Building research in diet and cognition (BRIDGE): Baseline characteristics of older obese African American adults in a randomized controlled trial to examine the effect of the Mediterranean diet with and without weight loss on cognitive functioning

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ABSTRACT

In the United States, >5.4 million people age 65 and older are affected by cognitive impairment and dementia, including Alzheimer’s disease. African Americans are more likely than non-Hispanic whites to suffer from these disorders. Obesity is linked to accelerated age-related cognitive decline, and weight loss through caloric restriction is a potential strategy to prevent this cognitive impairment. Adherence to a healthful dietary pattern, such as the Mediterranean Diet (MedDiet), has also shown positive effects on reducing risk for dementia. African Americans are disproportionately affected by obesity and have less healthful diets than non-Hispanic whites. We present baseline characteristics from a three-arm randomized controlled trial that randomized 185 obese (BMI ≥30 kg/m² and < 50 kg/m²) healthy older adults (55–85 years of age) to: 1) Typical Diet Control (TDC); 2) MedDiet alone (MedDiet-A) intervention; or 3) MedDiet caloric restricted intervention to promote weight loss (MedDiet-WL). The majority of the sample was African American (91.4%) and female (85.9%). The two active interventions (MedDiet-A and MedDiet-WL) met once weekly for 8 months, and the TDC received weekly general health newsletters. Baseline data were collected between January 2017 and July 2019 in Chicago, IL. In our sample, closer adherence to a MedDiet pattern was associated with higher attention and information processing (AIP) and higher executive functioning (EF). Consistent with the literature, we saw that older participants performed more poorly on the cognitive assessments than younger participants, and women outperformed men across verbally mediated tasks, especially ones related to learning and memory.

1. Introduction

In the United States (US), >5.4 million people age 65 and older are affected by cognitive impairment and dementia, including Alzheimer’s disease. (Alzheimer’s Association, 2020, 2016). African Americans are more likely than non-Hispanic whites to suffer from these disorders (Chen and Zissimopoulos, 2018; Lines et al., 2014; Plassman et al., 2007; Zhang et al., 2016). Alzheimer’s disease and related dementias (ADRD) are devastating and costly conditions, with a direct cost estimate to the US economy of $236 billion in 2016 (Alzheimer’s Association, 2016). Reductions in cardiovascular diseases (CVD) over the last half of the 20th century are linked to some noted leveling off in the rates of ADRD in most developed and industrialized countries (Larson et al., 2013). However, obesity rates have increased dramatically during the last...
several decades, particularly among underrepresented minority populations, including African Americans (Ogden et al., 2020, 2015). Since obesity is associated with cognitive decline (Cournot et al., 2006; Elias et al., 2005; Wolf et al., 2007), this places these populations at increased risk of ADRD.

The exact mechanisms that link the increased risk of ADRD with obesity are not well understood (Singh-Manoux et al., 2018), and whether intentional weight loss in obese individuals can positively influence cognitive performance has not been determined (Siervo et al., 2011). However, obesity likely negatively influences cognition through its effect on CVD and metabolic risk factors, as well as associated adipocytokines, cytokines, and inflammatory markers (Lambert et al., 2013; Tosto and Reitz, 2013). Improving obesity-related lifestyle behaviors such as unhealthful diets and sedentary behaviors can decrease obesity, and may reduce the risk of cognitive decline through downstream physiological effects (Sherzai and Sherzai, 2019; Wright et al., 2017). Weight loss via caloric restriction is the primary treatment strategy to treat obesity, and modest weight loss (5–7%) is associated with reduction in the risk of CVD and metabolic diseases (Fain, 2009; Logue et al., 2010; Mavri et al., 2011; Villareal et al., 2011). These changes are primarily due to the positive effects on metabolism, inflammatory markers, and oxidative stress (De Las Fuentes et al., 2009; Esposito et al., 2003).

Interventions focused on lifestyle factors such as a healthy diet and modest weight loss could provide a practical approach to prevent or offset the development of age-related cognitive decline (Kuczmarski et al., 2014). The Mediterranean Diet (MedDiet) pattern, defined as a plant-based diet, characterized by a high consumption of fruits, vegetables, and whole grains as well as fish, nuts, and legumes, unsaturated fatty acids, and low to moderate intake of alcohol (consumed with meal) is linked to slower cognitive decline, improved cognitive function, and decreased risk of dementia as evidenced in a number of observational studies (Arditi et al., 2017; Chen et al., 2019; Loughrey et al., 2017; Petersson and Philippou, 2016; Power et al., 2019; Solfrizzi et al., 2017). Adherence to the MedDiet is also associated with a reduced risk of multiple chronic diseases such as type 2 diabetes and cancer, among others, demonstrating its health benefits beyond cognition and contribution to overall well-being (Abenavoli et al., 2019).

Lourida et al. (2013) in a systematic review of 11 observational studies and one randomized controlled trial (RCT), reported a consistent pattern of associations between adherence to a MedDiet and lower risks of cognitive decline and better cognitive function. However, many of the observational studies had limitations that highlight the need for RCTs (Martinez-González et al., 2012). One RCT that tested the association in a sub-study of the “Primary Prevention of Cardiovascular Disease with a Mediterranean Diet” (PREVencion con Dieta MEDITerranea) (PRE-DIMED) (Valls-Pedret et al., 2015) reported cognitive improvement among participants randomized to the Med Diet group and cognitive decline in those randomized to the low-fat control group. The benefits of the Med Diet group were independent of sex, age, energy intake, cognitive associated variables such as education, APOE ε4 genotype and vascular risk factors. Results of this RCT provide stronger evidence of the effects of a MedDiet on cognition than those reported in observational studies (Lourida et al., 2013; Psaltopoulou et al., 2013; Singh et al., 2014).

To our knowledge, however, no RCTs have tested the combined effect on cognitive functioning of MedDiet with caloric restriction to promote weight loss. The MedDiet-WL (90 min) and MedDiet-A (60 min) interventions included 25 sessions and a final party. The group sessions occurred weekly, with dates skipped for holidays. For sessions 1–19, both groups received content on lifestyle changes to accommodate a MedDiet eating pattern. For the MedDiet-WL, there was additional content that focused on weight loss through caloric restriction and meeting physical activity guidelines consistent with current public health recommendations (CDC, 2018; USDA, 2015). For sessions 20–25, both intervention arms received instruction focused on maintaining lifestyle changes consistent with the MedDiet eating patterns, and the MedDiet-WL arm received content on weight loss maintenance.

