase 2 (Fig. 1). There

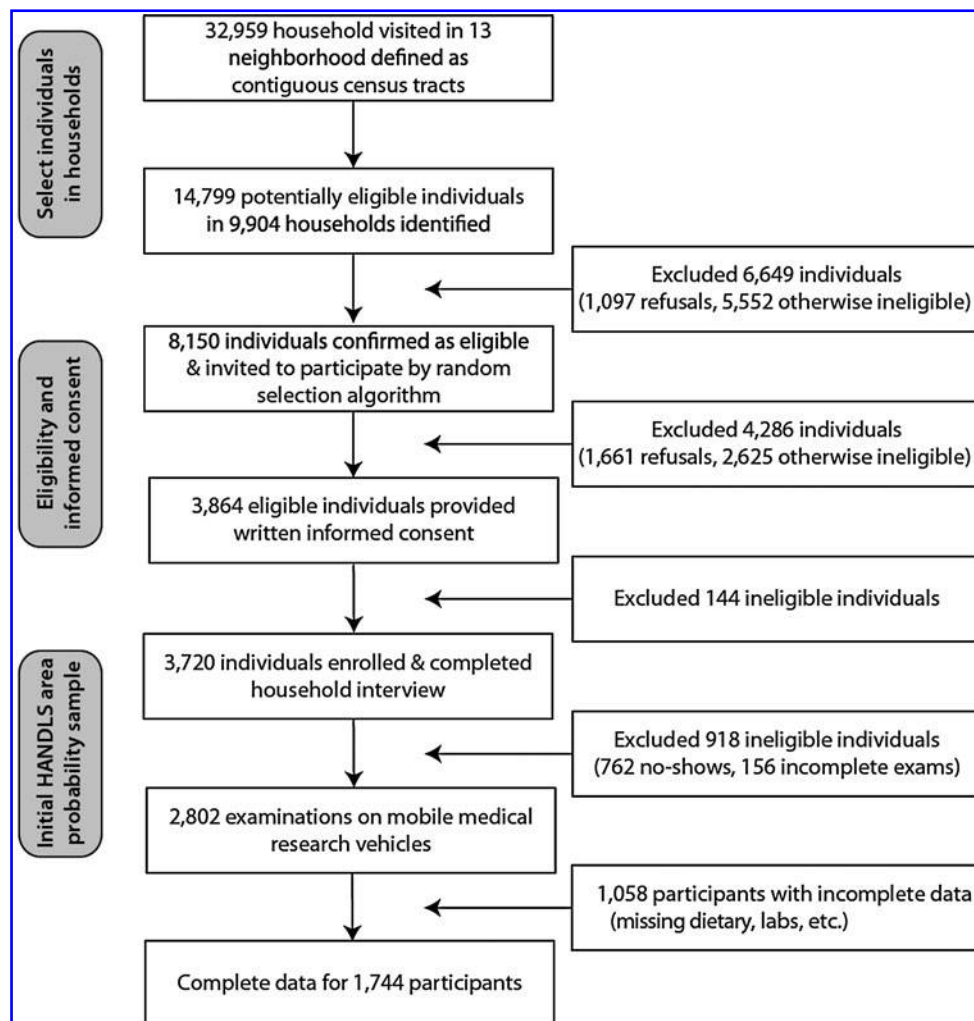


FIG. 1. Healthy Aging in Neighbors of Diversity across the Life Span Study household screening, participant eligibility, and response rates.

were no statistical differences in the distributions of demographic data or energy and nutrient profiles between participants who completed one or both days of dietary recall. Thus, the study sample is considered unbiased and representative of the entire HANDLS baseline sample.

Dietary method

Caffeine intake was assessed by 24-hour dietary recalls in the home and MRV. The United States Department of Agriculture (USDA) Automated Multiple Pass Method, a computer-assisted method, was used to collect both 24-hour dietary recalls.²⁷ The survey was supplemented by measurement aids such as measuring cups, spoons, ruler, and an illustrated Food Model Booklet to assist participants in estimating accurate quantities of foods and beverages consumed. Both 24-hour dietary recalls were administered in person by trained interviewers. The dietary recalls were coded using Survey Net, matching foods and beverages consumed with codes in the Food and Nutrient Database for Dietary Studies version 3.0.²⁸ Caffeine and theobromine intakes represent the mean intakes of two 24-hour dietary recalls.

