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Latent profile analysis of cognition in a non-demented diverse cohort: A focus on modifiable cardiovascular and lifestyle factors

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Abstract

Background/Objective.—Cognitively-defined subgroups are well-documented within neurodegeneration; less work has examined such profiles in diverse non-demented older adults, or considered how resulting subgroups relate to modifiable factors associated with neurodegeneration.

Method.—121 non-demented (MMSE=28.62) diverse (46% non-Latino Black, 40% non-Latino White, 15% Latino) community-dwelling adults (age=67.7 years) completed cognitive, cardiovascular, physical activity, and diet evaluations. Latent profile analyses (LPA) employed six cognitive scores (letter fluency, letter-number sequencing, confrontational naming, 'animal' fluency, list-learning delayed recall, and recognition discriminability) to characterize cognitively-defined subgroups. Differences between resulting subgroups on cardiovascular (composite scores of overall health; specific health components including fasting blood levels) and lifestyle

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(sedentary behavior; moderate-to-vigorous physical activity; Mediterranean Diet consumption) factors were examined using ANCOVAs adjusting for relevant confounders.

Results: Based on sample means across cognitive scores, LPA resulted in the following cognitive subgroups: (1) high-average cognition, 55% non-Latino White and 64% female participants; (2) average cognition, 58% non-Latino Black and 68% male participants; (3) lower memory, 58% non-Latino Black participants; and (4) lower executive functioning, 70% Latinos. The high-average subgroup reported significantly higher Mediterranean Diet consumption than the average subgroup (p=.001). The lower executive functioning group had higher fasting glucose and hemoglobin A1c than all other subgroups (p-values<.001).

Conclusion: LPA revealed two average subgroups reflecting level differences in cognition previously reported between non-Latino White and Black adults, and two lower cognition subgroups in domains similar to those documented in neurodegeneration. These subgroup, and their differences, suggest the importance of considering social determinants of health in cognitive aging and modifiable risk.

Keywords

latent profile analysis; aging; cognition; diversity; lifestyle; Mediterranean diet

INTRODUCTION

As anti-amyloid trials continue to fail [1], there is increasing interest in alternative approaches to preventing emergent Alzheimer's disease and related dementias (ADRD) via modifiable health and lifestyle factors. For example, mounting evidence from intervention studies suggest that controlling cardiovascular risk, engaging in appropriate physical activity, and modifying diet (e.g., [2]) mitigate against the emergence of ADRD in older adults regardless of age, sex, education, income, or global cognitive status [3]. While a multidomain intervention may be the most beneficial empirically, recommendations for multiple health and lifestyle modifications may not be feasible to implement for a given individual. Thus, it is important for researchers to identify how subgroups of otherwise healthy older adults may differ on modifiable health and lifestyle factors to assist clinicians in deciding which factors to highlight when considering recommendations for health and/or lifestyle modifications at the individual level.

Research suggests that it is possible to delineate subgroups of individuals with ADRD, as well as those in the at-risk stage known as mild cognitive impairment (MCI), on the basis of core cognitive parameters taken from a comprehensive neuropsychological assessment. For example, employing latent profile analysis (LPA), a statistical method of identifying unmeasured profile membership among individuals, we have revealed that profiles of patients with mild to moderate ADRD may be classified on the basis of their area/level of cognitive impairment on 6 cognitive parameters derived from 5 cognitive test. These profiles included pure amnestic, pure dysexecutive, mixed/mild impairment, and mixed/moderate impairment, with the mixed profiles consisting of impairments in memory, executive function, and language [4]. Consistent with these LPA findings, and using a similarly comprehensive set of cognitive parameters, cluster analysis of individuals diagnosed with

MCI reveals distinct cognitive subgroups including amnestic and dysexecutive/mixed subtypes [5–7]. The biological coherence of leveraging cognitively-defined subgroups in MCI and ADRD has been supported across genetic [8] and neuroimaging [9] studies. Additionally, cognitively-defined subgroups of MCI appear to differentially translate to Alzheimer's and, to a lesser extent, vascular dementia [10]. This work, conducted in studies comprised of ≥90% non-Latino White adults, suggests that cognitively-defined subgroups within MCI and ADRD may make it possible for a more precise characterization and earlier identification of disease progression in vulnerable individuals. However, few to no studies have employed this same approach to uncovering cognitive subgroups in diverse community-dwelling populations.

To our knowledge, work investigating cognitive subgroups in non-demented older adults has waxed and waned in recent years. This may be due, in part, to the increasing use of cognitive screening tools and/or conventional criteria for diagnosing risk and development of ADRD in large-scale studies rather than a broader canvassing of cognition via neuropsychological tests [11, 12]. Additionally, there has been an increasing focus on categorizing subgroups of clinically classified individuals according to neuropathological (e.g., [13]), neuroimaging (e.g., [14]), and/or CSF-based (e.g., [15]) biomarkers ([16] for review) as opposed to creating such categorizations using detailed cognitive assessments [11, 12]. While these studies have provided large-scale biological biomarker data, almost all have lacked participant diversity. Furthermore, while there is evidence – including some within the past 5 years – that subtle alterations within specific cognitive domains, e.g., episodic memory[17, 18], exist in normal aging [19, 20] and are indicative of later cognitive decline and progression to dementia [21, 22] [18], what is less evident is whether there is an association between cognitive profiles of normal aging using multiple cognitive parameters taken from a comprehensive neuropsychological assessment and modifiable health and lifestyle factors that may bolster successful aging at the individual level.