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For the MedDiet-WL group, at each group session, 30 min of supervised physical activity was offered, led by a physical activity instructor. Activities included stretching, flexibility, and moderate cardio exercises.

2. Materials and methods

2.1. Design

The BRIDGE trial is an RCT testing whether participants randomized to MedDiet-WL will achieve greater improvements in cognition, CVD and metabolic risk factors, body weight, and body composition, compared to participants randomized to MedDiet-A (weight stable) and a TDC group without caloric restriction or weight loss. The trial design, including methodology, is described in detail elsewhere (Tussing-Humphreys et al., 2017).

Setting. Both active interventions were conducted in local community sites that routinely deliver programming to older adults.

Participants. The study was conducted in 3 cohorts of about 60 participants each. Participants were randomly assigned to MedDiet-WL (n = 75), MedDiet-A (n = 73), or TDC (n = 37). Eligible participants were 55–85 years old, with BMI 30.0–50.0 kg/m², Montreal Cognitive Assessment (MoCA) score ≥ 19, MedDiet adherence screener score ≤ 6, able to participate in intervention classes at the scheduled time and location, planning to reside in the Chicago area for the duration of the study, able to understand English, and willing to participate in data collection and be randomized. Exclusion criteria have been discussed in detail elsewhere (Tussing-Humphreys et al., 2017); they include inability to exercise, significant health conditions, hemoglobin A1c (HbA1c) > 9%, Coumadin use, neurological or psychiatric conditions, bariatric surgery, enrollment in a formal weight loss program, or other memory/concentration research in the past 12 months.

Recruitment. We used passive recruitment strategies that included advertising in local neighborhoods and older adult specific listservs and publications. We placed brochures in senior facilities and senior exercise classes sponsored by local community sites. Participants in a previous study who had agreed to be contacted in the future were also contacted with information about the current study.

Interventions. The MedDiet-WL (90 min) and MedDiet-A (60 min) interventions included 25 sessions and a final party. The group sessions occurred weekly, with dates skipped for holidays. For sessions 1–19, both groups received content on lifestyle changes to accommodate a MedDiet eating pattern. For the MedDiet-WL, there was additional content that focused on weight loss through caloric restriction and meeting physical activity guidelines consistent with current public health recommendations (CDC, 2018; USDA, 2015). For sessions 20–25, both intervention arms received instruction focused on maintaining lifestyle changes consistent with the MedDiet eating patterns, and the MedDiet-WL arm received content on weight loss maintenance. For the MedDiet-WL group, at each group session, 30 min of supervised physical activity was offered, led by a physical activity instructor. Activities included stretching, flexibility, and moderate cardio exercises.

2.2. Measures

2.2.1. Socio-demographics

Participants were asked to report socio-demographic characteristics...
such as age, educational attainment, health insurance status, and self-reported medical conditions, among others.

2.2.2. Anthropometrics

Participant body weight was measured in duplicate using a digital scale (Tanita, Arlington Heights, IL). Participant height was measured in duplicate using a stadiometer. Body mass index (BMI) was calculated as weight (kg) divided by height (m²). Body composition including fat mass, fat free mass and regional body fat distribution was assessed using the General Electric Lunar IDXA machine (GE Healthcare, US).

2.2.3. Cognition

The cognitive domains outlined below reflect previously published work by our group generally (Boots et al., 2019; Gonzales et al., 2017; Lamar et al., 2015) and as it relates to MedDiet adherence more specifically (Karstens et al., 2019).

Attention/Information Processing domain (AIP). AIP was assessed via raw scores from the Digit Span Forward subtest and the Digit Symbol subtest of the Wechsler Adult Intelligence Scale – IV (WAIS-IV; Wechsler, 2008), time to completion on Part A of the Trail Making Test (TMT) (Reitan and Wolfson, 1985), and raw scores from the Stroop word and color subtests (Stroop, 1935).

The Executive Function domain (EF). EF was assessed using the raw scores from the Digit Span Backward and Sequencing subtests of the WAIS-IV, TMT Part B time to completion, total correct words produced on letter fluency (Lezak et al., 2004; Stroop, 1935), and the Stroop Color-Word Interference score.

Learning/Memory/Recognition domain (LMR). LMR was assessed using three measures from the California Verbal Learning Test – II (CVLT-II): total recall across the 5 learning trials, total delay free recall, and recognition discriminability scores (Delis et al., 2000).

Other Cognitive Measures. To screen for cognitive impairment during initial eligibility determinations, the MoCA screener (Nasreddine et al., 2005) was used as recommended by the National Institute of Neurological Diseases and Stroke and Canadian Stroke Network’s Neuropsychology working group (Hachinski et al., 2006). The MoCA screener assesses different cognitive domains including attention and concentration, executive functions, memory, language, visual construction skills, conceptual thinking, calculations, and orientation.

We calculated predicted verbal IQ from the raw word reading score from the Wechsler Test of Adult Reading (Wechsler, 2001); these metrics are considered more accurate means of assessing and adjusting for educational quality than years of education in racially/ethnically diverse samples of older adults (Manly et al., 2002). To monitor test-taking effort across the intervention, the CVLT-II forced choice recognition trial was administered, with > 14 correct considered adequate effort (Schwartz et al., 2016).

Cognitive Composite Scores. A composite score was created for each of the three domains outlined above (AIP, EF, and LMR) by converting the relevant raw scores to z-scores, then taking the mean of the z-scores. The z-scores for the TMT Parts A and B were multiplied by –1 so that a higher z-score indicated better performance to be consistent with all other individual z-scores.

2.2.4. Dietary intake

Habitual dietary intake was estimated using the Harvard Food Frequency Questionnaire (HFFQ) (Willett et al., 1985). The HFFQ is a semi-quantitative food frequency questionnaire consisting of 131 foods and beverages during the previous 12 months. Completed HFFQ surveys were processed by the Channing Lab at Harvard University.