Mental health measures

The presence of depressive symptomatology was assessed by trained interviewers, professionals with expertise in cognition, during the MRV examination. The CES-D scale, a 20-item instrument that describes behaviors and feelings, was used to identify individuals at risk for depression.²⁴ A score of ≥ 16 was used to classify persons at risk of depression,²⁴ which at this level is highly predictive of clinical depression on the basis of Diagnostic and Statistical Manual of Mental Disorders, 4th edition, criteria.²³

Global cognition was assessed by the Mini-Mental State Examination (MMSE), a standardized method. The MMSE has been proven to be a reliable and valid indicator of cognitive impairment with good test-retest reliability.^{12,29} It measures responses to a standard battery of memory and reasoning items, assessing orientation, attention, immediate and short-term recall, language, and the ability to follow simple verbal and written commands. The MMSE provides correct classification rates ranging between 80% and 90% compared to physician diagnosis of cognitive impairment and dementia.²⁹ $MMSE \leq 25$ was used as the cutoff to assess cognitive functioning based on the mean HANDLS education being a high school graduate.

Literacy assessment

Literacy was assessed by trained examiners on the MRV, using the reading subtest of the Wide Range Achievement Test-Third Edition (WRAT-3), a widely validated and used measurement of literacy.^{30,31} The WRAT-3 Reading subtest measures participants' ability

to recognize and name letters and words. The total WRAT-3 Reading score (total correctly pronounced letters by total correctly pronounced words) served as the literacy measurement. The total WRAT-3 Reading score was also converted to grade-level equivalents for descriptive purposes.³⁰

Clinical covariates: serum B12 and folate

Serum vitamin B12 and folate were examined, since low levels of either vitamin may lead to cognitive changes and depression. Fasting venous blood specimens were collected from participants during their MRV visit and analyzed by Quest Diagnostics, Inc. (Chantilly, VA). Folate and vitamin B12 were measured using enzyme immunoassay.³² Deficient levels of serum folate and vitamin B12 were defined as < 3 ng/mL³³ and < 200 pg/mL³⁴ respectively.

Statistical methods and analysis

Descriptive statistics were used to summarize and analyze preliminary unadjusted associations among demographic characteristics, cognitive measures, and clinical markers for the entire sample, as well as within race by sex classifications, using *t*- and chi-square tests. Pearson correlation analyses assessed the unconditional association of depressive risk and cognitive functioning scales with caffeine, theobromine, and clinical covariates (serum B12 and folate levels). Pearson correlation indicated no associating between the caffeine intake and the continuous outcomes of interest. Additional investigations using Spearman correlation analyses were also performed for quintile levels of intake and threshold-level outcomes of interest. Following preliminary analyses indicating low levels of dietary caffeine intake, the analyses then focused on the "bivariate relations" via the commonly used threshold values for depressive and cognitive scales.

Ordinal logistic regression was implemented to analyze and interpret the associations of both depressive risk and cognitive functioning with caffeine and theobromine. The first model assessed the relationship of exhibited depression ($CES-D \geq 16$) to the predictors of primary interest—caffeine and theobromine—while controlling for age and other demographic factors (race, sex, education, literacy, employment, and smoking). Similarly, the second model assessed the relationship of exhibited cognitive deficiency for the aforementioned predictors. CES-D and MMSE were also included as factors in the contrasting model.

Additionally, the preliminary lack of association of B12 and folate with the CES-D scale and folate with the MMSE scale excluded these covariates from the final models. Serum B12 was operationalized in the MMSE model as serum B12-deficient status. For both models, predictors with odds ratios and 95% confidence intervals

are presented in the results. Point estimates of the logistic regression were used to determine odds ratios of significant variables. No significant interactions were observed. Statistical significance was set to a two-tailed $p < 0.05$. Statistical analyses were performed with the SAS statistical software package v9.3 (SAS Institute, Cary, NC) and replicated in Stata v13 (StataCorp, College Station, TX).

