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Longitudinal associations between dietary quality and Alzheimer's disease genetic risk on cognitive performance among African American adults

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Abstract

Poor diet quality (DQ) is associated with poor cognition and increased neurodegeneration, including Alzheimer's disease (AD). We are interested in the role of DQ on cognitive functioning (by sex and increasing genetic risk for AD), in a sample of African American (AA) middle-aged adults. We analysed a sub-group of participants (about 55 % women; mean follow-up time of about 4·7 years) from the Healthy Aging in Neighborhoods of Diversity across the Life Span study with a genetic risk score for AD (hAlzScore). The Healthy Eating Index-2010, Dietary Approaches to Stop Hypertension and the mean adequacy ratio computed at baseline (2004–2009) and follow-up visits (2009–2013) were used to assess initial DQ and change over time. Linear mixed-effects regression models were utilised, adjusting for select covariates, selection bias and multiple testing. DQ change (ΔDQ) was associated with California Verbal Learning Test-List A – overall (0·15 (SE 0·06), $P = 0·008$) and in women (0·21 (SE 0·08), $P = 0·006$), at highest AD risk, indicating protective effects over time. Greater AD risk was longitudinally associated with poorer Clock Command Test scores in men. Poor DQ was positively and cross-sectionally associated with Trails B scores, but in women only. Better-quality diet was associated with a slower decline in verbal memory among AA women, with greater AD risk. Insufficient clinical evidence and/or mixed findings dictate that more studies are needed to investigate brain morphology and volume changes in relation to DQ in an at-risk population for AD, over time.

Key words: **Alzheimer's disease: Genetic risk: Diet quality: Cognitive decline: Health disparities: Adults**

Diet quality (DQ) has profound and long-term consequences on cognitive function[1–3]. An emerging literature is reporting protective benefits of some dietary factors (such as vitamins D and E, PUFA, etc.) against cognitive decline as well as delayed onset and progression of Alzheimer's disease (AD)[4–6]. Vitamin D has been implicated in cognitive decline due to possible neuronal loss with reduced number of vitamin D receptors in brain regions like the hippocampus and AD risk because of lower hippocampal vitamin D receptor mRNA[7]. PUFA (and their precursors) have numerous beneficial effects for improved brain health and cognition via optimal neurotransmission, better cell survival and reducing neuroinflammation in addition to influencing fluid intelligence, memory, gray and white matter volume and related microstructures[8]. Epidemiological evidence demonstrates a role for dietary intervention in the primary prevention of chronic diseases, even in old age[9]. Increasing evidence implicates certain dietary patterns as beneficial to brain health[1,5,10]. For instance, the Mediterranean diet, typically characterised by higher intakes of fruit, vegetables, whole grains, fish, unsaturated fatty acids and moderate alcohol consumption, is important for its role in preserving cognitive health[11]. A systematic review from 2016 found memory (i.e. delayed recognition, long-term and working memory), executive function and visual constructs benefited from Mediterranean

Abbreviations: AA, African American; AD, Alzheimer's disease; BVRT, Benton Visual Retention Test; CVLT, California Verbal Learning Test-List A; DASH, Dietary Approaches to Stop Hypertension; DQ, diet quality; ΔDQ, DQ change; hAlzScore, HANDLS Alzheimer's risk score; HANDLS, Healthy Aging in Neighborhoods of Diversity across the Life Span; HEI, Healthy Eating Index; MAR, mean adequacy ratio; MIND, Mediterranean-DASH Intervention for Neurodegenerative Delay; NAR, nutrient adequacy ratio.

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‡ S. H. had full access to the data used in this paper and completed all the statistical analyses.

diets[2]. However, the study population was predominantly White across the board, with a couple of exceptions that included Hispanic participants. Another recent review looking into the Mediterranean, Dietary Approaches to Stop Hypertension (DASH) and Mediterranean-DASH Intervention for Neurodegenerative Delay (MIND) diets suggested that higher adherence to these diets is associated with less cognitive decline and a lower risk of AD[12]. Diet that is very similar to a Mediterranean diet in composition, also widely used and recommended in the USA, is the DASH[13] diet. While most primary studies on DQ and cognition focused on one or possibly two DQ measures, this study aimed to expand the current literature on three validated scoring systems to measure DQ, establishing a comprehensive approach.

There is a paucity of research on association studies investigating diet and cognitive performance/decline among different racial groups in the progression of AD[14–18]. In fact, most research on the relation of race to cognitive function in AD has been cross-sectional[19]. Longitudinal studies assess rates of cognitive decline, but few have examined the association between cognitive decline[20] and DQ with genetic risk for AD. African Americans (AA) in particular suffer from higher incidence rates of AD, perhaps due to undiscovered genetic factors, disproportionately higher rates of risk factor diseases[21] (such as diabetes and stroke), biological or environmental exposures that erode 'cognitive reserve' which may protect against or accelerate disease expression or detection bias of existing testing methods[22]. They also struggle to adhere to a healthy diet more than their White counterparts[23–25].

In the present study, we examined the cross-sectional and longitudinal relationships of DQ and cognition in a socio-economically diverse sample of AA middle-aged adults. We hypothesised that initial better DQ would be associated with higher baseline cognitive functioning. We also examined whether those relationships differ across sex and by increasing genetic risk for AD.

Materials and methods

Database

Healthy Aging in Neighborhoods of Diversity across the Life Span (HANDLS) is a prospective cohort study initiated in 2004 to investigate health disparities in medical, metabolic and cognitive outcomes in a socio-economically diverse sample of Whites and AA (30–64 years old at baseline) recruited from selected neighbourhoods in Baltimore, MD. Initial data were collected in two phases (visit 1: 2004–2009). Phase 1 consisted of screening, recruitment, first 24-h dietary recall and household interviews in participants' homes. Phase 2 consisted of the second 24-h dietary recall and physical examinations in mobile medical research vehicles. The first follow-up examinations were performed approximately 5 years later (visit 2: 2009–2013; mean follow-up time of 4·62 (SE 0·95) years; range: 0·42–8·20) at which two 24-h dietary recalls were also collected. Neuropsychological tests were administered at both visits on the medical research vehicles. The numbers of participants with at least one of the eleven cognitive test scores at visits 1 or 2, dietary and covariate data at baseline ranged from 123 to 228 ($k = 1·70–1·95$ observations per participant), which yielded 5–15 % ($k = 1·0–1·7$) missing observations.

Written informed consent was obtained from all participants at each visit during which they were provided with a protocol booklet in layman's terms and a video that described all procedures and future re-contacts. HANDLS study was ethically approved by the National Institutes of Health, National Institute of Environmental Health Sciences Institutional Review Board.

Study sample

The initial HANDLS sample was recruited at visit 1 (n 3720) with complete data on demographics. In this study, we excluded participants from European ancestry (n 1522) due to non-availability of genetic data in this group and examined only AA participants (n 2198). Restricting our sample to participants over 50 years (n 979) and then excluding participants with missing data on valid cognitive tests, dietary assessment and genetic polymorphisms yielded a sample of 342 at visit 1 and 268 at visit 2. We restricted our sample to 'over 50 years' for a greater variability in cognitive decline measures across both racial groups compared. We calculated change in DQ over time for visit 1 (n 244) and visit 2 (n 249). After excluding participants with incomplete covariate data, our final sample for analyses was 228 for visit 1 and 230 for visit 2 (Fig. 1). This sample selectivity was adjusted for using a two-stage Heckman selection model[26].

Cognitive measures

A cognitive battery of tests was administered to participants consisting of Mini-Mental State Examination; California Verbal Learning Test-List A (CVLT-List A); CVLT-Free Recall Long Delay; Benton Visual Retention Test (BVRT); Brief Test of Attention; Trailmaking Test A (Trails A); Trailmaking Test B (Trails B); Digits Span Forward Test; Digits Span Backward Test; Clock Command Test; Identical Pictures Test; Card Rotation Test and Animal Fluency Test. Details of these tests are available in Appendix 1 in online Supplementary Material. Except for the BVRT and the Trailmaking Tests, higher scores reflect better cognition. For BVRT and Trailmaking Tests parts A and B, better performance on BVRT was measured by fewer errors; the Trailmaking Tests were measured by faster performance. Cognitive performance test scores at baseline (visit 1), follow-up (visit 2) and change between visits, by sex, for HANDLS participants >50 years are presented in online Supplementary Table S1.