Adherence to a MedDiet-like pattern. Data from the HFFQ were used to calculate a MedDiet adherence score. The MedDiet score, first developed by Panagiotakos et al. (Panagiotakos et al., 2007) and later modified for a Chicago-based population by Teyney and colleagues (Teyney et al., 2011), was adapted further for applicability to the HFFQ variables and data. Briefly, food and beverage items from the HFFQ were used to create adherence scores (0–5) for 11 components: non-refined grains (summary variable included in the HFFQ output file), potatoes (1 item), fruit (19 items), vegetables (24 items), legumes and nuts (8 items), fish (4 items), red meat and processed meat (12 items), poultry (3 items), full-fat dairy products (8 items), olive oil (3 items), alcohol (milliliters per week based on 5 items). The score ranges from 0 to 55 points, with 5 points maximum for each component awarded for full compliance and scores scaled proportionately based on intake (Table 2). For example, for non-refined grains, those consuming 33 or more servings weekly received 5 points, 19–32 servings 4 points, 13–18 servings 3 points, 7–12 servings 2 points, 1–6 servings 1 point and consuming 0 servings 0 points. MedDiet Adherence Screener. To assess eligibility, participants completed a 13-item screener (Martinez-Gonzalez et al., 2012) adapted for a U.S. population. One item was removed (sofrito) given that it is not a commonly known or consumed condiment/food in the US among our target population of African Americans. Scores can range from 0 to 13, and only those with scores ≤ 6 were eligible to participate.

2.2.5. Physical activity

To objectively measure physical activity, the ActiGraph wGT3x triaxial wrist accelerometer was used (Santos-Lozano et al., 2012), as compliance with accelerometers is higher when worn on the wrist (Freedson and John, 2013; Troiano et al., 2014). Participants were asked to wear the accelerometer on their non-dominant wrist for 7 days. Data were included if the participant wore the accelerometer for ≥ 4 days and ≥ 10 h/day. Data were processed via two methods. With the first method, ActiLife v6.13.4 software (ActiGraph, Pensacola, FL) was used to extract data, validate wear time, and compute physical activity levels with data converted to 60-s epochs. Average counts per minute (CPM) are reported. Additionally, moderate-to-vigorous physical activity (MVPA) was quantified using a cut-point of ≥ 7500 counts per minute (Camada et al., 2016), which was derived by examining the physical activity of older women assessed by hip- and wrist-worn accelerometers.

In the second method, accelerometer data were downloaded using ActiLife, saved in raw format as GT3X files, and converted to CSV format. Raw data files were processed in R (http://cran.r-project.org) using the GGIR package (Miguels et al., 2019; Sabia et al., 2014; van Hees et al., 2013). GGIR consists of two major processing components. In Part 1, raw triaxial acceleration values are converted into one omnidirectional measures of body acceleration by taking the vector magnitude from the three axes and subtracting by the value of gravity, after which negative values are rounded to zero. The resulting metric is referred to as the Euclidean norm minus one (ENMO) (van Hees et al., 2013). Data are further reduced by calculating the average values per 1-s epoch. In Part 2 of the data processing component, daily-level summary files are produced based on the acceleration summary data generated from Part 1. The daily summaries are generated using the intensity-specific milli-g cut-points from Hildebrand et al. regression equations (Hildebrand et al., 2014), which estimates minutes of MVPA.

Self-Reported Physical Activity. The Godin-Shepard Leisure Time Physical Activity Questionnaire was used to measure self-reported leisure time physical activity (Godin, 2011). A total score and an MVPA score were calculated using the standard scoring instructions, and participants were categorized as insufficiently active, moderately active, or active.

Mobility. Mobility and functional exercise capacity were measured using the six-minute walk test, in which participants were asked to walk as far as possible in 6 min (Guyatt et al., 1985; Naylor et al., 2014). An 18-meter walking course was marked with cones in a level, tiled hallway, and total distance walked was recorded. Participants were instructed to walk as quickly as possible for 6 min. Assistive devices could be used.

2.2.6. Clinical measures

Blood Lipids. Fasting total cholesterol, low density lipoprotein cholesterol (calculated), high density lipoprotein cholesterol and
triglycerides were measured by spectrophotometry at Quest Diagnostics (Wood Dale, IL).

**Blood Pressure.** Systolic and diastolic blood pressure and pulse rate were assessed in duplicate using the Omron HEM-907 (Lake Forest, IL) electronic blood pressure monitor with the participants seated (Pickering et al., 2005).

**Markers of Metabolic Risk.** Fasting insulin and glucose were assessed from serum via immunoassay (insulin) or spectrophotometry (glucose) at Quest Diagnostics (Wood Dale, IL). HbA1c was measured in whole blood via enzymatic assay by the same commercial lab.

**Systemic Inflammation.** Serum levels of high sensitivity C-reactive protein (hs-CRP) from fasting venipunctures were assessed via an immunoturbidimetric assay by Quest Diagnostics (Wood Dale, IL). The upper and lower limit of detection for this assay are 0.3–10.0 mg/L. Values coded as > 10 mg/L were excluded from analyses. Values below the lower limit of detection (usually 0.3, 0.2 for some early assays) were imputed as the limit of detection divided by the square root of 2 (Ong et al., 2013).

### 2.2.7. Psychosocial measures

**Quality of life.** Perceived quality of life was assessed using the Patient Reported Outcomes Measurement Information System (PROMIS) Global Health Scale version 1.2 (Reeve et al., 2007). Global scores for physical health and mental health were calculated and converted to T-scores. A score of 50 represents the mean for the U.S. general population; the SD for the U.S. is 10.

**Mood.** Depressive symptomatology was measured using the Center for Epidemiologic Studies of Depression Scale (CES-D) (Radloff, 1977), a

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**Fig. 1.** CONSORT Diagram (data collected January 2017 and July 2019 in Chicago, IL).
20-item scale with scores ranging from 0 to 60.

Social Support. This was evaluated by the Modified Medical Outcomes Study Social Support Survey (mMOS-SS) (Moser et al., 2012). The mMOS-SS includes 8 items covering two domains, emotional and instrumental (tangible) social support. Scores can range from 0 to 100.