Results

Sample characteristics

The characteristics of HANDLS study participants are presented in Table 1. The mean age of the baseline participants in this study was 49 years with a range of 30–64 years. There were no significant differences in education by sex within race. Approximately 30% of participants in this study had less than a high school education. The percentage of African American participants with less than an eighth grade literacy level, as measured by WRAT-3, was significantly higher than that of whites. More than half of participants reported being unemployed within the last month prior to their examination, with white males having the highest unemployment rate. The percentage of current cigarette smokers in the present sample ranged from 43% to 59%, a value higher than the national average of 19%.⁴ African American males smoked more than others in the study did.

More African American males than white males were at risk for depression. However, there was no significant difference in the proportion of African American (41%) and white females (44%) at risk for depression. Significantly more white females compared to white males ($p = 0.0014$) were at risk for depression. African American males scored the lowest in the MMSE, whereas white females had the lowest global cognitive impairment as indicated by the highest scores. The percentage of African American females with cognitive impairment was significantly higher than it was for their white counterparts ($p = 0.002$). In addition, more white males had cognitive impairment compared to white females ($p = 0.005$).

There were significant differences in body mass index (BMI) by sex within race for both African Americans and whites, with females having the greater BMI (Table 1). White males had a significantly greater BMI compared to African American males. The average BMI for both the males and females suggests the population was overweight or obese, which was corroborated by body fat determined by DXA (data not shown).

There were significant differences in mean serum folate and serum vitamin B12 levels within sex by race (Table 1). While the serum folate of African American males and females was lower than it was for their white counterparts, the reverse was seen for serum vitamin B₁₂. Mean serum vitamin B12 of African American

TABLE 1. CHARACTERISTICS OF HEALTHY AGING IN NEIGHBORS OF DIVERSITY ACROSS THE LIFE SPAN (HANDLS) STUDY PARTICIPANTS IN THIS STUDY

Characteristic	AA men (n=442)	W men (n=333)	p	AA women (n=530)	W women (n=439)	p	p-Values for comparison by sex within race (AAM vs. AAW, WM vs. WW)
<i>Demographic characteristics</i>							
Age, years, X ± SE	48.2 ± 0.44	48.8 ± 0.51	0.3871	48.5 ± 0.41	48.6 ± 0.45	0.8154	0.7089, 0.7448
Education, % < HS/GED	33.9 ± 2.3	31.8 ± 2.6	0.5374	30.6 ± 2.0	31.4 ± 2.2	0.7708	0.2624, 0.9065
Literacy, % < 8th grade	50.0 ± 2.4	25.8 ± 2.4	< 0.0001	45.6 ± 2.2	25.7 ± 2.1	< 0.0001	0.1774, 0.9875
Unemployed in last month, %	57.2 ± 2.4	69.4 ± 2.5	0.0006	53.4 ± 2.2	56.5 ± 2.4	0.3351	0.2302, 0.0003
Income < 125% PIR	48.4 ± 2.4	25.8 ± 2.4	< 0.0001	52.1 ± 2.2	34.4 ± 2.3	< 0.0001	0.2559, 0.0106
Smoker, % user	58.8 ± 2.3	45.1 ± 2.7	0.0001	43.0 ± 2.2	44.7 ± 2.4	0.6111	< 0.0001, 0.9123
<i>Cognitive measures</i>							
CES-D,* % ≥ 16	40.3 ± 2.3	32.4 ± 2.6	0.0252	41.3 ± 2.1	43.7 ± 2.4	0.4489	0.7404, 0.0014
Mini Mental,** % ≤ 25	19.0 ± 1.9	14.7 ± 1.9	0.1169	14.5 ± 1.5	7.1 ± 1.2	0.0002	0.0616, 0.0005
<i>Clinical measures</i>							
Body weight, kg, X ± SE	84.3 ± 0.8	88.3 ± 1.0	0.0037	83.3 ± 0.9	80.8 ± 1.0	0.0440	0.4281, < 0.0001
BMI, X ± SE	27.0 ± 0.3	28.4 ± 0.3	0.0044	31.0 ± 0.3	30.3 ± 0.4	0.1405	< 0.0001, < 0.0001
Serum folate, ng/mL, X ± SE	14.0 ± 0.33	15.1 ± 0.34	0.0252	13.9 ± 0.29	14.9 ± 0.32	0.0216	0.8277, 0.6986
Serum vitamin B12, pg/mL, X ± SE	528.7 ± 11.0	474.3 ± 10.7	0.0016	570.7 ± 12.0	472.3 ± 10.6	< 0.0001	0.0061, 0.9093