In the current research, we characterized cognitive profiles using LPA in a diverse community-dwelling sample of non-demented older adults and examined whether resulting subgroups differed on modifiable health and lifestyle factors. We focused on factors that have long been associated with ADRD in older adults regardless of race or ethnicity including cardiovascular health ([23] for review), physical activity, sedentary behavior, and diet [24]. Furthermore, we ensured that these factors were consistent with previous studies investigating modifiable risk factors associated with subtle alterations in cognitive trajectories in non-demented older adults (e.g., domain-specific episodic memory trajectories [17, 18] and test-specific cognitive screener trajectories [25]). We anticipated that LPA would reveal distinct subgroups of individuals across the spectrum of average to lower levels of cognitive functioning. We further hypothesized that when compared to individuals with average cognition, subgroups with lower cognitive performance would have higher sedentary behavior, lower levels of physical activity, poorer dietary intake, and higher cardiovascular risk. Lastly, individuals with average cognition would score most favorably across these health and lifestyle factors when compared to all other subgroups. Identifying modifiable factors associated with differing cognitive profiles derived from multiple cognitive parameters in a diverse community-dwelling sample of non-demented older adults

may help with more precise recommendations at the individual level and ultimately better cognitive health at the population level.

MATERIALS AND METHODS

Participants

Adults aged 60 years and older who self-identified as non-Latino White, non-Latino Black, or Latino were recruited via community outreach, including English and Spanish flyers, newspaper advertisements, and word of mouth to participate in a study of brain aging at the University of Illinois at Chicago (UIC) Department of Psychiatry. This study was approved by the UIC Institutional Review Board (IRB) and conducted in accordance with the Declaration of Helsinki with written informed consent obtained from all participants in their preferred language (Spanish or English). Additional IRB approval and all relevant data use agreements were completed with the Rush University Medical Center.

Described in detail elsewhere [26–28], interested individuals underwent a brief telephone screening in their preferred language to determine study eligibility. At this screen, exclusion criteria consisted of self-reported current or past history of neurological conditions (i.e., ADRD, MCI, Parkinson's disease or any other movement disorder, or stroke) or mood disorders (e.g., depression or generalized anxiety disorder); a history of head injury or loss of consciousness; a present or past history of substance abuse or dependence; or current psychotropic medication use. A self-reported history of stable (e.g., diabetes) or remitted medical illness (e.g., cancer) was not an exclusionary factor. Individuals were not eligible for this study if they had received cognitive testing within the past year, or if they reported current involvement in a cognitive aging study.

Eligible individuals were scheduled for further in-person evaluation of inclusion and exclusion criteria, including the Structured Clinical Interview for DSM-IV-TR (SCID) [29] and the Mini Mental State Examination (MMSE) [30]. These screening measures were administered by a trained research assistant fluent in English and/or Spanish and followed by an evaluation by a psychiatrist who completed the 17-item Hamilton Depression Rating Scale (HAM-D) [31] with the assistance of a translator as needed. Study staff were not privy to telephone screen information. Final inclusion criteria consisted of an absence of psychiatric symptoms based on the SCID, a score ≤8 on the HAM-D, an MMSE score ≥24, and a lack of subjective memory complaints. A total of 121 individuals met final inclusion criteria.

Study Protocol

Neuropsychological Evaluation.—All 121 participants completed a comprehensive neuropsychological evaluation in their preferred language, English (n=110) or Spanish (n=11), including standardized measures of attention, executive functioning, language, and episodic memory as outlined below.

Based on previous research [4], 6 core cognitive parameters derived from the following 5 cognitive test measures were chosen a priori to provide the raw scores used in our latent profile analysis (LPA): verbal fluency, letter-number sequencing, confrontational naming,

and learning and memory measures. Specifically, 1) total words correctly produced from Letter fluency, i.e., 'FAS' in English [32] and 'PMR' in Spanish [33]; 2) total Letter-Number Sequencing (LNS) score from the Wechsler Adult Intelligence Scale, 3rd Edition (WAIS-III) in either English [34] or Spanish [35]; 3) total correct from the 60-item Boston Naming Test (BNT) in English [36] or the 30-item BNT in Spanish [37] multiplied by 2 for comparison purposes; 4) total words correctly produced from Category fluency (i.e., 'animals' in both English and Spanish) [32]; and, from a 16-item verbal list learning task complete with distractor list, free and cued recall, and recognition testing; more specifically, the California Verbal Learning Test-II (CVLT-II) in English [38], and the Aprendizaje de Palabras from *La Batería Neuropsicológica en Español* [33]: 5) total correct from delayed free recall; and 6) recognition discriminability percent correct, i.e., [1 −(false positive + omissions / # possible correct)] × 100)].

Participants also completed self-reported measures of mood in either English or Spanish [39] including the Beck Depression Inventory (BDI) [40] and the Beck Anxiety Inventory [41] (BAI). Additionally, using The Language Experience and Proficiency Questionnaire (LEAP-Q) [42] we determined whether participants were native English speakers and then, as relevant, queried information on additional languages spoken including age of acquisition, current language exposure, and self-ratings of proficiency in speaking, understanding and reading based on a scale from 0 (none, i.e., no proficiency) to 10 (perfect proficiency).

Cardiovascular Disease Risk Factor Assessment ––Trained staff in the Center for Clinical and Translational Science's Clinical Research Center at UIC completed a medical history and physical examination in either English or Spanish, as well as two seated blood pressure readings separated by 5 minutes. A 12-h fasting blood draw quantified glucose, hemoglobin A1c, lipid profiles, and other blood-based biomarkers; an electrocardiogram was also performed. We chose two composite measures of overall cardiovascular disease health widely-used in the literature: 1) the recently revised [43] comprehensive Framingham Stroke Risk Profile score (FSRP) that predicts stroke risk in diverse populations and 2) the American Heart Association's Life's Simple 7 score (LS7) [44] cited as an ideal metric to study successful brain aging given its role in preserving cognition [45].