2.2.8. Randomization

A stratified block randomization sequence with a 2:2:1 allocation to MedDiet-WL, MedDiet-A, and TDC, respectively, was created in SAS and imported into the Research Electronic Data Capture (REDCap) randomization module. Randomization was stratified by program cohort (1–3), age (55–69 and 70–85 years), and MoCA score (19–25 and 26–30). The data manager, who had no contact with participants, was responsible for randomization.

2.2.9. Statistical analyses

We calculated Cronbach’s coefficient alpha for each of the cognitive composites to estimate internal consistency. We used Pearson correlations to explore the relationship between social support and global mental health or depressive symptoms. We used t-tests with pooled variances for tests of differences in MoCA and pVIQ. Scores can range from 0 to 100.

We randomized 185 participants: 75 to MedDiet-WL, 73 to MedDiet-A, and 37 to TDC. Table 1 reports the baseline demographic characteristics of study participants. Most of the participants were < 70 years of age and primarily identified as non-Hispanic Black or African American (91.4%). Most of the sample was female (85.9%), and 30.4% reported a graduate or professional degree. Reported income was < $20,000 for 22.2% of the sample, between $20,000 and $40,000 for 54.4%.

Table 1 also shows self-reported past or current medical conditions: 67.0% reported high blood pressure, 38.9% reported high cholesterol, 16.2% reported type 2 diabetes, and 24.9% reported sleep apnea. Mean BMI was 37.1 kg/m², with 35.7% of the sample in obesity class I (30 to < 35 kg/m²), 41.6% in obesity class II (35 to < 40 kg/m²), and 22.7% in obesity class III (≥ 40 kg/m²). The mean percent body fat for the sample was 47.7% (SD = 6.0%), and the mean estimated visceral mass was 1,621 g (SD = 774 g).

Table 2 shows MedDiet adherence at baseline, including the number of servings needed to score a full 5 points for a given component of the MedDiet adherence score (column 2), mean servings per week of each component (column 3) and corresponding mean score (column 4) estimated from HFFQ responses. The unadjusted mean total MedDiet score was 32.8 (SD = 5.5). Participants were most adherent with the full-fat dairy (4.6), poultry (3.9) and legumes and nuts (3.8) components and least adherent to the potatoes (0.9), olive oil (1.8) and fish (2.2) components.

Table 3 shows baseline cognitive characteristics of our sample, including composite domain scores and individual raw scores for each domain. It should be noted that standardized Cronbach’s alpha coefficients for our cognitive domains were deemed adequate: 0.68 for AIP, 0.65 for EF, and 0.85 for LMR. The mean MoCA score of 25.1 (SD = 2.5) fell between reported means for normal aging (∼27) and mild cognitive impairment (∼22) found in the literature and was well within limits set by our study eligibility threshold, i.e., ≥ 19. Additionally, the mean predicted verbal IQ (pVIQ) score from the WTAR, 94.5 (8.5), fell within the average range. Lastly, based on the CVLT-II Forced Choice Recognition Trial, over 98% of participants met the threshold for test taking effort during their baseline visit. Within this context, mean scores across AIP, EF, and LMR were commensurate with MoCA and pVIQ scores. For example, participants recalled, on average, 9.5 digits forward and 7.4 digits backward on the Digit Span Test (see Table 3).

**Table 1**

| Participant characteristics at baseline. | N   | Mean or SD | Median or | IQR |
|-----------------------------------------|-----|------------|-----------|-----|
| Age at randomization, yr                | 185 | 66.3 (6.1) | 66.0 (8.2) |
| 55–69                                   |     | 75.7% (140) |           |     |
| ≥ 70                                    |     | 24.3% (45)  |           |     |
| Gender                                  | 185 |            |           |     |
| Female                                  |     | 85.9% (159) |           |     |
| Male                                    |     | 14.1% (26)  |           |     |
| Race                                    | 185 |            |           |     |
| Black or African-American, not Hispanic |     | 91.4% (169) |           |     |
| Hispanic                                |     | 1.1% (2)    |           |     |
| White, not Hispanic                     |     | 1.1% (2)    |           |     |
| Native American                         |     | 0.5% (1)    |           |     |
| Multiracial                             |     | 5.9% (11)   |           |     |
| Education, yr                          | 184 | 15.1 (2.4)  | 16.0 (5.0) |
| Not HS graduate                        |     | 2.2% (4)    |           |     |
| HS graduate                             |     | 37.5% (69)  |           |     |
| Associate’s degree                     |     | 9.8% (18)   |           |     |
| College graduate                       |     | 20.1% (37)  |           |     |
| Graduate or professional degree         |     | 30.4% (56)  |           |     |
| Employed full or part-time             | 185 | 28.1% (52)  |           |     |
| Marital status                          | 185 |            |           |     |
| Single                                  |     | 25.4% (47)  |           |     |
| Married                                 |     | 27.6% (51)  |           |     |
| Widowed                                 |     | 15.7% (29)  |           |     |
| Divorced                                |     | 31.4% (58)  |           |     |
| Income (median)                        | 180 | 50,000 (40,000) |         |     |
| < $20,000                               |     | 22.2% (40)  |           |     |
| $20,000–$40,000                         |     | 23.3% (42)  |           |     |
| > $40,000                               |     | 54.4% (98)  |           |     |
| Has health insurance                    | 185 | 98.9% (183) |           |     |
| Medical conditions                      |     |            |           |     |
| High blood pressure                    | 185 | 67.0% (124) |           |     |
| High cholesterol                       | 185 | 38.9% (72)  |           |     |
| Type 2 diabetes                        | 185 | 16.2% (30)  |           |     |
| Sleep apnea                             | 185 | 24.9% (46)  |           |     |
| Total prescription medications         | 184 | 2.5 (2.1)   | 2.0 (3.0)  |     |
| MedDiet screener score (0–6)           | 185 | 4.2 (1.4)   | 4.0 (2.0)  |     |
| Weight, kg                              | 185 | 100.5 (14.5) | 98.8 (19.9) |     |
| Height, cm                              | 185 | 164.6 (7.4) | 164.2 (9.0) |     |
| BMI, kg/m²                              | 185 | 37.1 (4.8)  | 36.0 (5.9)  |     |
| BMl category                            | 185 |            |           |     |
| Obesity class I (30–35 kg/m²)           |     | 35.7% (66)  |           |     |
| Obesity class II (35–< 40 kg/m²)        |     | 41.6% (77)  |           |     |
| Obesity class III (> 40 kg/m²)          |     | 22.7% (42)  |           |     |
| Percent body fat                        | 184 | 47.7 (6.0)  | 48.4 (7.7)  |     |
| VAT mass, g                             | 174 | 1621 (774)  | 1492 (736) |     |