*CES-D ≥ 16 is the generally accepted cutoff for clinically relevant depressive symptoms.¹⁵

**MMSE ≤ 25 was used as the cutoff to assess cognitive functioning based on the mean HANDLS education being a high school graduate and the younger population.^{16,17}

AAM, African American men; AAW, African-American women; WM, white men; WW, white women; PIR, poverty income ratio; BMI, body mass index; CES-D, Center for Epidemiologic Studies Depression.

males was significantly lower than that of African American females ($p=0.0061$). The mean serum folate and vitamin B12 values were within normal reference range. Only 1% of the population had either serum folate or vitamin B12 levels indicative of a deficient state (<3 mg/mL and <200 pg/mL respectively).

Caffeine intakes and sources

Caffeine and theobromine intakes are shown in Table 2. The mean daily total intake of caffeine consumed by white males was significantly higher (threefold difference) than that of African American males ($p\leq 0.0001$). When mean caffeine intake was expressed per kilogram of body weight, intake by white males was again significantly higher than that of African American males ($p\leq 0.0001$). Mean total caffeine intake of white males was also significantly higher than the total caffeine intake of white females ($p=0.0407$). The same results were found for mean total theobromine but not mean theobromine intake per kilogram of body weight.

When daily caffeine intake was calculated for only consumers of caffeinated beverages, white males ($n=322$) ingested a mean \pm SEM of 259.8 ± 14.3 mg, while African American males ($n=378$) consumed 100.0 ± 5.1 mg ($p<0.0001$). It should be noted that 96.7% of the white males and 85.5% of the African American males reported consuming caffeinated beverages. In contrast, theobromine consumption was indicated for 221 of 333 (66.3%) white males and 265 of 442 (60.0%) African American males. The mean \pm SEM theobromine levels among users were 59.0 ± 5.2 mg and 51.4 ± 4.6 mg for white and African American males respectively.

Similar to the males, the daily total intake of caffeine consumed by white females was significantly higher (threefold difference) than that of African American females ($p\leq 0.0001$). When mean caffeine intake was expressed per kilogram of body weight, intake by white females was once again significantly higher than that of African American females ($p\leq 0.0001$). Mean total theo-

bromine intakes and mean theobromine intake per kilogram of body weight did differ significantly between white and African American females ($p=0.0115$ and $p=0.0241$ respectively).

When mean daily caffeine intake was calculated for only consumers of caffeinated beverages, there were significant differences between white and African American females ($p\leq 0.0001$). White females ($n=427$) ingested a mean \pm SEM of 232.0 ± 14.3 mg, while African American females ($n=454$) consumed 79.8 ± 4.0 mg. Caffeinated beverage consumption was reported among 97.2% of the white females and 85.7% of the African American females. Among females consuming theobromine, the mean \pm SEM theobromine consumption was 44.2 ± 3.0 mg and 39.5 ± 3.3 mg for white ($n=337$) and African American ($n=328$) females respectively.

When comparing intakes of caffeine and theobromine for users by sex and race, a few significant differences were found. White males consumed significantly more caffeine than white females did ($p=0.0328$). For both races, theobromine intake of male users was significantly greater than that of female users (African American $p=0.0296$; white $p=0.0098$).

The three main contributors of caffeine to the diets of HANDLS study participants were coffee, tea, and soft drinks (Fig. 2). Coffee was the primary contributor of caffeine in the diets of HANDLS study participants, ranging from about 67% for white males to 44% for African American females (Fig. 2). Except for white males, tea was the second highest dietary contributor of caffeine. For White males, caffeine from soft drinks exceeded that from tea. African American males and females had very similar distributions for caffeine by source, although a notable difference in tea consumption was observed between white males and females. African American males consumed about 2% of caffeine from energy drinks, which was notably higher than any other group. There were no significant associations between source of caffeine and either CES-D or MMSE.