Genetic data

In total, 1024 HANDLS participants were successfully genotyped to 907 763 SNP at the equivalent of Illumina 1M array coverage. Sample exclusion criteria were (1) call rate <95 %, discordance between self-reported sex and sex estimated from X-chromosome heterogeneity, cryptic relatedness, discordance between self-reported African ancestry and ancestry confirmed by genetic data. SNP exclusion criteria were (1) Hardy–Weinberg

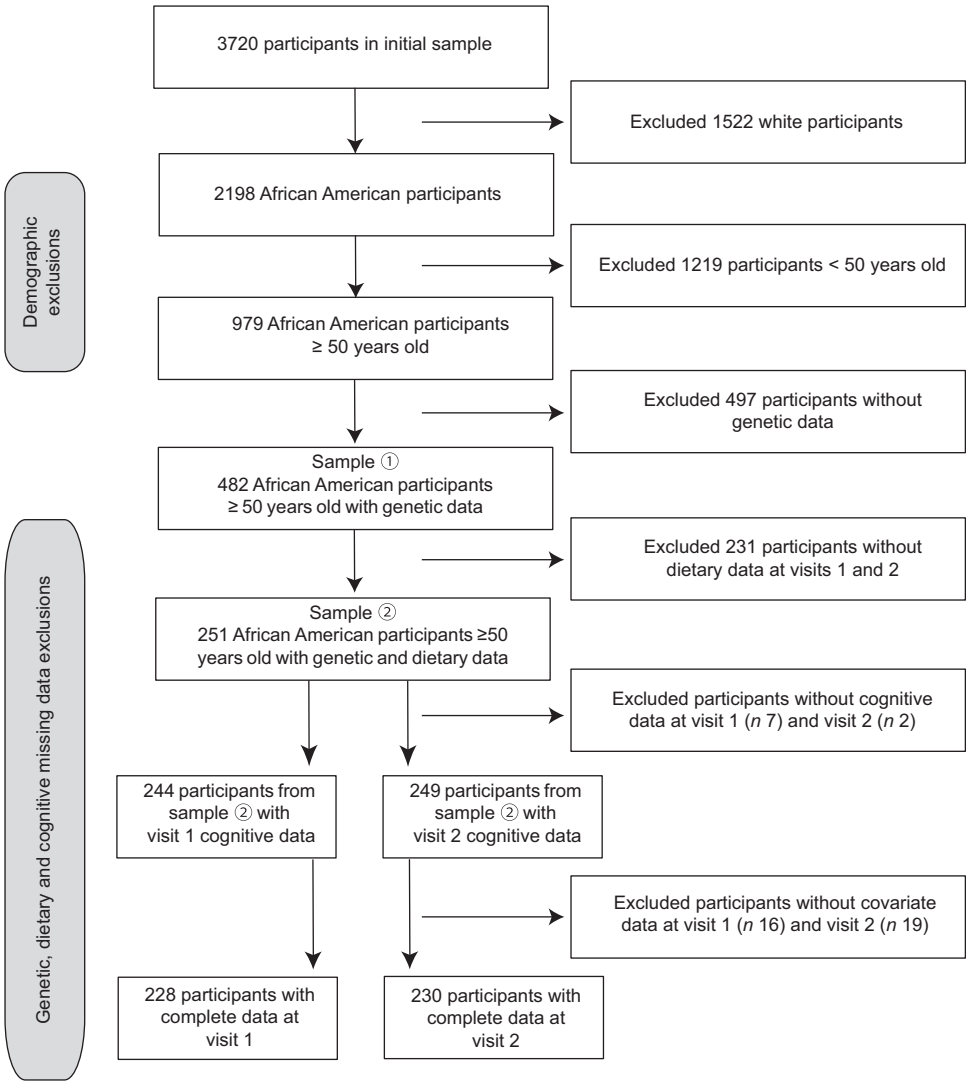

Fig. 1. Participant flowchart. Numbers of participants varied from 123 to 228 because there were missing data on cognitive tests ($k = 1{\cdot}70–1{\cdot}95$ observations/participant).

equilibrium *P*-value <10–7, (2) minor allele frequency <0·01 and (3) call rate <95 %. Genotype quality control and data management were conducted using PLINKv1.06 (PMID: 17701901). Cryptic relatedness was estimated via pairwise identity by descent analyses in PLINK and confirmed using RELPAIR (PMID: 11032786). HANDLS participant genotypes were imputed using MACH/minimac version 2.0 (https://genome.sph.umich.edu/wiki/Minimac) based on combined haplotype data for the 1000 Genomes Populations project phase 3 version 5 multi-ethnic reference panel. Our final sample includes subjects with complete genetic data as they are further narrowed down by the availability of complete dietary, cognitive and covariate information.

Genetic risk score calculation

Previously reported genetic variants at specific genetic loci implicated with phenotypes of AD were used for genetic risk score calculation (online Supplementary Table S2). Of the 130 reported genetic variants, seventy-seven had valid SNP identifier. Seventy out of seventy-seven SNP had imputed genotype data in the HANDLS study. After excluding two SNP with poor imputation quality score ($R^2 < 0{\cdot}30$), there were sixty-eight SNP for the final analysis. These SNP were then screened for significant associations with the Mini-Mental State Examination from the published literature. This was primarily because few studies used more than two tests (including Mini-Mental State Examination) to measure cognitive performance. Only twelve of the sixty-eight showed a significant association with baseline cognitive performance, across sex, age, race and geographical location[27–34]. The genotype dosages of the risk alleles of these twelve SNP were used for the calculation of the HANDLS AD genetic risk score (hAlzScore). The online Supplementary Table S2 describes those SNP. Table 1 presents with individual SNP and hAlzScore correlation. The SNP were located on the following genes: transferrin, *TF* (*n* 1); cystatin 3, *CST3* (*n* 1); presenilin 1, *PSEN1* (*n* 1); prion protein, *PRNP* (*n* 1); insulin

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Table 1. Individual SNP* correlations with hAlzScore (genetic risk score for Alzheimer's disease (AD) in Healthy Aging in Neighborhoods of Diversity Across the Life Span (HANDLS))†

	hAlzScore	rs1049~C	rs1064~A	rs1659~T	rs1799~A	rs2251~T	rs2306~C	rs4055~A	rs4291_A	rs4343_A	rs4496~A	rs4806~C	rs4845~G
hAlzScore	1·00												
rs1049296_C	0·23	1·00											
rs1064039_A	0·32	0·03	1·00										
rs165932_T	0·32	0·03	0·03	1·00									
rs1799990_A	0·36	−0·007	0·02	0·06	1·00								
rs2251101_T	0·23	0·03	0·004	0·007	0·03	1·00							
rs2306604_C	0·40	0·02	0·05	0·01	0·01	0·05	1·00						
rs405509_A	0·16	−0·03	−0·03	−0·07	0·03	−0·07	0·06	1·00					
rs4291_A	0·37	0·02	−0·05	0·02	0·009	0·01	−0·01	−0·03	1·00				
rs4343_A	0·31	−0·001	−0·004	−0·04	−0·02	−0·02	−0·03	0·02	0·11	1·00			
rs449647_A	0·17	−0·01	0·04	−0·002	−0·03	0·01	−0·007	−0·43	0·03	−0·05	1·00		
rs4806173_C	0·33	−0·002	−0·004	0·02	−0·03	−0·03	0·03	−0·03	−0·004	0·02	0·0230	1·00	
rs4845378_G	0·21	0·03	−0·02	0·02	0·01	−0·006	0·01	0·02	0·02	0·01	−0·01	0·003	1·00

TF, transferrin; *CST3*, cystatin 3; *PSEN1*, presenilin 1; *PRNP*, prion protein; *IDE*, insulin degrading enzyme; *TFAM*, transcription factor A, mitochondrial; *ACE*, angiotensin I converting enzyme; *GAPDH*, glyceraldehyde-3-phosphate dehydrogenase; *CHRNB2*, cholinergic receptor nicotinic beta 2 subunit.
* SNP dosages that were reverse-coded to create the hAlzScore, due to alternative allele increasing the risk of AD: rs165932, rs1799990, rs449647, rs4806173 and rs4845378.
† Genes/SNP: *TF* (rs1049296_C), *CST3* (rs1064039_A), *PSEN1* (rs165932_T), *PRNP* (rs1799990_A), *IDE* (rs2251101_T), *TFAM* (rs2306604_C), *APOE-ε2* (rs405509_A), *ACE* (rs4291_A), *ACE* (rs4343_A), *APOE-ε2* (rs449647_A), *GAPDHS* (rs4806173_C) and *CHRNB2* (rs4845378_G).

degrading enzyme, *IDE* (*n* 1); transcription factor A, mitochondrial, *TFAM* (*n* 1); *APOE* (*n* 2); angiotensin I converting enzyme, *ACE* (*n* 2); glyceraldehyde-3-phosphate dehydrogenase, *GAPDH* (*n* 1) and cholinergic receptor nicotinic beta 2 subunit, *CHRNB2* (*n* 1).