- **a** Medicare, Medicaid, or private insurance.
- **b** Self-reported, current or past conditions.
- **c** Screener scores can range from 0 to 13, with higher scores indicating greater adherence. Only those with scores < 7 were eligible for the study.
Inflammation. Clinical Measures: Blood Pressure, Glucose Metabolism, Cholesterol, and Inflammatory biomarkers. Mean systolic blood pressure was slightly above 133 mmHg (SD = 17.7), as was diastolic blood pressure, 79.8 (11.5) mmHg. Pulse per minute showed a mean of 73.1 (10.2). As per American Diabetes Association categorizations, mean HbA1c was within the prediabetes range at 6.1 (0.9)%, as was mean fasting insulin at 11.6 (8.7) uIU/mL. Average fasting insulin was 11.6 (8.7) uIU/mL. Mean total cholesterol was 188.9 (36.9) mg/dL, HDL was 59.2 (15.3) mg/dL, and LDL was 109.8 (32.6) mg/dL. Mean hs-CRP was 3.9 (2.5) mg/L.

### Table 2: Mediterranean Diet Adherence from MedDiet Score, N = 185.

| MedDiet score components (0-5) | Servings/wk for max score of 5 | Self-reported Servings/wk from FFQ | MedDiet scorea |
|-------------------------------|--------------------------------|-----------------------------------|-----------------|
|                               | Mean or % | SD or N | Mean | SD | Median | IQR |
| Non-refined grains ≥ 33       | 15.9 (9.8) |                  | 2.8 (1.2) | 3.0 (2.0) |
| Potatoes ≥ 14                 | 0.9 (1.2)  |                  | 0.9 (0.7) | 1.0 (1.0) |
| Fruit ≥ 23                    | 17.0 (11.6) |              | 3.4 (1.2) | 3.0 (3.0) |
| Vegetables ≥ 34               | 21.0 (14.5) |              | 3.1 (1.2) | 3.0 (2.0) |
| Legumes and nuts ≥ 7          | 7.5 (6.9)  |                  | 3.8 (1.2) | 4.0 (2.0) |
| Fish ≥ 7                      | 2.3 (2.3)  |                  | 2.2 (1.2) | 2.0 (2.0) |
| Red meat and processed meat ≤ 1 | 5.1 (5.4) |                  | 3.0 (1.7) | 3.0 (2.0) |
| Poultry ≤ 3                   | 4.3 (4.0)  |                  | 3.9 (1.4) | 4.0 (2.0) |
| Full-fat dairy products ≤ 10  | 7.1 (6.5)  |                  | 4.6 (0.8) | 5.0 (1.0) |
| Olive oil ≥ 7                 | 1.8 (3.2)  |                  | 1.8 (1.6) | 2.0 (3.0) |
| Alcohol (mL)b ≥ 299           | 28.1 (64.9) |              | 3.3 (2.4) | 5.0 (5.0) |

### Table 3: Cognitive Composite Scores and Raw Scores for the Underlying Variables.

| Composites and Raw Scoresa | N | Mean or % | SD or N | Min | Max | Median | IQR |
|----------------------------|---|-----------|---------|-----|-----|--------|-----|
| Attention/Information Processing (AIP) Composite | 184 | 0.0 | (0.7) | -1.8 | 2.2 | 0.0 | (0.9) |
| Digit Span Forward | 185 | 9.5 | (2.0) | 5 | 15 | 9.0 | (2.0) |
| Digit Symbol | 185 | 56.3 | (11.5) | 26 | 87 | 56.0 | (18.0) |
| Trail Making Test Part Aa | 184 | 35.1 | (12.1) | 16 | 107 | 34.0 | (14.0) |
| Stroop Color Score | 185 | 86.1 | (14.0) | 52 | 131 | 87.0 | (19.0) |
| Executive Function (EF) Composite | 179 | 0.0 | (0.6) | -1.5 | 1.7 | 0.1 | (0.9) |
| Digit Span Backward | 185 | 7.4 | (2.1) | 2 | 15 | 7.0 | (3.0) |
| Digit Span Sequencing | 185 | 7.4 | (2.1) | 1 | 12 | 8.0 | (3.0) |
| Trail Making Test Part Bb | 179 | 105.6 | (51.1) | 40 | 300 | 88.0 | (53.0) |
| Letter Fluency | 185 | 36.9 | (10.0) | 14 | 69 | 36.0 | (12.0) |
| Stroop Color-Word Interference Score | 185 | 31.8 | (7.9) | 10 | 51 | 33.0 | (11.0) |
| Learning/Memory/Recognition (LMR) Composite | 185 | 0.0 | (0.9) | -3.0 | 1.8 | 0.0 | (1.2) |
| CVLT-II Trials 1 thru 5 Total Learning | 185 | 45.2 | (9.3) | 5 | 67 | 46.0 | (12.0) |
| CVLT-II Delay Free Recall | 185 | 9.2 | (3.2) | 0 | 16 | 9.0 | (4.0) |
| CVLT-II Recognition Discriminability | 185 | 88.7 | (9.1) | 54.2 | 100 | 89.6 | (10.4) |