TABLE 2. CAFFEINE AND THEOBROMINE INTAKES OF HANDLS STUDY PARTICIPANTS

Dietary component	AA men (n=442)*	W men (n=333)*	p	AA women (n=530)*	W women (n=439)*	p	p-Values for comparison by sex within race (AAM vs. AAW, WM vs. WW)
Total caffeine, mg	85.5 \pm 4.7	251.2 \pm 14.0	<0.0001	68.3 \pm 3.6	225.7 \pm 10.6	<0.0001	0.1210, 0.0407
Caffeine, mg/kg body weight	1.05 \pm 0.06	3.01 \pm 0.19	<0.0001	0.86 \pm 0.04	3.00 \pm 0.16	<0.0001	0.2247, 0.9861
Total theobromine, mg	30.8 \pm 3.0	39.2 \pm 3.8	0.0477	24.4 \pm 2.2	33.9 \pm 2.5	0.0115	0.0897, 0.2163
Theobromine, mg/kg body weight	0.37 \pm 0.04	0.47 \pm 0.05	0.0884	0.33 \pm 0.03	0.45 \pm 0.03	0.0241	0.4340, 0.6953
Total caffeine of caffeine users, mg	100.0 \pm 5.1	259.8 \pm 14.3	<0.0001	79.8 \pm 4.0	232.0 \pm 10.7	<0.0001	0.1001, 0.0328
Total theobromine of theobromine users, mg	51.4 \pm 4.6	59.0 \pm 5.2	0.2041	39.5 \pm 3.3	44.2 \pm 3.0	0.3559	0.0296, 0.0098

*X \pm SE.

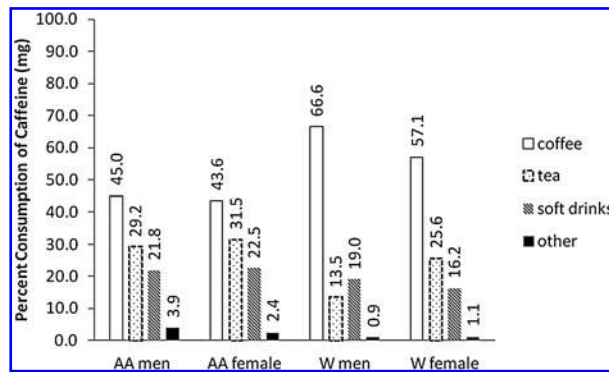


FIG. 2. Percent of caffeine consumption, stratified by source, distributed by race and sex.

Caffeine and depressive symptomatology

There were no significant correlations with CES-D and caffeine or theobromine. The results of the logistic analysis revealed that neither caffeine nor theobromine were associated significantly with risk for depression in the HANDLS study participants. Sex (female), age (younger), literacy (having a literacy equivalent to 5th grade or less), education (having less than a high school education), smoking status (current smoker), and employment (unemployed within last month) were associated significantly with CES-D, displaying a higher risk for depression (Table 3). Point estimates of the logistic regression were used to determine odds ratios of significant variables. With respect to risk for depression, current smokers have a 43% greater risk, and women have a 30% greater risk.

Caffeine and cognition

Neither caffeine nor theobromine was correlated with global cognition measured by MMSE. Logistic regression analyses indicated global cognition was not significantly affected by intake of either caffeine or theobromine

(Table 4). Significant predictors of MMSE included sex (male), age (older), literacy (5th grade or less), education (less than a high school education), and serum vitamin B12 (deficient levels; Table 4). With respect to cognitive impairment, the greatest risk was associated with deficient serum vitamin B12 levels (OR 0.278 [95% CI 0.095, 0.812]).

Discussion

Caffeine intakes

The HANDLS study provided sample sizes robust enough to give reliable estimations of caffeine intake for both urban white and African American groups. The mean caffeine intake for white HANDLS study participants was close to those reported in NHANES for white adults ($M=263.6$ mg for males and 219.8 mg for females).³⁵ Conversely, the HANDLS African American population was about three times below the national average. In a study by Boggs *et al.*,³⁶ it was noted that African American females drink less tea and coffee than their white counterparts do. When expressed as caffeine (in mg) per kilogram of body weight, the caffeine intake of the African Americans was lower than that reported by Mitchell *et al.*¹⁴ from a U.S. Beverage Consumption Panel, while the whites were similar to those reported from this panel.