The revised FSRP metric uses a regression-based algorithm that incorporates age, sex, systolic blood pressure, anti-hypertensive therapy, diabetes, smoking, cardiovascular disease, and atrial fibrillation to calculate 10-year risk of stroke (FSRP-10) ([43] for calculation specifics). FSRP-10 was log-transformed to normalize its distribution. Using criteria set forth by the American Heart Association ([44] for specifics), we calculated participants' LS7 scores (min=0, max=14) based on levels of ideal (2 points), intermediate (1 point) or poor (0 points) health status across self-reported smoking, diet, and physical activity as well as the objectively obtained metrics of body mass index, blood pressure, total cholesterol, and fasting blood glucose.

Previous work from our group has highlighted the key role that systolic blood pressure played in FSRP-10 scores of this sample [26]; thus, we also investigated systolic blood pressure as a secondary outcome. Furthermore, to ensure that our work was consistent with previous studies investigating modifiable cardiovascular risk factors associated with specific

cognitive profiles in non-demented older adults [17, 18, 25], we also investigated pulse pressure (the discrepancy between systolic and diastolic BP) and mean arterial pressure [systolic BP + (2*diastolic BP)]/3 as well as fasting glucose, hemoglobin A1c, total cholesterol, and triglyceride levels as secondary outcomes.

Sedentary Behavior and Physical Activity Assessment ––—As described elsewhere [27], sedentary behavior was assessed using the Sedentary Behavior Questionnaire (SBQ) [46] for English speakers and the SBQ-S for Spanish-speakers [47]. These comparable questionnaires measure the amount of time spent engaging in activities such as watching television or reading a book or magazine. Each activity was queried for the amount of time spent on a typical weekday and weekend day, separately. Sedentary behavior was calculated as (reported weekday hours × 5) + (reported weekend day hours × 2), for an approximate total hours per week of sedentary activity.

The Community Healthy Activities Model Program for Seniors (CHAMPS) Physical Activity questionnaire, designed for older adults in English [48] and adapted to Spanish [49], was used to determine levels of physical activity based on a self-report interview both for LS7 calculations and as a metric of moderate to vigorous activity more generally as outlined below. Participants were asked to report on their frequency of activities over the past 4 weeks in “times per week,” and classify duration of the activity into six categories ranging from “less than 1 hour/week” to “9 or more hours/wk.” MET (metabolic equivalent) values were obtained for each activity of interest for categorization into Moderate (MET value ≥ 3.0) and Vigorous (MET value ≥ 5.0) activities. Moderate activities included swimming gently or riding a bicycle while Vigorous activities included singles tennis or jogging/running [50]. For the purpose of this research we used a measure of moderate-to-vigorous physical activity (MVPA) displaying a MET value ≥ 3.0.

Dietary Assessment ––—The Block 2015 Food Frequency Questionnaire (FFQ) was administered by trained research assistants in either English [51] or Spanish [52] in person or over the phone to assess self-reported dietary intake of ~110 food items over the past year. Details of administration instructions including the Block Dietary Data Systems portion guide used, and validation data against repeated 4-day diet records collected over 1 year may be found in previous publications [28, 53]. In addition to the dietary items used when computing the LS7 score described above, we also calculated a separate Mediterranean Diet (MedDiet) score using self-reported weekly-portion consumption of the 7 components indicative of the MedDiet (i.e., nonrefined grains, fruits, vegetables, potatoes, fish, legumes, and nuts) using the following scale: 0 = never, 1 = rare, 2 = frequent, 3 = very frequent, 4 = weekly, and 5 = daily consumption. This scale was reversed for consumption of the 3 components that were counter indicative of the MedDiet (i.e., red and processed meat, poultry, full-fat dairy). Alcohol consumption was scored separately, with higher scores given for more moderate daily alcohol consumption. The total MedDiet score ranged from 0 to 55, with higher scores representing greater MedDiet adherence. Four participants’ MedDiet scores were excluded from analyses due to implausibly low or high daily caloric intakes (<500 or >4,000 kcal for men and <400 or >3,800 kcal for women), which has been shown

to suggest invalid responding and inaccurate and/or skewed estimates of MedDiet adherence [54].

Covariates

All covariates were chosen given their known associations with our variables of interest, particularly our outcomes of modifiable health and lifestyle factors [55, 56]. Thus, in addition to age and sex, covariates included word reading and, for all analyses except those involving LS7, body mass index (BMI). Word reading was measured by raw scores on the 50-item Wechsler Test of Adult Reading (WTAR) [57] for individuals tested in English, and the 30-item Word Accentuation Test (WAT) [58] for individuals tested in Spanish. The WAT was developed to be equivalent to English language measures of word reading [59]; thus, we created a proportionate WAT score from raw totals using the following equation x=(WAT score*50)/30. WTAR and WAT scores were then converted to z-scores and used as a covariate in all analyses instead of years of education given that educational quality derived from word reading is more robustly associated with cognition in diverse populations than educational quantity derived from years of education [55]. BMI, calculated based on height and weight using the following formula: kg/m^2.