### Table 4: Clinical Measures: Blood Pressure, Glucose Metabolism, Cholesterol, and Inflammation.

| N | Mean | SD | Median | IQR |
|---|------|----|--------|-----|
| Systolic BP, mmHg | 185 | 133.6 | (17.7) | 123.0 | (21.0) |
| Diastolic BP, mmHg | 185 | 79.8 | (11.5) | 80.0 | (15.0) |
| Pulse, per minute | 185 | 73.1 | (10.2) | 73.0 | (13.0) |
| HbA1c, % | 185 | 6.1 | (0.9) | 5.8 | (0.7) |
| Glucose, mg/dL | 185 | 102.6 | (24.1) | 96.0 | (16.0) |
| Insulin, uIU/mL | 185 | 11.6 | (8.7) | 9.2 | (6.7) |
| Total chol, mg/dL | 185 | 188.9 | (36.9) | 187.0 | (46.0) |
| HDL, mg/dL | 185 | 59.2 | (15.3) | 58.0 | (17.0) |
| LDL, mg/dL | 185 | 109.8 | (32.6) | 108.0 | (43.0) |
| Non-HDL chol, mg/dL | 185 | 129.7 | (35.9) | 129.0 | (47.0) |
| Cholesterol/HDLc | 185 | 3.4 | (1.0) | 3.3 | (1.2) |
| Triglycerides, mg/dL | 185 | 99.4 | (42.0) | 91.0 | (53.0) |
| hs-CRP, mg/L | 156 | 3.9 | (2.5) | 3.6 | (4.1) |

### Table 5: Physical Activity, Measured by Accelerometer, N = 183.a

| N | Mean | SD | Median | IQR |
|---|------|----|--------|-----|
| Counts per minuteb | 1528 | (504) | 1454 | (639.2) |
| MVPa/day, fixed cutoffs | 9.4 | (8.3) | 7.0 | (10.0) |
| MVPa/day, intensity-specific cutoffs | 8.9 | (10.9) | 5.5 | (9.6) |

### Notes

- a A higher score indicates greater adherence to the Mediterranean diet.
- b A score of 0 was assigned for either 0 or ≥ 700 mL/wk of alcohol.
- c Higher trail-making raw scores indicate lower performance.

Nearly 90% (see Table 3 for details).

Table 4 shows clinical and circulating cardiometabolic and inflammatory biomarkers. Mean systolic blood pressure was slightly above average fasting insulin was 11.6 (8.7) uIU/mL. Mean total cholesterol was 118.9 (36.9) mg/dL, HDL was 59.2 (15.3) mg/dL, and LDL was 109.8 (32.6) mg/dL. Mean hs-CRP was 3.9 (2.5) mg/L.

### References

- American Heart Association cut-points for normal at 133.6 mmHg (SD = 17.7), as was diastolic blood pressure, 79.8 (11.5) mmHg. Pulse per minute showed a mean of 73.1 (10.2). As per American Diabetes Association categorizations, mean HbA1c was within the prediabetes range at 6.1 (0.9)%, as was mean fasting glucose at 102.6 (24.1) mg/dL; average fasting insulin was 11.6 (8.7) uIU/mL. Mean total cholesterol was 188.9 (36.9) mg/dL, HDL was 59.2 (15.3) mg/dL, and LDL was 109.8 (32.6) mg/dL. Mean hs-CRP was 3.9 (2.5) mg/L.
- Calculated using the ActiLife program; MVPA was defined as ≥ 7500 counts per day; one record was lost due to accelerometer malfunction.
- Calculated in R using the GGIR package; MVPA was calculated using intensity-specific cutpoints (Hildebrand et al., 2014).
Table 5 shows baseline accelerometer-assessed physical activity. Wear time ranged from 10.0 to 24.0 h per day with a mean wear time of 21.1 (SD = 4.5) hours per day. With the ActiLife data processing method, mean number of minutes of MVPA per day was 9.4 (8.3), and the mean counts per minute was 1528 (504). With the GGIR data processing method, the mean number of minutes of MVPA was 8.9 (10.9).

Table 6 (Table 6), the mean for physical health was 49.8 (SD = 7.5) and for mental health, 52.7 (7.8). The mean score on the CES-D, measuring depressive symptoms, was 7.3 (6.1). The mean score for social support (mMOS-SS) was 74.8 (22.4), and social support was associated with both better reported overall mental health (r = -0.41, p < 0.001) and fewer depressive symptoms (r = -0.28, p < 0.001).

Table 7 explores associations between age, BMI, and gender and both the cognitive composite scores and the energy-adjusted MedDiet adherence score. Attention/Information Processing performance was lower for older (>70 y) compared to younger (55-69 y) participants (mean = -0.3 vs 0.1, p = 0.002) and higher in participants with higher (>40 kg/m²) BMI (0.2 vs -0.1, p = 0.006). Compared to men, women showed lower AIP scores (0.1 vs -0.4, p = 0.001). Higher Executive Functioning was associated with higher BMI (0.3 vs -0.1, p < 0.001). Compared to women, men showed lower Learning/Memory/Recognition Processing performance (0.1 vs -0.4, p = 0.02). The energy-adjusted MedDiet adherence score did not differ significantly by age, BMI, or gender (Table 7). Additional Pearson partial correlation analyses between MedDiet adherence score and individual cognitive domains, adjusted for energy, had the following results: r = 0.19 (p = 0.01) for Attention/Information Processing r = 0.21 (p = 0.006) for Executive Functioning, and r = 0.13 (p = 0.08) for Learning/Memory/Recognition Processing, indicating that higher MedDiet scores were associated with higher cognitive performance.

When considering age, BMI, gender, and MedDiet score together as predictors of individual cognitive composite scores in three multivariable linear regression models (Table 8), results were somewhat different from the unadjusted results reported above and shown in Table 7. After adjusting for energy and the WTAR raw score, age (b = -0.04, p < 0.001) and gender (b = -0.41, p = 0.002) were still significantly associated with AIP, but BMI and MedDiet were not. For EF, age was a significant independent predictor of performance (b = -0.02, p = 0.002), and MedDiet score was also a significant predictor (b = 0.02, p = 0.047). For LMR, gender continued to significantly associate with performance (b = -0.42, p = 0.02), and there was a suggestion that age was also a predictor (b = -0.02, p = 0.050).