Diet quality assessment

Method. All 24-h dietary recalls were collected using the United States Department of Agriculture computerised automated multiple-pass method[35]. The automated multiple-pass method was designed to provide prompts throughout all five steps of the recall to capture all the foods and drinks consumed throughout the previous day. The steps are described in detail elsewhere[13]. Trained interviewers provided an illustrated food model booklet, rulers and measuring cups and spoons to participants to help them estimate accurate quantities of foods and beverages consumed. The approximate time between recalls was 4–10 d. Each recall was coded using the United States Department of Agriculture Survey Net data processing system, matching foods consumed with codes in the Food and Nutrient Database for Dietary Studies[36]. Of the 3720 participants examined at visit 1, 2177 individuals and at visit 2, 2140 persons completed two 24-h dietary recalls.

Healthy Eating Index 2010. Food-based DQ was also evaluated with the Healthy Eating Index 2010 (HEI-2010). The National Cancer Institute's Applied Research website provided the basic steps for calculating the HEI-2010 component and total scores and statistical codes for 24-h dietary recalls[37]. A detailed description of the procedure used for this study is available on the HANDLS website[38]. The HEI-2010 includes twelve components, nine of which assess adequacy of the diet and the remaining three should be consumed in moderation. The nine components are: (1) total fruit; (2) total vegetables; (3) whole fruit; (4) greens and beans; (5) whole grains; (6) dairy products; (7) total protein foods; (8) seafood and plant proteins and (9) fatty acids. Refined grains, Na and empty energy content reflect components that should be consumed in moderation[39]. Component and total HEI-2010 scores were calculated for each recall day and were averaged to obtain the mean for both days combined.

Dietary Approaches to Stop Hypertension. The score for DASH diet adherence, based on nine nutrients, was determined for each participant using the formula reported by Mellen *et al.*[40]. The nine target nutrients were total fat, saturated fat, protein, fibre, cholesterol, Ca, Mg, Na and K. Micronutrient goals were expressed per 1000 kcal. The total DASH score was generated by the sum of all nutrient targets met. If the participant achieved the DASH target for a nutrient, a value of 1 was assigned, and if the intermediate target for a nutrient was achieved, a value of 0·5 was assigned. A value of zero was assigned if neither target was met. The maximum DASH score was 9; individuals meeting approximately half of the DASH targets (DASH score = 4·5) were considered DASH adherent[40].

Mean adequacy ratio. DQ was also assessed using nutrient adequacy ratio (NAR) for seventeen micronutrients and mean adequacy ratio (MAR) scores[41,42]. The NAR score was determined

by dividing each participant's daily intake of a micronutrient divided by the RDA for that micronutrient. The micronutrients were vitamins A, C, D, E, B_6, B_{12}, folate, Fe, thiamin, riboflavin, niacin, Cu, Zn, Ca, Mg, P and Se. The RDA was adjusted for participants' ages and sexes, and vitamin C was adjusted for smokers[43]. The NAR score was converted into percentage with values exceeding 100 truncated to 100. The formula used to calculate the MAR score was: MAR = (ΣNAR scores)/17[44]. NAR and MAR were calculated separately for each daily intake and then averaged. MAR scores represented nutrient-based DQ since they were based on intakes of foods and beverages and no supplements.

Diet quality score. Two principal components analyses[45] were conducted whereby baseline DQ indices (HEI-2010, DASH and MAR) as well as their annual rates of change were reduced into two measures, namely DQ and DQ Change (ΔDQ), respectively, using the Kaiser rule for component extraction (Eigen value > 1) and examining the scree plot. In both cases, 46–54 % of the total variance was explained by the single component[45]. Those measures were used in the main analysis, for data reduction purposes.

Covariates

Socio-demographic, lifestyle and health-related potential confounders. All regression models adjusted for socio-demographic factors, namely age, sex, race, educational levels (less than high school coded as '0'; high school coded as '1'; and more than high school coded as '2') and poverty status (below *v.* above 125 % the federal poverty line). Additional adjustment factors include BMI (kg/m^2), current drug use ('opiates, marijuana or cocaine' = 1 *v.* not = 0) and current smoking status ('never or former smoker' = 0 *v.* 'current smoker' = 1). These models were further adjusted for self-reported history of type 2 diabetes, hypertension, dyslipidaemia, CVD (stroke, congestive heart failure, non-fatal myocardial infarction or atrial fibrillation), inflammatory disease (multiple sclerosis, systemic lupus, gout, rheumatoid arthritis, psoriasis, thyroid disorder and Crohn's disease) and use of non-steroidal anti-inflammatory drugs (prescription and over-the-counter) during visit 1.

Statistical analysis. Stata 15.0 (StataCorp) was used to conduct all analyses. First, participants' characteristics, including covariates and exposures, were compared by sex using *t* tests for continuous variables and χ^2 tests for categorical variables. Second, several mixed-effects regression models on continuous initial DQ and ΔDQ scores calculated from total scores of HEI-2010, MAR and individual components were conducted to test associations with cognitive performance measures, while adjusting for potential confounders. We used linear mixed-effects models to characterise the overall pattern of change in cognitive function and to examine the relation of a specific predictor (e.g. DQ or hAlzScore) to initial level of cognitive function and annual rate of change. In this approach, both initial level of cognition and individual rate of change are explicitly modelled as sources of random variability and possible correlates of how rapidly cognition changes. Everyone is assumed to follow the mean path of the group except for random effects which cause the initial level of cognition to be higher or lower and the rate of change to be faster or slower. Thus, we added a random effect for the intercept and another for the slope. Specifically, each model included years elapsed between visits (*TIME*), exposures/covariate main effects and two-way interaction terms between *TIME* and exposures/covariates. We assumed the unavailability of outcomes to be missing at random[46]. Sex-specific associations were examined through stratified analyses separately among men and women. Effect modification by sex was formally tested for effects of hAlzScore/DQ/ΔDQ on baseline cognitive performance (two-way interaction terms) and on cognitive change over time (three-way interaction terms). These models were adjusted for covariates (see Covariates section) that include socio-demographics, lifestyle and health-related factors. Scores for Trails A and B were log-transformed before modelling due to the extreme distribution of both. All other cognitive tests were not skewed.

Three sets of models were tested: (1) models with hAlzScore as the main predictor, for cross-sectional and longitudinal cognitive performance, (2) models with DQ and ΔDQ as the main predictors for cross-sectional and longitudinal cognitive performance and (3) models with DQ and ΔDQ interacting with hAlzScore to determine cross-sectional and longitudinal cognitive performance. In addition, to test for clinical significance, the exposures and outcomes were transformed into *z*-scores. They were then run in the same mixed models in lieu of the unstandardised variables, and the effect sizes were noted. An effect size >0·2 was considered strong, while >0·1 was moderate.

To account for multiple testing, given that there were two exposures, type I error was reduced to 0·05/2 = 0·025 for main effects and for interaction terms for the mixed-effects regression models. Three-way interaction terms were deemed statistically significant at an α-error level of 0·05.

Results

Descriptive findings are outlined in Table 2. Women had higher HEI-2010 and DASH scores than men represented by means across visits (48·0 and 2·3 *v.* 43·6 and 1·4, $P = 0·03$ and $P = 0·004$), respectively. Other notable differences include current smoking status, current use of illicit drugs and BMI. Table 3 displays findings from the linear mixed-effects regression models for hAlzScore on cognitive test performance over time. After adjustment for multiple testing, none of the tests was associated with hAlzScore longitudinally, except Clock Command in men (0·04 (SE 0·01), $P = 0·01$), showing a protective effect. However, hAlzScore was significantly associated with a decline in CVLT-DFR (−0·41 (SE 0·14), $P = 0·004$) in men and BVRT (0·69 (SE 0·26), $P = 0·009$) in women. Other longitudinal effects were inconsistent overall and within sex. Table 4 presents the associations between DQ and cognitive change by time. None of the tests survived multiple testing, except Trails B in women: longitudinal association with ΔDQ reflecting a worsening of performance (−0·04 (SE 0·01), $P = 0·01$). We also conducted a sensitivity analysis with total energy intake (data not shown) that did not affect our current findings.