Statistical Analyses

In order to assess cognitive subgroups in our non-demented community-dwelling sample, we conducted a latent profile analysis (LPA; Mplus Version 8) using the following six cognitive raw scores: letter fluency, LNS, BNT, animal fluency, and verbal list-learning delayed free recall and recognition discriminability. Raw scores were used to maximize the variability in scores, though all variables were z-scored (M=0, SD=1) so that they were on the same scale prior to inclusion in the LPA [60, 61]. LPA uses a step-wise procedure, and a variety of fit indices and conceptual considerations to determine whether the addition of profiles improves the fit to the data [62]. We fit a one-profile (unconditional) model to the data, and we then increased the number of profiles one at a time until there was no additional improvement to the model [60, 61]. LPA fit statistics including the Bayesian Information Criterion (BIC), the Akaike Information Criterion (AIC), and the sample-size adjusted Bayesian Information Criterion (ABIC), were used to evaluate the resulting subgroups [63–65], with lower values indicating improved fit. Additionally, a Bootstrap Likelihood Ratio Test (BLRT) compared the model with *k* profiles to the model with *k*-1 profiles; if the BLRT *p*-value is significant, then the model with one additional profile is a better fit to the data than the model with one fewer profile. Monte Carlo simulation studies suggest that the BIC and BLRT are the most robust fit indices and thus were given the most weight [60]. Finally, profiles were examined to determine whether they were theoretically sound and clinically meaningful.

Following identification of LPA-derived cognitive subgroups, these groups were submitted to separate analyses of covariance (ANCOVA) to investigate between-group differences in participant characteristics, modifiable health and lifestyle factors. All analyses adjusted for age, sex, word reading, and (as relevant) BMI. Where significant, post-hoc analyses were performed using Fisher's Least Significant Difference (LSD) testing. All between-group analyses were conducted in SPSS Version 27, with significance set at $p \leq .05$ for primary

analyses and at $p \leq 0.007$ for our seven secondary outcomes (i.e., 0.05/7) given the number of additional comparisons they added to our statistical analyses.

RESULTS

Characteristics of the Entire Analytic Sample

Described in detail in Table 1, participants (N=121) were, on average, 67 years of age at time of testing (age range: 60 to 89) with approximately 15 years of education. Women comprised roughly half of the entire analytic sample. Over half of the analytic sample self-identified as either non-Latino Black or Latino. Average MMSE (28.62±1.42; min=25, max=30) and HAM-D scores (1.32±1.74; min=0, max=8) suggested study inclusion/exclusion criteria were successful in identifying non-demented, non-depressed participants. Lastly, of the 16 non-native English speakers in the entire analytic sample (13.2%), all were native Spanish speakers with the majority reporting Spanish as their dominant (n=14) or only (n=1) language. For the 14 reporting English as a second language (L2), average age of L2 acquisition was 20 years (19.61±12.85; min=5, max=50), with current L2 exposure estimated, on average, at 38% (min=0, max=97) when compared to L1; overall L2 proficiency was rated at 6.09±2.84 (min=0.67, max=10). Table 1 has additional LEAP-Q details.

Missingness ––Of the 121 participants enrolled in the overall study, 96 completed the SBQ and 97 completed the CHAMPS (all but 10 in English for both questionnaires), while 85 completed the FFQ (all but one in English). This was due, in part, to the late introduction of these questionnaires into our study. In direct comparisons, those with and without data from these questionnaires did not differ on key participant characteristic from Table 1 with the exception of age (p-values≤.043) and aspects of education (p-values≤.004). More specifically, participants who completed the SBQ, the CHAMPS, and the FFQ were *older* than participants that did not complete these questionnaires and had higher levels of word reading (SBQ and CHAMPS participants) or years of education (FFQ participants) (Supplemental Tables 1 and 2). As noted above, participants who completed the FFQ were less likely to be Latino or to have been tested in Spanish (p-values<.001) than participants that did not complete the FFQ. In order to maximize our analytic sample, we chose listwise deletion (as opposed to imputation methods) as our method for handling missing data. This approach allowed the number of participants, and hence the degrees of freedom in analyses reported below, to fluctuate based on available data. We report sample sizes by group in all reported analyses where they deviate from Table 1 reporting.

LPA-Derived Subgroups and Subgroup Characteristics

As shown in Table 2, the statistical fit indices supported the 4-profile solution as the best-fitting model; thus, we chose to interpret this model for use in our work. More specifically, the 4-profile solution resulted in consistently smaller BIC, AIC, and ABIC statistics, and the BLRT statistic was significant (p<.001). As demonstrated by Figure 1, the four cognitive subgroups included a high-average cognition subgroup (50.4% of the analytic sample, n=61) who scored +½ to 1 SD above the sample mean on all six cognitive test scores, an average cognition subgroup (25.6% of the analytic sample, n=31) who scored within ±½ SD of the

sample mean on all 6 cognitive test scores, and two subgroups reflective of lower memory (Memory; 15.7% or n=19) and lower executive functioning (Executive; 8.3% or n=10). Each of these lower subgroups scored within 0 to −1 SD below the sample mean on 5 of 6 test scores but had select difficulty on either memory or executive function tasks.

As seen in Table 3, LPA-defined subgroups did not differ in age (p=.358), word reading (p=.074), BMI (p=.316), or BAI (p=.083) scores; however, subgroups differed on sex (p=.011), race/ethnicity (p<.001), years of education (p<.001), and depressive symptoms as measured by the BDI (p=.002). More specifically, the high-average subgroup had disproportionately more women and more non-Latino Whites than the other three subgroups. Those with average cognition or lower memory were more likely to be male and self-identify as non-Latino Black. Individuals in the lower executive function subgroup were more likely to self-identify as Latino, to self-report fewer years of formal education, and to obtain higher scores on the BDI. Given these between-group differences, race/ethnicity and BDI scores were included as additional covariates in all analyses. Nonetheless, we remained confident about the non-depressed nature of our sample given that groups did not differ in HAM-D scores (p=.145).