4. Discussion

Epidemiologic data show that approximately one third of US older adults are obese, with the highest rates of obesity among African American older adults, aged 65-74 years (Fakhouri et al., 2012). African Americans are also at increased risk for adverse subclinical brain changes and associated cognitive impairment and ADRD (Gottesman et al., 2015; Ho et al., 2010). Weight loss, through caloric restriction, that can positively influence vascular (e.g., hypertension) and metabolic (e.g., insulin resistance, inflammation, dyslipidemia) risk factors in obese individuals, may provide secondary benefits for cognitive functioning (Passini and Wolfe, 2001). Different dietary strategies have also been found to affect cognitive functioning depending on the energy content and macronutrient composition. (D-Anci et al., 2020; Gillette-Guyonnet et al., 2003) Current research does not provide complete conclusions on the effect of dietary patterns on ADRD (Vinegrruera et al., 2020). However, of the available evidence, the MedDiet, a particularly antioxidant-rich dietary pattern, has been shown to confer cognitive benefits and a reduced risk of dementia (Valls-Pedret et al., 2015). More specifically, in observational studies, close adherence to a MedDiet pattern is associated with reduced cognitive decline and decreased risk of ADRD (Anastasiou et al., 2017; Dinu et al., 2018; Louhreby et al., 2017; Polletier et al., 2015; Samieri et al., 2013; Tangney et al., 2014).

However, we know of no RCTs that have tested whether the combined effects of a caloric restricted MedDiet designed to achieve modest weight loss (MedDiet-WL) will achieve greater improvements in cognition compared to an isocaloric MedDiet (MedDiet-A) designed to be weight stable and a typical diet control (TDC). Additionally, whether MedDiet-WL will achieve greater improvements in cognition compared to MedDiet-A will be assessed.

To our knowledge, the baseline results for our sample of obese, predominantly African American older adults are the first to document that closer self-reported adherence to a MedDiet like pattern is associated not only with higher AIP, but also with higher EF. There are several differences between our study and previous reports. Specifically, in studies outlined in the Van Den Brink 2019 review (Van Den Brink et al., 2019) only one found higher MedDiet adherence was associated with higher EF (i.e., (Anastasiou et al., 2017)). This may be due, in part, to across study variations in ethnicity, age, baseline overall physical and mental health status, as well as variations in the approaches to assessing adherence to a MedDiet like pattern. Notably, in the Coronary Artery Risk Development in Young Adults (CARDIA) study, a longitudinal cohort of >2000 individuals recruited as young adults, 45% black and 57% female, a higher adherence to a MedDiet was associated with statistically superior cognitive performance, including EF, at 30-year follow-up (McVoy et al., 2019). Other studies have reported that higher MedDiet adherence is significantly associated with higher LMR (e.g., (Karstens et al., 2019)); while our results did not reach significance, they did suggest a similar association was present in our sample regardless of adjustments.

Additional results of our baseline evaluation revealed similarities to other cohort studies of dietary patterns, which supports generalizability of the results of our intervention when completed. For example, the Chicago Health and Aging Project (CHAP) (Tangney et al., 2011), a longitudinal cohort study of Midwest, urban, older adults (>65 years), included 2280 African Americans and 1510 non-Hispanic whites, and the sample had a mean BMI of 27.1 kg/m² (SD = 5.5), and mean MedDiet adherence scores of 27.6 (CI 95%: 27.4, 27.7) and 29.2 (CI 95%: 29.0, 29.4), for African American and non-Hispanic whites, respectively. In our sample of Midwest urban obese predominantly African American older adults, adherence to a MedDiet like pattern, evaluated using a similar dietary survey and dietary index score as CHAP, had a slightly
associated with improved cognitive functioning, which is not consistent. In our sample, in unadjusted analyses, a higher BMI was related to our composite scores with and without adjustment are consistent with previous studies. However, other studies do not support what is referred to as the "obesity paradox" (Nilsson and Nilsson, 2009; Strandberg et al., 2013; Tobias et al., 2014). The outcomes from our Med Diet-WL group will help to shed light on these initial conflicting results. Our study fills a gap for the need to help clarify the directionality of the relationship between BMI and cognitive performance, particularly as our study is assessing cognitive performance prior to, and following, intentional weight loss. It is also important to highlight that our participants reflect a relatively healthy older adult population, with clinical measures such as blood pressure, heart rate, HbA1c, insulin, total cholesterol, and triglycerides all within normal ranges. Excluding potential participants with significant medical conditions provides us with the opportunity to more clearly assess the association between elevated BMI and AIP, EF, and LMR. More than half of our sample were classified as insufficiently active based on self-reported leisure activity which is consistent with other studies conducted with diverse samples of overweight/obese older adults (Diaz et al., 2016; Emerson and Gay, 2017; Gothe, 2018; Zhu et al., 2017). Our accelerometer results do demonstrate that that our sample is sedentary, with an average of 9.4 min (SD = 8.3) of MVPA per day. Cross-sectional and some prospective studies in predominantly non-Hispanic white samples suggest that aerobic fitness can enhance cognitive function (Barnes et al., 2013; Kramer et al., 2006, 2003). The mechanisms by which physical activity affects cognitive function remain to be fully elucidated, but this study will allow us to assess the associations between objectively measured physical activity and specific domains of cognition. It was evident that the wrist-worn accelerometers are acceptable to this population, and adherence to wear-time protocol was high. At baseline, 99% of our participants had a valid record. This is in contrast to a prior study we conducted with obese African American women, where only 74% (70/94) of the participants had valid records (Fitzgibbon et al., 2008), which is similar to the 71% adherence reported by the National Health and Nutritional Examination Survey (NHANES) for hip-worn accelerometers (Troiano et al., 2008). This suggests that the wrist placement may be an ideal location for objective activity measurement in older African American adults (Diaz et al., 2018; Doberty et al., 2017; Wolpern et al., 2019). On the measure of mobility, the mean 6-minute walk distance was 352.9 m (SD = 76.0), which is similar to another study we conducted with overweight and obese older African Americans with osteoarthritis (356.3 m) (Fitzgibbon et al., 2018), but lower than another RCT (N = 401) of younger (mean age, 56.3 years) higher mean 32.8 (5.5). This may reflect our participants’ interest in diet and chronic disease prevention given their desire to participate in a dietary lifestyle intervention trial.