Online Supplementary Table S3 shows cross-sectional (baseline *v.* baseline) and longitudinal (baseline *v.* change, change *v.* change) associations between cognitive test scores

Table 2. Characteristics of Healthy Aging in Neighborhoods of Diversity across the Life Span (HANDLS) study participants (>50 years) by sex (mean across waves)
(Mean values with their standard errors; percentages)

	By sex				
	Men (*n* 102)		Women (*n* 126)		*P**
	Mean	SEM	Mean	SEM	Men *v.* women
Main exposures					
HEI-2010	43·6	1·4	48·0	1·6	0·03
DASH	1·4	0·1	2·3	0·2	0·004
MAR	80·5	1·7	76·4	2·4	0·17
hAlzScore	12·7	0·2	12·4	0·2	0·36
Changes in diet quality					
Delta HEI-2010	1·0	0·4	0·5	0·3	0·29
Delta DASH	−0·0	0·02	−0·9	0·04	0·10
Delta MAR	−0·5	0·4	−0·4	0·4	0·86
Diet PCA score	−0·01	0·2	−0·2	0·2	0·17
Socio-demographic characteristics					
Age (years)	57·1	0·5	56·0	0·8	0·22
African American (%)	44·7		55·3		0·80
Education (%)					
<HS	8·8		6·4		0·59
HS	51·0		57·1		
>HS	40·2		36·5		
PIR ≥ 125 % (%)	60·0		73·0		0·89
Lifestyle and health-related factors					
Current smoking status (%)	47·1		32·5		0·03
Current use of illicit drugs (%)	16·7		7·1		0·02
BMI (kg/m^2)	29·3	1·0	33·3	1·1	0·01
Co-morbid conditions and NSAID (%)					
Diabetes	22·0		30·0		0·17
Hypertension	55·0		88·0		0·08
Dyslipidaemia	32·0		52·0		0·07
CVD†	22·0		33·0		0·45
Inflammatory conditions‡	9·0		31·0		0·08
NSAID§	34·0		35·0		0·09

HEI-2010, Healthy Eating Index 2010; DASH, Dietary Approaches to Stop Hypertension; MAR, mean adequacy ratio; hAlzScore, HANDLS Alzheimer's risk score; PCA, principal component analysis; HS, high school; PIR, poverty income ratio; NSAID, non-steroidal anti-inflammatory drugs.
* *P* value was based on independent-samples *t* test when row variable is continuous and χ^2 test when row variable is categorical.
† CVD includes self-reported stroke, congestive heart failure, non-fatal myocardial infarction or atrial fibrillation.
‡ Inflammatory conditions include multiple sclerosis, systemic lupus, gout, rheumatoid arthritis, psoriasis, thyroid disorder and Crohn's disease.
§ Includes over the counter and prescription drugs in that category.

and hAlzScore, and DQ (DQ and ΔDQ). Annual rate of change in the CVLT-List A was associated with an interaction between ΔDQ and hAlzScore in the total population (Time × ΔDQ × hAlzScore: 0·15 (SE 0·06), $P = 0·008$) as well as in women (Fig. 2) (0·21 (SE 0·08), $P = 0·006$), indicating protective effects of DQ at higher AD risk levels. No other associations were statistically significant after correcting for multiple testing.

Finally, to tease apart the dietary index/indices driving the findings, we conducted two additional sensitivity analyses with just main findings from our principal component analyses. The results for DQ in cognition are presented in online Supplementary Table S4, while the results of gene × diet interactions are presented in online Supplementary Table S5. We found that all three indices had significant contributions to Trails B test scores over time. However, only HEI-2010 and DASH scores influenced the gene × diet interactions for CVLT-List A and delayed free recall.

Discussion

This study prospectively examined the relationship between change in DQ and a genetic risk for AD on cognition in urban-dwelling AA adults. Our findings indicated that improvements in DQ over time were associated with a slower rate of decline on a test of verbal memory particularly among AA women with higher genetic risk for AD (Fig. 2). The association was not present in men but persisted overall in mixed-sex analyses. No cross-sectional associations (initial diet and related findings) were detected in our present analyses, except for Trails A and B in women only.

AD is a progressive cognitive decline that diminishes social and occupational functioning. AD is typically characterised by memory deficits, cognitive deterioration, functional impairment in activities of daily living and neuropsychiatric symptoms[47]. It has been poorly identified and assessed in AA[48,49], resulting in an escalating public health crisis as reflected by an increased prevalence of the disease in AA.

Examining gene variations may be one pioneering method to explain the pathophysiological and clinical symptoms observed in persons with AD, a multifactorial disorder. The pathogenesis of AD in AA elders may be related to the amyloid-β cascade and pathogenesis of neuropsychiatric symptoms. Several neuroanatomical structures and neurotransmitters

Table 3. Coefficient estimates for associations between cognitive test performance and Healthy Aging in Neighborhoods of Diversity across the Life Span (HANDLS) Alzheimer's risk score (hAlzScore) by time, for HANDLS participants >50 years of age with complete and reliable cognitive test scores derived from mixed-effects linear regression models
(β-Coefficients and standard errors)‡

	All			Women			Men		
	β	SE	P	β	SE	P	β	SE	P
MMSE	n 225; k = 1·82			n 123; k = 1·85			n 102; k = 1·77		
Time	0·02	0·17	0·90	−0·54	0·55	0·33	−0·13	0·26	0·62
hAlzScore	−0·11*	−0·07	0·09	−0·04	0·09	0·62	−0·13	0·11	0·20
hAlzScore × time	0·02	−0·02	0·31	0·01	0·02	0·74	0·02	0·03	0·39
CVLT, List A	n 223; k = 1·76			n 122; k = 1·8			n 101; k = 1·71		
Time	−0·68	0·44	0·12	−2·32	1·58	0·14	−0·56	0·54	0·30
hAlzScore	−0·32	−0·2	0·10	−0·39	0·25	0·11	−0·15	0·32	0·63
hAlzScore × time	0·05	−0·05	0·33	0·13*	0·07	0·07	−0·06	0·07	0·42
CVLT, DFR	n 219; k = 1·74			n 121; k = 1·78			n 98; k = 1·7		
Time	−0·38	0·19	0·05	−0·94	0·63	0·14	−0·84	0·27	0·002
hAlzScore††	−0·19*	−0·1	0·18	0·04	0·14	0·75	−0·41***	0·14	0·004
hAlzScore × time	0·03	−0·02	0·18	0·01	0·03	0·62	0·03	0·03	0·37
BVRT	n 227; k = 1·89			n 123; k = 1·92			n 104; k = 1·85		
Time	0·77	0·42	0·08	−2·97	1·48	0·05	0·96	0·48	0·05
hAlzScore††	0·25	−0·19	0·05	0·69***	0·26	0·009	−0·14	0·26	0·59
hAlzScore × time	−0·06	−0·05	0·24	−0·10	0·07	0·12	0·02	0·06	0·68
Brief test of attention	n 220; k = 1·78			n 121; k = 1·81			n 99; k = 1·75		
Time	0·21	0·15	0·17	0·18	0·54	0·73	0·27	0·25	0·28
hAlzScore	−0·07	−0·08	0·40	−0·13	0·11	0·27	−0·05	0·13	0·69
hAlzScore × time	0·01	−0·02	0·71	0·00	0·02	0·85	0·02	0·03	0·40
Animal fluency	n 228; k = 1·95			n 124; k = 1·96			n 104; k = 1·93		
Time	0·32	0·27	0·23	0·60	0·78	0·45	0·67	0·39	0·08
hAlzScore	0·02	−0·18	0·90	0·08	0·22	0·71	0·12	0·28	0·67
hAlzScore × time	−0·03	−0·03	0·31	−0·02	0·03	0·61	−0·08*	0·04	0·07
Digits span, forward	n 226; k = 1·85			n 123; k = 1·83			n 103; k = 1·86		
Time	0·13	0·11	0·25	0·27	0·35	0·45	0·27	0·16	0·09
hAlzScore	0·02	−0·07	0·74	0·00	0·09	0·10	0·12	0·10	0·24
hAlzScore × time	0	−0·01	0·96	0·00	0·02	0·94	−0·00	0·02	0·10
Digits span, backward	n 226; k = 1·84			n 123; k = 1·82			n 103; k = 1·86		
Time	−0·23	0·15	0·12	−0·30	0·51	0·55	−0·15	0·21	0·46
hAlzScore†	−0·04	−0·07	0·51	−0·16*	0·09	0·08	0·11	0·09	0·23
hAlzScore × time	0·01	−0·02	0·73	0·03	0·02	0·23	−0·01	0·02	0·64
Clock Command Test	n 228; k = 1·93			n 125; k = 1·95			n 103; k = 1·89		
Time	0·07	0·09	0·46	0·15	0·32	0·64	0·04	0·12	0·73
hAlzScore	0	−0·04	0·93	−0·01	0·06	0·86	−0·03	0·07	0·64
hAlzScore × time	0·01	−0·01	0·37	−0·01	0·01	0·40	0·04**	0·01	0·01
Trailmaking test, part A	n 224; k = 1·84			n 123; k = 1·87			n 101; k = 1·81		
Time	−0·00	0·04	0·84	0·09	0·12	0·46	0·03	0·05	0·59
hAlzScore	0·00	0·02	0·94	0·03	0·02	0·27	0·00	0·02	0·93
hAlzScore × time	−0·00	0·00	0·24	−0·00	0·01	0·42	−0·01	0·01	0·17
Trailmaking test, part B	n 222; k = 1·77			n 123; k = 1·76			n 99; k = 1·78		
Time	−0·07	0·05	0·16	−0·32	0·15	0·04	−0·06	0·06	0·26
hAlzScore	−0·00	0·02	0·98	0·00	0·04	0·86	−0·02	0·03	0·54
hAlzScore × time	0·00	0·01	0·93	−0·00	−0·01	0·87	0·00	0·00	0·56