LPA-defined subgroups did not differ on L2 exposure (p=0.084); although levels of self-rated proficiency in L2 speaking, F(3,13)=3.67, p=0.051, understanding, F(3,13)=4.33, p=0.034, and reading, F(3,13)=4.31, p=0.034 either approached or reached significance. This was driven primarily by 2 native Spanish speakers in the average cognition subgroup who appeared to be monolingual, i.e., they provided little to no data on L2 proficiency variables and chose to be tested in Spanish. Excluding these individuals and rerunning subgroup analyses on self-rated L2 proficiency, only reading proficiency approached, but did not reach, significance (p=0.057). We did not adjust for any LEAP-Q variable in our analyses.

LPA-Derived Subgroups and Modifiable Factors

Health ——The ANCOVA investigating group differences in 10-year risk of stroke using the FSRP-10 controlling for age, sex, race/ethnicity, word reading, BMI, and BDI indicated that there were no significant differences between groups, F(3, 110)=1.217, p=.307, η_p^2=.032. A similar fully-adjusted analysis was applied to the LS7 score (note BMI was not included as a covariate given it is part of the LS7 score). Results were not significant; this was regardless of whether we examined LS7 in the subset of 80 participants with complete LS7 data, F(3, 71)=1.387, p=.254, η_p^2=.0–55, or whether we modified the LS7 score to excluded diet and physical activity in order to increase the sample size to 113, F(3, 104)=0.411, p=.745, η_p^2=.012.

Secondary analyses for specific health components including individual blood pressure values and fasting blood levels were conducted controlling for age, sex, race/ethnicity, word reading, BMI, and BDI. Results were not significant for systolic blood pressure, F(3, 111)=0.340, p=.797, η_p^2=.009, pulse pressure F(3, 111)=0.478, p=.698, η_p^2=.013, or MAP, F(3, 111)=0.782, p=.506, η_p^2=.021. As may be seen by Figure 2, there was a significant difference between cognitive subgroups for fasting glucose levels, F(3, 109)=11.819, p<.001, η_p^2=.245, and hemoglobin A1c, F(3, 110)=12.090, p<.001, η_p^2=.248; both p=values

met our corrected threshold for significance. Pairwise comparisons suggested that the participants with lower executive performance had higher levels of fasting glucose and hemoglobin A1c compared to all other groups (all p-values<.001). There were no significant differences between groups in fully-adjusted models investigating total cholesterol, F(3, 109)=1.737, p=.164, η_p^2=.046, or triglyceride levels F(3, 109)=0.635, p=.594, η_p^2=.017.

Lifestyle ––There were no significant differences between cognitive subgroups for sedentary behavior [F(3, 86)=0.482, p=.695, η_p^2=.017] or MVPA scores [F(3, 86)=0.070, p=.976, η_p^2=.002] adjusting for age, sex, race/ethnicity, word reading, BMI, and BDI. In similarly adjusted analyses, there was a significant difference between cognitive subgroups for MedDiet consumption, F(3, 79)=3.677, p=.016, η_p^2=.123. Post-hoc Fisher's LSD analyses revealed participants with high-average cognition (n=47) had higher MedDiet scores than those with average cognition (n=23; p=.001; Figure 2).

Given that BMI is often seen as a modifiable lifestyle factor in its own right, we investigated cognitive subgroup differences in BMI (post-hoc) controlling for age, sex, race/ethnicity, word reading, and BDI. ANCOVA results did not indicate a significant differences between groups, F(3, 112)=1.918, p=.131, η_p^2=.049.

DISCUSSION

We characterized cognitive profiles using LPA on 6 cognitive parameters in a diverse cohort of 121 non-demented older adults and examined whether resulting cognitively-derived subgroups differed on modifiable factors known to be associated with ADRD and other domain-specific cognitive subgroups found in the literature. LPA fit indices supported a 4-profile solution that included two levels of normal cognition, i.e., high average and average, that represented the majority of participants and two smaller subgroups with either lower memory or lower executive functioning performance. Distinctions in cognitively-derived subgroups existed across several sociodemographic factors. Specifically, the high average cognitive subgroup was disproportionately non-Latino White and female, while those in the average cognitive and lower memory subgroups were disproportionately non-Latino Black adults and male; the lower executive function subgroup was more likely to self-identify as Latino and reported fewer years of education. Results investigating whether these resulting subgroups differed on health and/or lifestyle factors suggest the lower executive function subgroup differed from all other groups on blood glucose and hemoglobin A1c levels and the high average and average cognitive subgroups differed in Mediterranean Diet consumption. No other differences in modifiable factors were evident. Taken together, results suggest that even within a diverse group of non-demented older adults, cognitive profiles are discernible and have associations with select modifiable factors reflective not of composite scores of overall health (e.g., FSRP-10 or LS7) but of more specific cardiovascular and lifestyle components (i.e., blood levels and MedDiet adherence).

This study extends the cognitive literature in several ways. First, studies to date investigating cognitively-defined subgroups derived from multiple cognitive domains have primarily been conducted in overwhelmingly (≥90%) non-Latino White adults and/or clinical populations diagnosed with MCI or ADRD. Our study sample, only 40.5% non-Latino White, represents