Longitudinal studies based on food frequency assessments all reported a higher daily intake of caffeine compared to the intake reported for the HANDLS study. The intake of white females who participated in the Nurse's Health Study had a mean of 236 mg/day and a range of 73 ± 75 mg/day to 649 ± 220 mg/day.⁵ Among Portuguese males and females older than 65 years, mean caffeine intake was 75 mg/day.³⁷ Ruusunen *et al.*⁶ reported an average caffeine intake of 494 ± 221 mg/day for Finnish men.

Different concentrations of caffeine, even when standardized to 6 fl. oz., have been reported, posing a challenge when comparing the findings of dietary intake studies. The HANDLS study participants' caffeine intake

TABLE 3. FACTORS INFLUENCING HANDLS PARTICIPANTS' RISK FOR DEPRESSION BY LOGISTIC REGRESSION¹

Parameter	β Estimate \pm SE	p	Odds ratio	95% Confidence limits
Caffeine	0.00046 \pm 0.0003	0.1299	1.000	[0.999, 1.000]
Theobromine	0.00071 \pm 0.0009	0.4209	1.001	[0.999, 1.002]
Sex: men vs. women	-0.1311 \pm 0.0529	0.0132	0.769	[0.625, 0.947]
Race: African American vs. white	-0.0946 \pm 0.0607	0.1192	0.828	[0.652, 1.050]
Age	-0.0131 \pm 0.0057	0.0212	0.987	[0.976, 0.998]
Global cognitive function: normal vs. impaired	-0.1095 \pm 0.0819	0.1812	0.803	[0.583, 1.107]
Education: <high school vs. high school+	0.1323 \pm 0.0601	0.0276	1.303	[1.130, 1.649]
Literacy: \leq 5th grade vs. post-high school	0.3637 \pm 0.1044	0.0005	1.853	[1.336, 2.571]
Literacy: 6th-8th grade vs. post-high school	-0.0323 \pm 0.1056	0.7599	1.247	[0.902, 1.726]
Literacy: high school vs. post-high school	-0.0781 \pm 0.089	0.3804	1.192	[0.905, 1.568]
Current Smoker: no vs. yes	-0.1793 \pm 0.0543	0.001	0.699	[0.565, 0.864]
Employment: no vs. yes	0.415 \pm 0.0546	< 0.0001	2.293	[1.852, 2.840]

¹CES-D used to determine risk for depression.¹⁵

TABLE 4. FACTORS INFLUENCING HANDLS PARTICIPANTS' COGNITIVE FUNCTION BY LOGISTIC REGRESSION¹

Parameter	β Estimate \pm SE	p	Odds ratio	95% Confidence limits
Caffeine	0.000099 \pm 0.000446	0.82	1.000	[0.999, 1.001]
Theobromine	0.00146 \pm 0.00135	0.28	1.001	[(0.999, 1.004)]
Sex: men vs. women	0.2095 \pm 0.0816	0.01	1.520	[1.104, 2.094]
Race: African American vs. white	0.0302 \pm 0.096	0.75	1.062	[0.729, 1.548]
Age	0.0395 \pm 0.00938	< 0.0001	1.040	[1.021, 1.060]
Depression: not at risk vs. at risk	-0.1057 \pm -0.1057	0.0824	0.809	[0.586, 1.118]
Education: < high school vs. high school +	0.277 \pm 0.0864	0.001	1.740	[1.240, 2.441]
Literacy: \leq 5th grade vs. post-high school	1.7417 \pm 0.1427	< 0.0001	37.068	[17.369, 79.112]
Literacy: 6th-8th grade vs. post-high school	0.347 \pm 0.1742	0.05	9.190	[4.110, 20.546]
Literacy: high school vs. post-high school	-0.2176 \pm 0.1687	0.20	5.225	[2.371, 11.516]
Current smoker: no vs. yes	-0.013 \pm 0.0842	0.88	0.974	[0.700, 1.355]
Employment: no vs. yes	0.1112 \pm 0.0856	0.20	1.249	[0.893, 1.747]
Serum vitamin B12: deficient vs. normal	-0.6406 \pm 0.2737	0.02	0.278	[0.095, 0.812]

¹Cognitive function assessed with Mini Mental State Examination.

was calculated from analytically derived values reported in the USDA Food and Nutrient Database for Dietary Surveys.²⁸ These values are similar to those reported by the National Coffee Association. The caffeine content in a cup of coffee, defined as 6 fl. oz. (177.4 mL), varies by the bean type and brew methods.^{14,35} According to the National Coffee Association, the average cup of coffee contains 72 mg of caffeine per 6 fl. oz.³⁵ Yet, Ruusunen *et al.*⁶ used the value of 177 mg of caffeine for a 6 fl. oz. cup of coffee and 70.8 mg of caffeine for a 6 fl. oz. cup of tea.