MMSE, Mini-Mental State Examination; k, total number of observations/total number of groups per test; CVLT-List A, California Verbal Learning test – List A; CVLT-DFR, California Verbal Learning Test-Long-Delayed Free Recall; BVRT, Benton Visual Retention Test.
* P < 0·10, ** P < 0·05, *** P < 0·01.
Significant interaction with sex: † P < 0·10, †† P < 0·5.
‡ Continuous covariates were mean-centred.

are shared in the pathogenesis of AD and neuropsychiatric symptoms such as schizophrenia, major depression and personality alterations. These derive from abnormalities in the limbic system and frontal and temporoparietal regions with altered function of the serotonergic, noradrenergic and cholinergic systems in the brain. Collectively, these neurochemical and neuroanatomical changes can result in the clinical symptoms manifested in AA elders with AD. This theory of the pathogenesis of AD in AA elders with AD may also support the temporal nature of the clinical symptoms given the increased abnormalities in neurotransmitters and neuroanatomy specific to the limbic system. However, further analysis is warranted about this theory since it is based on the limited number of clinical symptoms reported and examined in AA elders with AD as well as indications of mixed pathologies[50].

In terms of the genetics of AD, ApoE ϵ4 increases the risk of both age-related cognitive decline and the transition from mild to severe cognitive impairment[51]. Moreover, there is evidence that AD patients who are ϵ4 carriers have a faster rate of cognitive decline[52,53], although the data are equivocal. A few studies have investigated this issue reporting that ϵ4 carriers exhibit

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Table 4. Coefficient estimates for associations between diet quality and cognitive change by time, for Healthy Aging in Neighborhoods of Diversity across the Life Span (HANDLS) participants >50 years of age with complete and reliable cognitive test scores derived from mixed-effects linear regression models (β-Coefficients and standard errors)†††

	All			Women			Men		
	β	*n*	SE	β	*n*	SE	β	*n*	SE
MMSE		225			123			181	
Time	0·02		0·17	0·11		0·21	−0·10		0·26
Diet change‡‡‡	0·02		0·14	−0·09		0·16	0·07		0·25
Diet change × time	−0·01		0·04	0·04		0·04	0·02		0·07
Initial diet§§§	−0·06		0·11	−0·17		0·13	−0·00		0·21
Initial diet × time	0·01		0·03	0·03		0·03	0·05		0·05
CVLT, List A††		223			122			173	
Time	−0·64		0·43	−1·31**		0·66	−0·56		0·52
Diet change	0·23		0·36	0·16		0·42	0·75		0·63
Diet change × time	−0·01		0·10	−0·15		0·13	0·22		0·14
Initial diet	−0·06		0·31	−0·05		0·37	−0·12		0·55
Initial diet × time	−0·03		0·08	−0·08		0·11	0·06		0·12
CVLT, FRLD†		219			121			167	
Time	−0·34*		0·19	−0·36		0·28	−0·79***		0·26
Diet change	−0·06		0·18	−0·25		0·23	0·38		0·27
Diet change × time	0·03		0·04	0·07		0·06	−0·03		0·07
Initial diet	−0·02		0·16	−0·16		0·21	0·29		0·24
Initial diet × time	−0·02		0·04	0·01		0·05	−0·09		0·06
BVRT††		227			123			192	
Time	0·64		0·42	0·14		0·68	1·03**		0·48
Diet change	−0·30		0·37	−0·16		0·47	−0·51		0·61
Diet change × time	−0·07		0·10	−0·05		0·14	−0·07		0·15
Initial diet	−0·20		0·31	−0·20		0·38	0·06		0·52
Initial diet × time	0·01		0·08	0·08		0·10	−0·15		0·12
Brief test of attention‡§‖		220			121			173	
Time	0·24		0·24	0·19		0·20	0·26		0·24
Diet change	−0·25*		0·17	−0·24		0·20	−0·22		0·27
Diet change × time	0·04		0·05	0·02		0·04	0·13*		0·07
Initial diet	−0·35**		0·15	−0·45***		0·17	0·01		0·24
Initial diet × time	0·03		0·02	0·04		0·03	0·01		0·06
Animal fluency†‖		228			124			201	
Time	0·31		0·27	0·10		0·66	0·67*		0·39
Diet change	−0·08		0·35	−0·10		0·43	0·28		0·65
Diet change × time	0·11*		0·06	0·16		0·14	−0·01		0·11
Initial diet	0·06		0·29	0·19		0·36	−0·23		0·55
Initial diet × time	0·02		0·05	0·03		0·11	−0·03		0·09
Digits span, forward†§§		226			123			192	
Time	0·15		0·11	−0·05		0·15	0·29*		0·16
Diet change	0·25**		0·11	0·39**		0·16	0·19		0·24
Diet change × time	0·00		0·03	0·01		0·03	−0·02		0·05
Initial diet	0·14		0·11	0·19		0·14	0·13		0·20
Initial diet × time	−0·01		0·02	−0·01		0·03	−0·01		0·04
Digits span, backward††¶		226			123			192	
Time	−0·23		0·15	−0·43**		0·21	−0·12		0·21
Diet change	0·06		0·13	0·11		0·17	0·00		0·22
Diet change × time	0·02		0·04	0·06		0·05	−0·01		0·06

Table 4. (*Continued*)

	All			Women			Men		
	β	*n*	SE	*β*	*n*	SE	*β*	*n*	SE
Initial diet	−0·13		0·11	−0·20		0·14	0·06		0·19
Initial diet × time	0·05*		0·03	0·06*		0·04	0·01		0·05
Clock, Command‡‡		228			125			195	
Time	0·08		0·09	0·02		0·14	0·05		0·13
Diet change	0·12		0·08	0·10		0·10	0·15		0·15
Diet change × time	−0·02		0·02	−0·02		0·03	−0·02		0·04
Initial diet	−0·00		0·07	−0·10		0·09	0·10		0·13
Initial diet × time	0·02		0·02	0·03		0·02	0·02		0·03
Trailmaking test, part A§§‖‖		224			123			101	
Time	−0·01		0·04	−0·04		0·05	0·02		0·05
Diet change	0·03		0·04	−1·81		5·50	0·03		0·06
Diet change × time	−0·01		0·01	1·02		1·87	−0·02		0·01
Initial diet	−0·01		0·03	0·37		4·52	0·00		0·05
Initial diet × time	−0·01		0·00	2·74***		1·39	0·00		0·01
Trailmaking test, part B††§‖¶		222			123			99	
Time	−0·07		0·05	−0·14**		0·06	−0·06		0·05
Diet change	0·07		0·05	0·13**		0·06	−0·06		0·07
Diet change × time	−0·02		0·01	−0·04***		0·01	0·02		0·02
Initial diet	−0·02		0·04	−0·01		0·01	−0·03		0·06
Initial diet × time	−0·00		0·01	−0·01		0·01	−0·03**		0·06

MMSE, Mini-Mental State Examination; CVLT-List A, California Verbal Learning test-List A; CVLT-DFR, California Verbal Learning Test-Delayed Free Recall; BVRT, Benton Visual Retention Test.
* $P < 0·10$, ** $P < 0·05$, *** $P < 0·01$.
Significant interaction between time and sex: † $P < 0·10$, †† $P < 0·05$.
Significant interaction between sex and diet: ‡ $P < 0·10$, ‡‡ $P < 0·05$.
Significant interaction between sex and diet (change): § $P < 0·10$, §§ $P < 0·05$.
Significant interaction between sex and diet (change) and time: ‖ $P < 0·10$, ‖‖ $P < 0·05$.
¶ Significant interaction between sex and diet and time ($P < 0·10$).
††† Continuous covariates were mean-centred.
‡‡‡ Represents change in diet quality over time (about 5 years from baseline).
§§§ Represents diet quality at baseline (time 0).