a departure from this historic lack of diversity both in terms of race/ethnicity as well as recruitment. Specifically, our sample was additionally comprised of older non-Latino Black (44.6%) and Latino (15%) adults with all participants representing community-dwelling individuals not seen in or recruited from a memory clinic. Additionally, these same prior studies have shown that statistically-determined cognitive profiles exist across MCI and ADRD and cognitive subgroups of memory and executive function are highly prevalent [4, 5, 7, 11, 12, 66]. We extended this work to include cognitive profiles in a cohort of non-demented older adults albeit at lower levels of average (as opposed to impaired) memory and executive function performance. Our results also revealed that, much like there are two levels of mixed cognitively impaired subgroups often reported in MCI and ADRD research [4, 5, 11, 12, 66], there are two levels of 'normal' cognition in otherwise healthy individuals, specifically, high average and average. Our results are consistent with domain-specific studies of non-demented older adults that report two levels of average memory performance [17, 18], and extend this work to include two levels of average attention, executive functioning, and language performance as well. Third, we extended the investigation of statistically-derived cognitive subgroups derived from multiple cognitive parameters to include modifiable health and lifestyle factors. Although levels of sedentary behavior and physical exercise did not distinguish our cognitively-defined subgroups, there were subgroup differences in Mediterranean Diet consumption as well as individual cardiovascular disease risk factors. While our findings must be interpreted with caution given our generally small sample size and modest numbers of participants within each LPA-derived subgroup for these analyses, our work suggests that those working with non-demented individuals expressing concern about their cognitive health may point to the Mediterranean Diet as a lifestyle factor option that may be associated with better cognitive performance and cite high blood sugar levels as a health-related associate of lower executive performance.

The two levels of average cognition resulting from the LPA, i.e., high average and average, were distinguished by several sociodemographic factors including sex, race, and ethnicity. Women have been shown to outperform men on several of the measures used in our LPA including our verbally-mediated memory tasks with these differences in performance thought to reflect a number of biological differences [67]. In contrast, level differences in cognition between older Black and older White adults have no basis in biology but reflect differences in lived experiences between Black and White adults including systemic racism and discrimination experienced across the lifespan [68, 69]. How these social determinants negatively impact MedDiet consumption is less well understood [70]; however, increasing attention is being given to geospatial disparities resulting from historic redlining practices including supermarket readlining that results in food deserts and a subsequent lack of access to MedDiet-like foods [71]. We are actively investigating how these geospatial disparities may have contributed to our MedDiet results. The lower executive function subgroup while small in number, was 70% Latino. Patterns of language use across older monolingual and bilingual Latinos have been associated with executive function scores [72], and lived experiences of acculturation and discrimination may also negatively impact cognitive performance [73] as well as cardiovascular risk factor profiles including blood sugar levels [74] of Latinos. While sex as a biological variable and race and ethnicity as socially constructed ones may help explain the emergence of the cognitively-determined

subgroups in the current study (and the additional distinctions found therein), more work is needed exploring how sociodemographic factors and associated social determinants of health contribute to statistically-determined cognitive profiles using larger, yet equally diverse, cohorts of non-demented older adults.

It remains to be seen whether the cognitively-defined subgroups revealed in this study may be replicated, and whether they predict development of domain-specific subtypes of MCI or ADRD. While there is a temptation to liken our results to other studies of subtle cognitive decline [9, 12, 22], several distinctions make comparisons difficult including our use of raw scores and LPA as opposed to age-, sex-, and/or education-based normative scores for use with actuarial thresholding. In addition to our previously noted LPA methodological considerations for using raw scores, we chose to adjust for educational quality – a more robust cognitive associate than educational quantity in diverse populations [55] – rather than attempt to use years of education to norm our participant data. The issue of educational quantity versus quality is further illuminated by comparing years of education in the lower executive function group to their word reading scores; the former does not necessarily suggest the latter in this small primarily Latino sample. Lastly, our overall sample, albeit smaller than the analytic samples employed in studies of subtle cognitive decline [9, 12, 22], was more diverse consisting of only 40% non-Latino White to their larger >90% non-Latino White participant group. Regardless of these distinctions, mounting evidence suggests that investigating cognitively-determined profiles in non-demented older adults either using core parameters from mulitiple cognitive tests or investigating domain-specific trajectories of decline [17, 18, 25] may be an important, and relatively more accessible means by which to predict neurodegeneration [20] than PET- and/or CSF-based biomarker data.

Results of this study should be interpreted within a larger discussion of its limitations. In addition to lacking metrics on systemic factors like racism or discrimination to better understand differences in our cognitive-determined subgroups, the cross-sectional nature of this study makes it impossible to determine causality in our reported dietary relationships. There is evidence to suggest that LNS, a test measure used in our LPA, may underestimate performance in Latino participants in the US [35]; this, combined with the small number of participants in the lower executive function subgroup more generally – only 8% of the overall sample – suggest less emphasis should be placed on results related to this subgroup. Additionally, although native Spanish speakers were present (with some tested in Spanish) across all subgroups, LEAP-Q results would suggest that levels of bilingualism may have varied, particularly in reading proficiency. Given our small sample of native Spanish speakers, how this may (or may not) have impacted our results is difficult to determine and requires further investigation in a larger sample. Despite the fact that participants were screened for cognitive impairment and depressive symptoms at study entry, six individuals (4.95% of the sample) met Jak-Bondi actuarial neuropsychological criteria for MCI based on sample-derived z-scores [11], and cognitively-derived subgroups differed in depressive symptoms. Sample-derived z-scores may have underestimated performance as outlined above, and while self-reported depressive symptoms may have differed by subgroups, HAM-D scores did not. Furthermore, both BDI and HAM-D scores were below cut-points for clinical depression. As with all LPA analyses, variables for inclusion were chosen a priori based on previous research [4]; this may have biased our resulting subgroups as different

choices of variables for inclusion may have resulted in different subgroups. Lastly, we relied on self-report measures of some modifiable risk factors that may have disadvantaged the low cognition subgroups; however, we would note that the low cognition subgroups did not show differences (or even uniformly low scores) in these self-report metrics.