It is widely recognized that the caffeine content of a cup of coffee can be affected by many factors including the type of bean used, roasting procedures, grinding procedures, and preparation procedures.^{14,38-40} A 2012 study by Crozier *et al.*³⁸ found that high performance liquid chromatography (HPLC) analysis of 20 commercial espresso coffees revealed a sixfold difference in caffeine levels. They noted that the serving size of one cup had a range between 23 and 100 mL, and the caffeine per cup had a range between 51 and 322 mg.³⁸ A study conducted by Chou and Bell⁴¹ noted that caffeine content differs by brand and type of soft drink. This variance suggest that future research use plasma levels of caffeine as well as dietary caffeine intakes to explore the relationships of caffeine to mental health.

Caffeine and depressive symptomatology

To the best of our knowledge, no studies have compared caffeine intake and risk for depression in a socioeconomically diverse sample of urban African American compared to white females and males, aged 30-64 years. The most significant and unexpected finding emerging from this study was that neither caffeine intake nor cups of coffee or tea consumed were associated with risk for depression for these population groups. However, sex, age, smoking, and socioeconomic factors, specifically literacy, education, and employment, were significant predictors

for risk of depression. To our knowledge, no previous studies have examined literacy, a better measure of the quality of education, in relation to risk for depression in adults.

A lower risk for depression with increased caffeine intake has been reported for select population groups, notably Finnish men⁶ and white nurses,⁵ in longitudinal studies spanning \geq 8 years. Although the current study did not find similar relationships, this difference might be explained by the fact that the mean caffeine consumption of the HANDLS study population is lower than that reported in these other studies. Thus, caffeine intake might be in the bottom range of the J-shaped curve, suggesting a lack of effect.⁶

Another explanation for the lack of association of caffeine and depression may be attributed to the effects of tobacco smoking. Caffeine and smoking require CYP1A2 enzyme for metabolism. Smoking induces this enzyme. Thus, it is considered a factor that can determine tolerance and response to caffeine.^{5,7,8,40,42} In this study, both African American and white smokers consumed significantly greater quantities of caffeine per kilogram of body weight than nonsmokers (data not shown). de Leon *et al.*²⁰ found that the median plasma caffeine concentration was two- to threefold higher in nonsmokers for each level of caffeine intake compared to smokers. The high prevalence of smokers in HANDLS in combination with relatively low caffeine intake may explain the lack of association of caffeine with risk for depression.

Lastly, methodological differences in the dietary data collection and in caffeine databases may have resulted in overestimations of caffeine intakes. For instance, Lucas *et al.*⁵ used food frequency questionnaires seven times over a 22-year period and used a sensitivity analysis with an 8-year lag of exposure. It should be noted that the food frequency methods were not the same as the Nurse's Health Study, and sometimes there was no indication of fluid ounces associated with a cup, which could

result in imprecise estimations of caffeine intake.⁵ Although the food frequency method attempts to estimate usual individual intake of foods over the past month or even year, there are many weaknesses associated with the food frequency such as the respondent's memory and the lack of details about foods with limited or no portion size estimation, and is prone to bias. Most importantly, it requires a literate population.