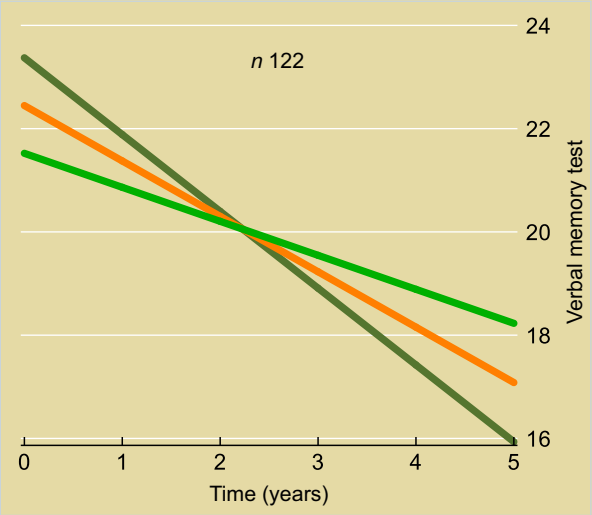

Fig. 2. Predictive margins for California Verbal Learning test-List A by time, across levels of diet change, among women (*n* 122) with highest genetic risk for Alzheimer's disease: mixed-effects linear regression models. ▬, Diet change (mean − 1SD); ▬, Diet change (mean + 1SD); ▬, diet change (mean).

a phenotype characterised by greater memory impairment[54]. In other words, AD patients who have memory complaints are significantly more likely to be ϵ4 carriers. In addition, greater memory deficits on formal neuropsychological testing have been observed in AD patients who are ϵ4 carriers. Studies on ApoE ϵ4 status and episodic memory have involved predominantly White samples except for Fillenbaum *et al.* who compared the effects of ϵ4 status on baseline cognitive functioning in AA *v.* White AD patients[55]. Our risk score in HANDLS (hAlzScore) contained two ApoE SNP which could elucidate the observed, long-term memory association in women. Although we have ApoE information on all 1024 genotyped HANDLS participants, the current analyses did not specifically focus on the overlapping subjects (those included in the final sample who also had complete ApoE data) as we continued with the risk score calculation. The lack of more current literature on racial difference in AD further justifies the need for studying ApoE in a unique study population such as ours.

Interestingly, and in contrast to our current finding, there were racial differences in cognitive abilities such that the ϵ4 allele was related to faster decline in semantic memory and working memory for Whites but not for AA.

Dietary modification may have the potential to reduce the risk of developing AD. A recent meta-analysis (*n* 34 168) showed that the highest Mediterranean diet score was associated with reduced risk of developing cognitive disorders (relative risk = 0·79, 95 % CI 0·70, 0·90)[56], while supplementation with olive oil or nuts was associated with improved cognitive function[57]. A study that investigated a relationship between Southern diet (high in added fats, fried food, eggs, processed meats and sugar-sweetened beverages) and Prudent diet (rich in vegetables, fruit, cereals and legumes, whole grains, rice/pasta, fish, low-fat dairy products, poultry and water) in individuals at risk for AD found an association between Southern diet and reduced cognitive performance among AA[58]. In both Whites and AA adults, greater adherence to a Prudent dietary pattern was associated with better cognitive outcomes suggesting differential effects of diet on cognitive function in middle-aged individuals at high risk for AD. This suggests that diet could be a non-pharmaceutical tool to reduce cognitive decline in racially diverse populations[59]. Mediterranean, DASH[60–62] and MIND[63,64] have all been linked to reduced risk of AD and lower cognitive decline in a recent publication[12]. Suggested mechanisms include: olive serves as one of the building block components of MedDi and MIND diets and the exerted potential health beneficial might be suggested due to the presence of its bioactive constituents such as oleic acids and phenolic compounds in olives, for example, as well as the combined neuroprotective functions of the antioxidants, MUFA and PUFA.

Confidence in our findings is strengthened by several factors. First, we used a longitudinal design to ascertain temporality of these relationships while stratifying by sex that is important in cognitive decline. Second, we used a composite measure of eleven cognitive tests that assessed a range of cognitive abilities, reducing the opportunity for floor and ceiling effects and other sources of measurement error to affect results. Finally, the availability of a mean of repeated measurements of cognition per individual allowed us to simultaneously but separately model initial level of cognition and rate of change, thereby allowing us to more effectively adjust for the former while testing for sex differences in the latter.

Nevertheless, some study limitations should be noted. First, our final sample size after using multiple selection variables was rather small. We were also unable to determine the statistical power of our selected samples since the process in mixed models is more complex than in linear models and requires more assumptions[65]. It is also often estimated using simulations which are not always reliable. Second, although our models were adjusted for a wealth of potentially confounding covariates, causality cannot be inferred given the observational nature study and the possible role played by residual confounding. Third, outcome measures were only repeated up to twice over an average follow-up of 5 years, leaving room for improvement in studies with three or more time points. Fourth, although we performed our risk score calculation based on over 100 AD-related genes and reported SNP, hundreds of more SNP have been discovered since the *Nature* publication[66], and we are unable to claim our list as comprehensive. Fifth, we excluded those <50 years to have greater variability in cognitive decline measures at the expense of statistical power with a larger sample size. Finally, no additional analyses were performed with complete ApoE allele status to further explore the associations.

This study aimed to investigate longitudinal associations of genetic risk for AD and DQ with cognitive outcomes, in a sample of <500 people. While we were well powered to do the study, we might have missed significant gene variations while creating our genetic risk score. It might be equally important to study who are <50 years in hopes of detecting some early changes that was outside the scope of this study. In addition, because of the projected growth of minority populations in the coming decades,

larger multi-racial/ethnic studies of cognitive function in older people are needed.

Conclusions and implications

We conclude that among AA women with increased genetic risk for AD, a better-quality diet was associated with a slower rate of decline in verbal memory. It is evident that DQ and its change over time can impact memory in the long run, especially in people with higher risk for AD. Mechanistically speaking, the changes observed begin long before the detected impairments are manifest. While we cannot change the genetic risk for a disease, shifting to a better-quality diet offers possible long-term health benefits, as it has been well established in the literature. More studies are needed to investigate brain morphology and volume changes in relation to DQ, in an at-risk population for AD, over time.

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The authors declare that there are no conflicts of interest.

The views expressed in this article are those of the author(s) and do not reflect the official policy of the Department of the Army/Navy/Air Force, Department of Defense, or the US Government.

Supplementary material

For supplementary material referred to in this article, please visit https://doi.org/10.1017/S0007114520001269