Strengths of this study include its diverse sample, including 60% non-Latino Black and Latino participants, as well as its detailed evaluation of cognition and multiple primary and secondary modifiable health and lifestyle factors including both composite scores of overall health (e.g., FSRP-10 or LS7) and more specific health components (e.g., blood pressure, blood levels, and MedDiet adherence). This study not only extended the concept of cognitively-defined subgroups derived from core cognitive parameters taken from multiple cognitive tests to include normal aging in a diverse community-based cohort, but it is one of the first using this specific approach to investigate these cognitive profiles as they relate to modifiable cardiovascular and lifestyle factors including physical health and activity, sedentary behavior, and diet. It suggests that associations between levels of cognition including average and high average as well as lower memory and/or executive function are a complex exchange of sex-differences and social determinants of health that may underlie not only profiles of cognitive aging but their associates with select cardiovascular and lifestyle choices. If replicated and validated with larger, longitudinal studies, our results may lay the foundation for a more inclusive approach to identifying cognitively-determined subgroups in otherwise healthy older adults that considers the lived experiences of participating individuals and the role of social determinants of health to provide more precise approaches to promote cognitive health and successful cognitive aging for *all* older adults.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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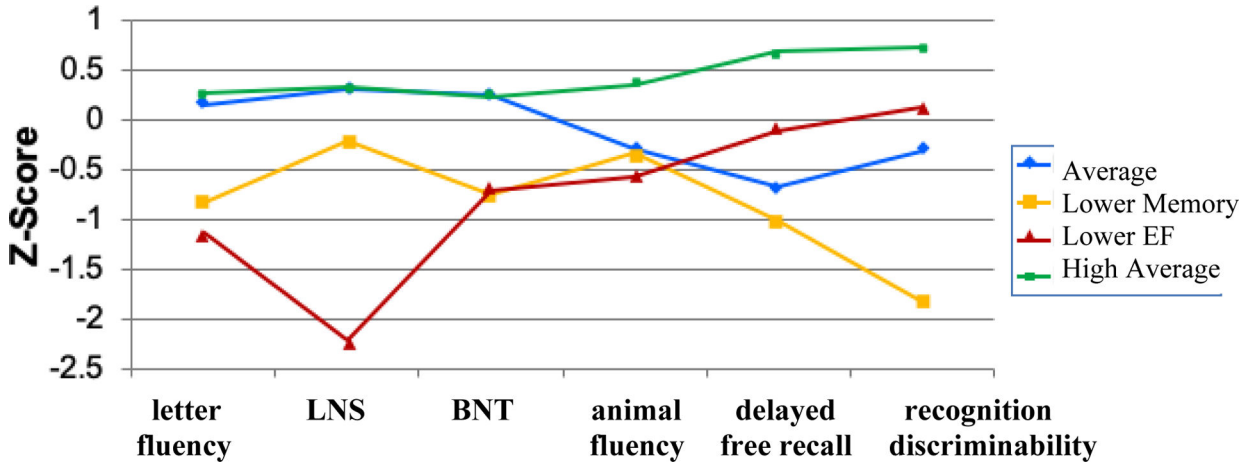

Figure 1.

Plot of the averaged z-scored cognitive test items used in the latent profile analysis including letter fluency ('FAS' or 'PMR'), letter-number sequencing (LNS), Boston Naming Test (BNT), animal fluency, and delayed free recall and recognition discriminability from verbal list-learning and memory testing by LPA-derived cognitive subgroups; EF=executive functioning.

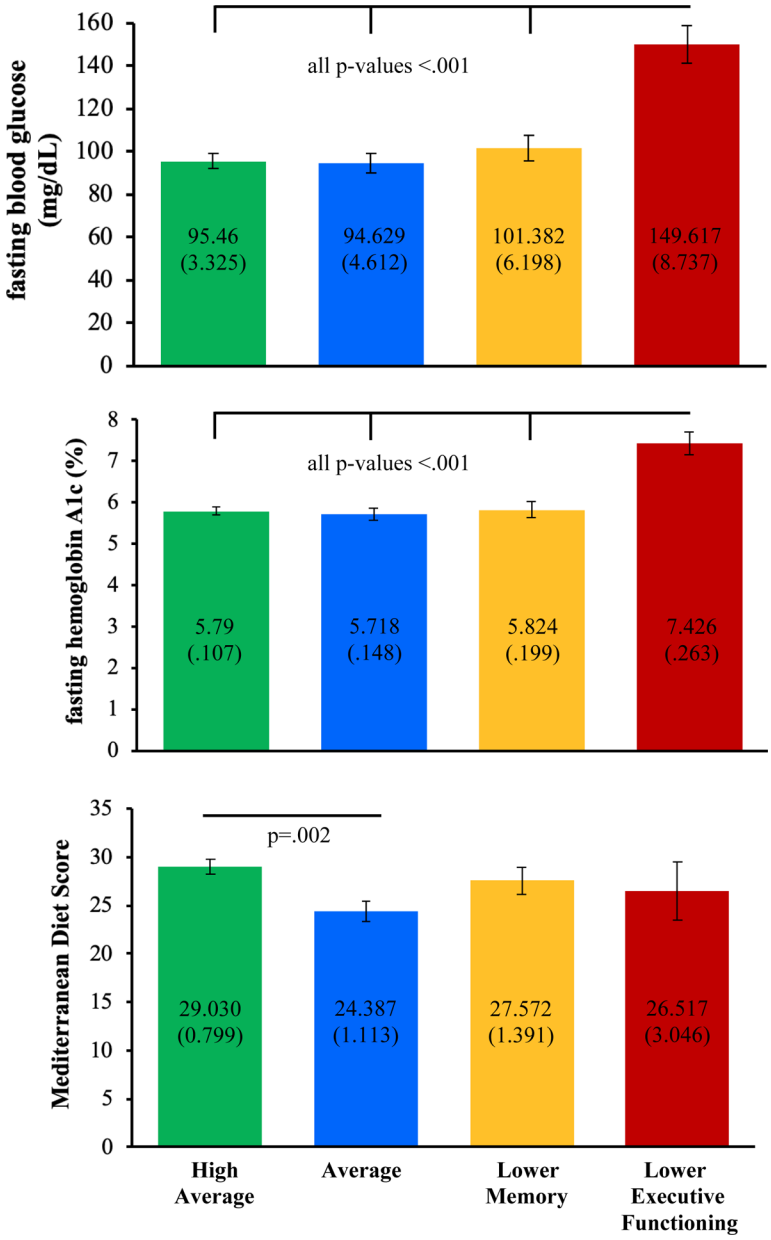

Figure 2.