The results of the current study demonstrate that risk of depression among both African American and white HANDLS participants was associated with their lower education and literacy status, age, sex, and smoking. Other researchers have also found that smoking, age, and education are factors affecting risk for depression. Similar to our findings, other studies have found sex-dependent effects with risk for depression, showing significant results with females.^{8,42} Additionally, younger adults tend to report more symptoms of depression than middle-aged adults do.⁴³

Caffeine and cognition

Similar to the findings for depression, the findings from this study of HANDLS African American and white participants were that neither caffeine intake nor cups of coffee or tea consumed were associated with impaired cognition. Sex, age, education, literacy, and employment were significant predictors for global cognitive status. It was anticipated that literacy would be a significant predictor, since the associations between literacy and cognitive ability have been well documented, and longitudinal associations between literacy and cognitive decline have also been reported.^{44,45} In fact, Dotson *et al.*⁴³ found that racial minority status and low SES affect the relative influence of literacy and years of education on cognition and that reading ability better predicts cognitive function than education does in these population groups.⁴³ Deficient levels of serum vitamin B12 were also associated with impaired global cognition, which is consistent with the findings reported by other researchers.^{46,47}

The effect of caffeine on cognition might be explained by the role of caffeine acting as an antagonist of adenosine receptors in the brain, which consequently stimulates cholinergic neurons. These neurons protect against β amyloid-induced neurotoxicity, a precursor of cognitive decline.^{12,48} Van Gelder *et al.*¹² reported an inverse and J-shaped association between 10-year cognitive decline and cups of coffee consumed per day. Healthy adult men consuming three cups of coffee per day had the least cognitive decline. Unfortunately, the amount of caffeine ingested by the HANDLS study participants does not appear to be at the level to influence global cognition significantly. Arab *et al.*⁸ reported an association between coffee consumption and attenuated rates of cognitive decline in women. A systematic review of six longitudinal cohort studies revealed that cognitive decline measured with the MMSE was lower in consumers of caffeine bev-

erages, but there was a lack of a distinct dose response.⁴⁸ A randomized, double blind, crossover designed study reported that individuals ingesting 3 mg/kg of body weight compared to individuals ingesting a placebo improved cognitive performance.⁴⁹ It has also been noted that elderly people (≥ 65 years) may increase their cognitive performance by increasing their levels of caffeine.³⁷ Yet, the findings describing the effects of caffeine on cognitive processes are inconsistent, suggesting the need for more research in this area.^{16,50}

Strengths and limitations

There are many strengths of this study. A major strength is that it investigated an understudied urban population of diverse SES, allowing the comparison of African American and white adults. Another strength was the dietary data collection method. Using two 24-hour recalls provided accurate representation of usual caffeine consumption. Since these interviews were administered by trained interviewers, the participants' literacy did not impact the reports. Third, the MMSE measures global cognitive functioning and can discriminate among cognitively intact and mildly cognitively impaired individuals. Fourth, the CES-D is suitable for African American and white populations with a wide range of age and SES and can accurately classify people at risk for depression. Lastly, it demonstrates the importance of including literacy when exploring diet-health relationships.

A limitation of the study, as with all dietary studies, is that measurement error is inevitable. Until caffeine databases improve, the challenge of obtaining accurate and current data will continue. Another limitation is the cross-sectional study design for this analysis. However, the HANDLS study is prospective, which will support future longitudinal analyses over the life span. Lastly, the results describe a sample that resided in Baltimore, Maryland. Although the findings may not generalize to a national population, independent demographic analyses found this sample was representative of urban populations from U.S. cities with similar population densities and racial distribution, namely, Atlanta, GA; Bridgeport, CT; Bridgeton, NJ; Buffalo, NY; Camden, NJ; Carson, CA; Chicago, IL; Cleveland, OH; Detroit, MI; Harrisburg, PA; Hartford, CT; Oakland, CA; Springfield, MS; and Trenton, NJ (Lepkowski J. HANDLS Generalizability, 2010 and HANDLS Principle Cities Clusters Analysis, 2011, unpublished internal National of Institutes on Aging documents).

Conclusion

This study contributes to the literature as the first to describe caffeine intake in relation to depressive symptomatology and cognition in urban African American adults compared to urban white adults. Among HANDLS participants, coffee, tea, and caffeine consumption was not

associated with the risk for depression or cognitive impairment. Education, literacy, employment, and sex had greater associations than caffeine on risk for depression and impaired cognitive performance. To enhance our knowledge of the relationship between caffeine consumption, cognitive function, and risk for depression, future research should examine both dietary and plasma caffeine values, and explore other lifestyle factors such as physical activity, alcohol, and illegal drug use, which may influence mental health measures and caffeine metabolism.

Author Disclosure Statement

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