References

1. Alosco ML, Spitznagel MB, Raz N, *et al.* (2013) Dietary habits moderate the association between heart failure and cognitive impairment. *J Nutr Gerontol Geriatr* **32**, 106–121.
2. Hardman RJ, Kennedy G, Macpherson H, *et al.* (2016) Adherence to a Mediterranean-style diet and effects on cognition in adults: a qualitative evaluation and systematic review of longitudinal and prospective trials. *Front Nutr* **3**, 22.
3. Petersson SD & Philippou E (2016) Mediterranean diet, cognitive function, and dementia: a systematic review of the evidence. *Adv Nutr* **7**, 889–904.
4. Gu Y & Scarmeas N (2011) Dietary patterns in Alzheimer's disease and cognitive aging. *Curr Alzheimer Res* **8**, 510–519.
5. Solfrizzi V, Panza F, Frisardi V, *et al.* (2011) Diet and Alzheimer's disease risk factors or prevention: the current evidence. *Expert Rev Neurother* **11**, 677–708.
6. Yannakoulia M, Kontogianni M & Scarmeas N (2015) Cognitive health and Mediterranean diet: just diet or lifestyle pattern? *Ageing Res Rev* **20**, 74–78.
7. Wilson VK, Houston DK, Kilpatrick L, *et al.* (2014) Relationship between 25-hydroxyvitamin D and cognitive function in older adults: the Health, Aging and Body Composition Study. *J Am Geriatr Soc* **62**, 636–641.
8. Richard EL, Laughlin GA, Kritz-Silverstein D, *et al.* (2018) Dietary patterns and cognitive function among older community-dwelling adults. *Nutrients* **10**, 1088.
9. Charlton KE (2002) Eating well: ageing gracefully! *Asia Pac J Clin Nutr* **3**, S607–S617.
10. Dacks PA, Shineman DW & Fillit HM (2013) Current evidence for the clinical use of long-chain polyunsaturated *n*-3 fatty acids to prevent age-related cognitive decline and Alzheimer's disease. *J Nutr Health Aging* **17**, 240–251.
11. Moore K, Hughes CF, Ward M, *et al.*(2018) Diet, nutrition and the ageing brain: current evidence and new directions. *Proc Nutr Soc* **77**, 152–163.
12. van den Brink AC, Brouwer-Brolsma EM, Berendsen AAM, *et al.* (2019) The Mediterranean, Dietary Approaches to Stop Hypertension (DASH), and Mediterranean–DASH Intervention for Neurodegenerative Delay (MIND) diets are associated with less cognitive decline and a lower risk of Alzheimer's disease – a review. *Adv Nutr* **10**, 1040–1065.
13. Appel LJ, Moore TJ, Obarzanek E, *et al.* (1997) A clinical trial of the effects of dietary patterns on blood pressure. DASH Collaborative Research Group. *N Engl J Med* **336**, 1117–1124.
14. Graff-Radford NR, Besser LM, Crook JE, *et al.* (2016) Neuropathologic differences by race from the National Alzheimer's Coordinating Center. *Alzheimers Dement* **12**, 669–677.
15. Morris JC, Schindler SE, McCue LM, *et al.* (2019) Assessment of racial disparities in biomarkers for Alzheimer disease. *JAMA Neurol* **76**, 264–273.
16. Gavett BE, Fletcher E, Harvey D, *et al.* (2018) Ethnoracial differences in brain structure change and cognitive change. *Neuropsychology* **32**, 529–540.
17. Rajan KB, Barnes LL, Wilson RS, *et al.* (2019) Apolipoprotein E genotypes, age, race, and cognitive decline in a population sample. *J Am Geriatr Soc* **67**, 734–740.
18. Weuve J, Barnes LL, Mendes de Leon CF, *et al.* (2018) Cognitive aging in Black and White Americans: cognition, cognitive decline, and incidence of Alzheimer disease dementia. *Epidemiology* **29**, 151–159.
19. Barnes LL, Wilson RS, Li Y, *et al.* (2006) Change in cognitive function in Alzheimer's disease in African-American and white persons. *Neuroepidemiology* **26**, 16–22.
20. Wilson RS, Li Y, Aggarwal NT, *et al.* (2006) Cognitive decline and survival in Alzheimer's disease. *Int J Geriatr Psychiatry* **21**, 356–362.
21. Hajjar I, Wharton W, Mack WJ, *et al.* (2016) Racial disparity in cognitive and functional disability in hypertension and all-cause mortality. *Am J Hypertens* **29**, 185–193.
22. Bachman DL, Stuckey M, Ebeling M, *et al.* (2009) Establishment of a predominantly African-American cohort for the study of Alzheimer's disease: the South Carolina Alzheimer's disease clinical core. *Dement Geriatr Cogn Disord* **27**, 329–336.
23. Hossain S, Beydoun MA, Kuczmarski MF, *et al.* (2019) The interplay of diet quality and Alzheimer's disease genetic risk score in relation to cognitive performance among urban African Americans. *Nutrients* **11**, 2181.

24. Savoca MR, Arcury TA, Leng X, *et al.* (2009) The diet quality of rural older adults in the South as measured by healthy eating index-2005 varies by ethnicity. *J Am Diet Assoc* **109**, 2063–2067.
25. Richards Adams IK, Figueroa W, Hatsu I, *et al.* (2019) An examination of demographic and psychosocial factors, barriers to healthy eating, and diet quality among African American adults. *Nutrients* **11**, 519.
26. Yosef Hochberg AC (1987) *Multiple Comparison Procedures*. New York: John Wiley & Sons.
27. Antonell A, Balasa M, Oliva R, *et al.* (2011) A novel *PSEN1* gene mutation (L235R) associated with familial early-onset Alzheimer's disease. *Neurosci Lett* **496**, 40–42.
28. Berr C, Richard F, Dufouil C, *et al.* (1998) Polymorphism of the prion protein is associated with cognitive impairment in the elderly: the EVA study. *Neurology* **51**, 734–737.
29. de Oliveira FF, Bertolucci PH, Chen ES, *et al.* (2014) Brain-penetrating angiotensin-converting enzyme inhibitors and cognitive change in patients with dementia due to Alzheimer's disease. *J Alzheimers Dis* **42**, Suppl. 3, S321–S324.
30. Finckh U, von der Kammer H, Velden J, *et al.* (2000) Genetic association of a cystatin C gene polymorphism with late-onset Alzheimer disease. *Arch Neurol* **57**, 1579–1583.
31. Lillenes MS, Stoen M, Gunther CC, *et al.* (2017) Mitochondrial transcription factor A (TFAM) rs1937 and AP endonuclease 1 (APE1) rs1130409 alleles are associated with reduced cognitive performance. *Neurosci Lett* **645**, 46–52.
32. Ma C, Zhang Y, Li X, *et al.* (2016) The TT allele of rs405509 synergizes with APOE epsilon4 in the impairment of cognition and its underlying default mode network in non-demented elderly. *Curr Alzheimer Res* **13**, 708–717.
33. Ozturk A, DeKosky ST & Kamboh MI (2006) Lack of association of 5 SNPs in the vicinity of the insulin-degrading enzyme (IDE) gene with late-onset Alzheimer's disease. *Neuroscience Lett* **406**, 265–269.
34. Tisato V, Zuliani G, Vigliano M, *et al.* (2018) Gene-gene interactions among coding genes of iron-homeostasis proteins and APOE-alleles in cognitive impairment diseases. *PLOS ONE* **13**, e0193867.
35. Moshfegh AJ, Rhodes DG, Baer DJ, *et al.* (2008) The US Department of Agriculture Automated Multiple-Pass Method reduces bias in the collection of energy intakes. *Am J Clin Nutr* **88**, 324–332.
36. FNDDS https://www.ars.usda.gov/northeast-area/beltsville-md-bhnrc/beltsville-human-nutrition-research-center/food-surveys-research-group/docs/fndds/ (accessed March 2020).
37. HEI Tools for Researchers https://epi.grants.cancer.gov/hei/tools.html (accessed March 2020).
38. Healthy Eating Index (2010) https://handls.nih.gov/06Coll-w01HEI.htm (accessed March 2020).
39. Guenther PM, Kirkpatrick SI, Reedy J, *et al.* (2014) The Healthy Eating Index-2010 is a valid and reliable measure of diet quality according to the 2010 Dietary Guidelines for Americans. *J Nutr* **144**, 399–407.
40. Mellen PB, Gao SK, Vitolins MZ, *et al.* (2008) Deteriorating dietary habits among adults with hypertension: DASH dietary accordance, NHANES 1988–1994 and 1999–2004. *Arch Intern Med* **168**, 308–314.
41. Murphy SP, Foote JA, Wilkens LR, *et al.* (2006) Simple measures of dietary variety are associated with improved dietary quality. *J Am Diet Assoc* **106**, 425–429.
42. Fanelli Kuczmarski M, Mason MA, Beydoun MA, *et al.* (2013) Dietary patterns and sarcopenia in an urban African American and White population in the United States. *J Nutr Gerontol Geriatr* **32**, 291–316.
43. Vitamin C Fact Sheet. https://ods.od.nih.gov/factsheets/VitaminC-HealthProfessional/ (accessed March 2020).
44. Fanelli Kuczmarski M, Bodt BA, Stave Shupe E, *et al.* (2018) Dietary patterns associated with lower 10-year atherosclerotic cardiovascular disease risk among urban African-American and White adults consuming western diets. *Nutrients* **10**, 158.
45. Jake Lever MKNA (2017) Principal component analysis. *Nature Methods* **14**, 641–642.
46. Ibrahim JG & Molenberghs G (2009) Missing data methods in longitudinal studies: a review. *Test* **18**, 1–43.
47. Holston EC (2005) Stigmatization in Alzheimer's disease research on African American elders. *Issues Ment Health Nurs* **26**, 1103–1127.
48. Wilson RS, Capuano AW, Sytsma J, *et al.* (2015) Cognitive aging in older Black and White persons. *Psychol Aging* **30**, 279–285.
49. Corsi M, Di Raimo T, Di Lorenzo C, *et al.* (2016) Cognitive disability in Alzheimer's disease and its management. *La Clinica Terapeutica* **167**, e123–e126.
50. Barnes LL, Leurgans S, Aggarwal NT, *et al.* (2015) Mixed pathology is more likely in black than white decedents with Alzheimer dementia. *Neurology* **85**, 528–534.
51. Mount DL, Ashley AV, Lah JJ, *et al.* (2009) Is ApoE epsilon4 associated with cognitive functioning in African Americans diagnosed with Alzheimer disease? An exploratory study. *South Med J* **102**, 890–893.
52. Hendrie HC, Murrell J, Baiyewu O, *et al.* (2014) APOE epsilon4 and the risk for Alzheimer disease and cognitive decline in African Americans and Yoruba. *Int Psychogeriatr* **26**, 977–985.
53. Stewart R, Russ C, Richards M, *et al.* (2001) Apolipoprotein E genotype, vascular risk and early cognitive impairment in an African Caribbean population. *Dement Geriatr Cogn Disord* **12**, 251–256.
54. Potter GG, Plassman BL, Burke JR, *et al.* (2009) Cognitive performance and informant reports in the diagnosis of cognitive impairment and dementia in African Americans and whites. *Alzheimers Dement* **5**, 445–453.
55. Barnes LL, Arvanitakis Z, Yu L, *et al.* (2013) Apolipoprotein E and change in episodic memory in blacks and whites. *Neuroepidemiology* **40**, 211–219.
56. Wu L & Sun D (2017) Adherence to Mediterranean diet and risk of developing cognitive disorders: an updated systematic review and meta-analysis of prospective cohort studies. *Sci Rep* **7**, 41317.
57. Rajaram S, Valls-Pedret C, Cofán M, *et al.* (2016) The Walnuts and Healthy Aging Study (WAHA): protocol for a nutritional intervention trial with walnuts on brain aging. *Front Aging Neurosci* **8**, 333.
58. Nutaitis AC, Tharwani SD, Serra MC, *et al.* (2019) Diet as a risk factor for cognitive decline in African Americans and Caucasians with a parental history of Alzheimer's disease: a cross-sectional pilot study dietary patterns. *J Prev Alzheimers Dis* **6**, 50–55.
59. Gorelick PB, Furie KL, Iadecola C, *et al.* (2017) Defining optimal brain health in adults: a presidential advisory from the American Heart Association/American Stroke Association. *Stroke* **48**, e284–e303.
60. Wu J, Song X, Chen GC, *et al.* (2019) Dietary pattern in midlife and cognitive impairment in late life: a prospective study in Chinese adults. *Am J Clin Nutr* **110**, 912–920.
61. Abbatecola AM, Russo M & Barbieri M (2018) Dietary patterns and cognition in older persons. *Curr Opin Clin Nutr Metab Care* **21**, 10–13.
62. Berendsen AAM, Kang JH, van de Rest O, *et al.* (2017) The dietary approaches to stop hypertension diet, cognitive function, and cognitive decline in American older women. *J Am Med Dir Assoc* **18**, 427–432.