Results of LPA-derived cognitive subgroup differences for modifiable cardiovascular and lifestyle variables. Graphs display estimated means and standard errors adjusting for age, sex, race, word reading, body mass index, and Beck Depression Inventory scores by LPA-derived cognitive subgroups.

Table 1.

Analytic sample characteristics

Characteristic	N=121
Age, years	67.69 (6.63)
Female, %	49.6
Race/Ethnicity, %	
Non-Latino White	40.5%
Black	44.6%
Latino	14.9%
Spanish used for Testing, %	8.3%
LEAP-Q defined native Spanish speaker, %	13.2%
Current exposure to English (i.e., L2)*, %	37.86%
Self-rated English (i.e., L2) proficiency*	
Speaking	6.54 (2.29)
Understanding	6.69 (2.05)
Reading	6.31 (3.22)
Word Reading (max=50)	38.4 (10.41)
Degree Years of Education	14.83 (3.26)
Body Mass Index, kg/m^2	28.94 (5.99)
BDI Total (max=63)	3.63 (4.31)
BAI Total (max=63)	2.95 (4.14)

Values are mean (SD) and for the entire analyltic sample unless otherwise stated.

Note: LEAP-Q = Language Experience and Proficiency Questionnaire [42]; L2 = second language of native Spanish speakers *(n=16 reporting); Word Reading derived from either the Wechsler Test of Adult Reading [57] for participants tested in English or the Word Accentuation Test [58] for individuals tested in Spanish; BDI = Beck Depression Inventory; BAI = Beck Anxiety Inventory.

Table 2.

Fit indices for latent profile analysis (LPA) models with 1 to 5 profiles

Number of profiles	Number of free parameters	Log likelihood	AIC	BIC	ABIC	BLRT	entropy
1	12	−1003.015	2030.029	2063.579	2025.639	0	1
2	19	−942.468	1922.936	1976.056	1915.984	0	0.81
3	26	1893.846	1966.536	1966.536	1884.333	0	0.875
4	**33**	**-898.924**	**1863.849**	**1956.110**	**1851.775**	**0**	**0.875**
5	40	−880.870	1841.739	1953.571	1827.105	0	0.829

Bolded values indicate the best fitting model.

Note: AIC=Akaike information criterion; BIC=Bayesian information criterion; ABIC=sample-size adjusted BIC; BLRT=Bootstrap Likelihood Ratio Test.

Table 3.

LPA-derived subgroup characteristics

LPA Profile Characterization	High Average	Average	Lower Memory	Lower Executive Functioning
	+½ to 1 SD above mean	Within ±½ SD of mean	0 to −1 SD below mean on 5/6 tests	0 to −1 SD below mean on 5/6 tests
n	61	31	19	10
Age, years	68.57 (6.93)	67.00 (5.99)	65.68 (6.17)	68.40 (7.32)
Female, %§	63.9	32.3	31.6	50.0
Race/Ethnicity, %§				
Non-Latino White	55.7	32.2	26.3	0.0
Black	36.1	58.1	57.9	30.0
Latino	8.2	9.7	15.8	70.0
Spanish used for Testing, %	1.6 (n=1)	6.5 (n=2)	0 (n=0)	70 (n=7)
native Spanish speaker, n	4	2	3	7
L2/English exposure, %	46.98 (37.69)	0 (0)	70.00 (20.00)	24.28 (21.49)
L2/English proficiency				
Speaking	7.75 (0.95)	0	7.50 (3.53)	5.57 (2.37)
Understanding	7.75 (0.95)	2	8.50 (2.12)	5.57 (1.98)
Reading	8.25 (0.95)	0	9.00 (1.41)	4.43 (3.30)
Word Reading (max=50)	40.02	38.00	33.00	39.96
Degree Years of Education*	15.89 (2.98)	14.42 (2.79)	14.42 (2.69)	10.40 (3.41)
Body Mass Index	29.45 (5.68)	29.45 (7.64)	26.60 (4.31)	28.72 (4.27)
BDI Total* (max=63)	3.80 (4.18)	2.45 (2.72)	2.63 (3.11)	8.10 (7.61)
BAI Total (max=63)	3.18 (4.04)	2.19 (3.11)	2.00 (2.77)	5.70 (7.12)
HAM-D Total (max=53)	1.38 (1.64)	1.00 (1.78)	1.00 (1.32)	2.40 (2.41)

Values are mean (SD) unless otherwise stated;

* Independent-samples t-test, $p < .05$;

§ χ^2, $p < .05$

Note: L2 = second language of native Spanish speakers (n=16) as determined by the Language Experience and Proficiency Questionnaire [42]; Word Reading derived from either the Wechsler Test of Adult Reading [57] for participants tested in English or the Word Accentuation Test [58] for individuals tested in Spanish; BDI = Beck Depression Inventory; BAI = Beck Anxiety Inventory; HAM-D = Hamilton Depression Rating Scale.