Likewise, a review of our cognitive data and the associations with basic demographic characteristics suggests that our participants reflect the larger current literature on cognitive aging. For example, it is well documented that older adults perform more poorly on cognitive assessments than mid-to young-old adults (Park et al., 1999), particularly within the areas of attention and information processing (Rabbitt and Goward, 1994). Likewise, women traditionally outperform men across basic demographic characteristics suggests that our participants reflect the need to help clarify the directionality of the relationship between BMI and cognitive performance, particularly as our study is assessing cognitive performance prior to, and following, intentional weight loss. It is also important to highlight that our participants reflect a relatively healthy older adult population, with clinical measures such as blood pressure, heart rate, HbA1c, insulin, total cholesterol, and triglycerides all within normal ranges. Excluding potential participants with significant medical conditions provides us with the opportunity to more clearly assess the association between elevated BMI and AIP, EF, and LMR. More than half of our sample were classified as insufficiently active based on self-reported leisure activity which is consistent with other studies conducted with diverse samples of overweight/obese older adults (Diaz et al., 2016; Emerson and Gay, 2017; Gothe, 2018; Zhu et al., 2017). Our accelerometer results do demonstrate that that our sample is sedentary, with an average of 9.4 min (SD = 8.3) of MVPA per day. Cross-sectional and some prospective studies in predominantly non-Hispanic white samples suggest that aerobic fitness can enhance cognitive function (Barnes et al., 2013; Kramer et al., 2006, 2003). The mechanisms by which physical activity affects cognitive function remain to be fully elucidated, but this study will allow us to assess the associations between objectively measured physical activity and specific domains of cognition. It was evident that the wrist-worn accelerometers are acceptable to this population, and adherence to wear-time protocol was high. At baseline, 99% of our participants had a valid record. This is in contrast to a prior study we conducted with obese African American women, where only 74% (70/94) of the participants had valid records (Fitzgibbon et al., 2008), which is similar to the 71% adherence reported by the National Health and Nutritional Examination Survey (NHANES) for hip-worn accelerometers (Troiano et al., 2008). This suggests that the wrist placement may be an ideal location for objective activity measurement in older African American adults (Diaz et al., 2018; Doberty et al., 2017; Wolpern et al., 2019). On the measure of mobility, the mean 6-minute walk distance was 352.9 m (SD = 76.0), which is similar to another study we conducted with overweight and obese older African Americans with osteoarthritis (356.3 m) (Fitzgibbon et al., 2018), but lower than another RCT (N = 401) of younger (mean age, 56.3 years)
obese individuals with arthritis that included approximately 44% African Americans (M = 493.0 m) (Hughes et al., 2020).

Regarding psychosocial variables, the results for our sample are consistent with other studies. On average, participants reported few depressive symptoms, with a mean CES-D score of 7.3. Scores ranged from 0 to 27, with 20 participants (10.8%) at or above the 16-point cut-off identifying those at high risk for depression (Radloff, 1977; Zich et al., 1990). There is a growing literature reporting that older African Americans have a lower prevalence of mood disorders than their younger counterparts and that African Americans populations, in general, have lower prevalence rates than non-Latino whites of mood disorders (Mezuk et al., 2013). We will administer this measure at each study visit to continue to investigate these profiles.

On measures of global health, our participants scored similarly to a sample of participants who were recruited via an internet survey company (www.op4g.com) that maintains a panel of respondents from the general population. In this sample of 2025 participants, 49% were male, and the mean age was 46 years (SD = 18). Scores were 48.3 (9.0) and 48.5 (10.0), for global physical health and global mental health, respectively (Schalet et al., 2015). Self-reported social support (mMOS-SS) for our participants was relatively high, with a score of 74.8 out of a possible 100. In a study of early stage breast cancer patients (N = 541) and matched controls (N = 542), mean age = 57.7 y, that included 23% African American women, the mean mMOS-SS score was slightly higher, 84.6 (SD = 17.9) (Thompson et al., 2013). In another study of African American women participating in a two-year RCT, the reported baseline social support score was 81.9 (SD = 19.8) (Thompson et al., 2017). Not surprisingly, in our sample, social support was associated with both better reported overall mental health and fewer self-reported depressive symptoms.

5. Conclusions

Strengths of the present study include the RCT design, a sample of relatively healthy older obese African American adults, a well-validated dietary questionnaire, well-validated psychosocial measures, objectively measured physical activity, and the inclusion of a number of tests to measure cognitive functioning. The cognitive domain scores were drawn from previously published literature in aging and cognition (Boots et al., 2019; Gonzales et al., 2017; Lamar et al., 2015) as well as MedDiet adherence studies (Blumenthal et al., 2017; Karstens et al., 2019). While certain cognitive domains are not represented, e.g., visuospatial abilities, our represented cognitive domain scores were extracted from a larger neuropsychological protocol. Thus, we will be able to assess other cognitive abilities, albeit not at the composite level. The opportunity to assess other cognitive abilities including visuospatial skills may also counter the female advantage seen for several of our composite scores.

Our ability to generalize our baseline findings to other populations may be limited in several ways. Our sample was predominantly African American, so we cannot necessarily extend our findings to other racial/ethnic groups. Our participants also resided in a large urban city, so we cannot necessarily generalize our findings to rural settings. We also do not have information on the duration of obesity for our participants. We know of no studies that have examined the duration of obesity and cognitive performance in relatively healthy older adults, but it is possible that individuals with a longer history of obesity perform differently on tests of cognition (Wagner et al., 2020). We also do not have information about physical activity earlier in life. Some findings suggest that midlife physical activity may play a role in preserving cognitive health as people age (Najar et al., 2019). In addition, people with high MedDiet adherence at baseline (screener scores ≥ 7) were ineligible for the study, so the associations seen in our baseline analyses may not apply at higher levels of adherence. Lastly, our study did not account for genetic predisposition to ADRD, which has been shown to be associated with cognitive decline later in life (Deary et al., 2004).

Despite these potential limitations, to our knowledge ours is the first RCT to directly compare the independent effect of the MedDiet and combined effects of the MedDiet and weight loss on cognition in obese African American older adults. Our study will help to clarify the relationship between BMI and cognitive performance, particularly as it relates to cognitive assessment before and after intentional weight loss.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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