63. Omar SH (2019) Mediterranean and MIND diets containing olive biophenols reduces the prevalence of Alzheimer's disease. *Int J Mol Sci* **20**, 2797.
64. Cherian L, Wang Y, Fakuda K, *et al.* (2019) Mediterranean-Dash Intervention for Neurodegenerative Delay (MIND) diet slows cognitive decline after stroke. *J Prev Alzheimers Dis* **6**, 267–273.
65. Evangelos Kontopantelis DAS, Parisi R & Reeves D (2016) Simulation-based power calculations for mixed effects modeling: idpower in Stata. *J Stat Softw* **74**, 25.
66. Bertram L, McQueen MB, Mullin K, *et al.* (2007) Systematic meta-analyses of Alzheimer disease genetic association studies: the AlzGene database. *Nat Genet* **39**, 17–23.

Appendix 1: Cognitive Tests

Mental Status – The Mini Mental State Examination (MMSE) concentrates only on the cognitive aspects of mental functions. It has eleven questions, easy to administer and is practical to use serially and routinely [1]. The MMS is divided into two sections. First section requires vocal responses only and covers orientation, memory, and attention; with a maximum score of 21. Second section tests the ability to name, follow verbal and written commands, with a maximum score is nine. Because of the reading and writing involved in Part II, patients with severely impaired vision may have some extra difficulty that can usually be eased by large writing and allowed for in the scoring.

Verbal learning and memory—The California Verbal Learning Test-II (CVLT-II) [2] as described by Delis *et al.* measures verbal learning and memory by immediate and delayed recall and recognition of two sixteen-word lists. As administered to HANDLS participants, List A consists of three trials, followed by list B with one trial. After testing with list B, short-delay short free recall and cued recall of list A are tested. After ~ 30 min delay, long-delay free recall, cued recall and yes/no-recognition attempts of list A conclude the test.

Non-verbal memory—The Benton Visual Retention Test [3] consists of ten designs and their reproduction by participants, as accurately as possible. It measures visual memory, perception and visuo-constructional abilities. It is an untimed test scored by the examiner with a reliability range of 0·74 to 0·84 [4].

Working memory—The Digit Span subscale of the Wechsler Adult Intelligence Scale consists of forward and backward test measurements [5]. In both tests, seven pairs of increasing, random number sequences, are presented verbally at a rate of one per second. In Digits Forward, the subject repeats the same number sequence after the examiner. In Digits Backward the participant is asked to repeat the number sequence in reverse order. The test is discontinued when the subject fails both the forward and backward trial of any given sequence string. Digits Forward and Backward are measured by the number of correct trials. This is used as a valid test of attention, working memory and concentration.

Attention and cognitive flexibility—The Trail Making Test [6] is administered in two timed-parts, lasting 5 to 10 min each. Trails A is administered first, where subjects connect, in ascending order, randomly numbered circles on a page by drawing lines. In Trails B, subjects connect alternating numbered and lettered circles, in ascending order the same way as Trails A. Following of the correct sequence is required to complete each test. Cognitive task burden in Trails B is greater than Trails A. The Trails Making Test, therefore, provides a composite measure of attention, visuomotor tracking, and cognitive flexibility.

Visuospatial ability—The Card Rotations Test measures two-dimension visuospatial ability with the help of different card shapes [7]. Ten rows of eight cards each are compared with a sample card shape to determine if each card is rotated or flipped over. The completion is marked by identifying two sets of ten card rows in 3 min each. The score is the difference between cards marked correctly vs. incorrectly.

Perceptual speed—The Identical Pictures Test includes three components of perceptual speed: perceptual fluency, decision-making speed and immediate perceptual memory. In this timed test, sample objects are matched with an identical picture in the adjacent row of test objects [7]. The score is the number of correct answers, minus a fraction of the number of incorrect answers.

Semantic fluency—The Semantic Fluency Test is used to assess spontaneous generation of words from specific categories in a preset amount of time [4]. In HANDLS, participants were asked to name as many animals as possible within 60s. Then, the total number of unique animals named is aggregated to generate a categorical animal fluency score.

1. Folstein Mf Fau - Folstein SE, Folstein Se Fau - McHugh PR, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician.
2. Delis D KJ, Kaplan E et al. CVLT-II. New York: The Psychological Corporation. 2000.
3. AL B. Benton Visual Retention Test, 5th ed. San Antonio, TX: The Psychological Corporation. 1992.
4. Strauss E SESO. A Compendium of Neuropsychological Tests: Administration, Norms and Commentary, 3rd ed. New York: Oxford University Press. 2006.
5. D W. Wechsler Adult Intelligence Scale – Revised. New York: The Psychological Corporation. 1981.

6. RM R. Trail Making Test: Manual for administration and scoring. Tucson, AZ: Reitan Neuropsychology Laboratory. 1992.
7. Ekstrom RB FJ, Harman HH et al. . Kit of Factor-Referenced Cognitive Tests, revised ed. Princeton, NJ: Educational Testing Service. 1976.

Table S1. Cognitive performance test scores at baseline (Visit 1), follow-up (Visit 2), and change between visits, by sex, for HANDLS participants >50y of age with complete hAlzScore

	All	**Women**	**Men**
Mini-Mental State Exam, total score			
Visit 1	27.314±0.249 *(N=220)*	27.305±0.371 *(N=123)*	27.324±0.335 *(N=97)*
Visit 2	27.4491±0.168 *(N=192)*	27.691±0.199 *(N=107)*	27.267±0.265 *(N=85)*
P (Visit2-Visit1)	*0.556*	*0.359*	*0.894*
California Verbal Learning Test (CVLT), List A			
Visit 1	22.365±0.539 *(N=191)*	23.006±0.667 *(N=112)*	21.75±0.87 *(N=79)*
Visit 2[a]	16.204±0.769 *(N=191)*	17.616±0.1.138 *(N=106)*	14.63±0.91 *(N=85)*
P (Visit2-Visit1)	*<0.001*	*<0.001*	*<0.001*
CVLT, free delayed recall			
Visit 1	6.322±0.288 (N=187)	6.267±0.323 (N=110)	6.375±0.468 (N=77)
Visit 2	4.042±0.281 (N=191)	4.272±0.416 (N=106)	3.786±0.382 (N=85)
P (Visit2-Visit1)	<0.001	<0.001	<0.001
Benton Visual Retention Test			
Visit 1	6.191±0.478 (N=219)	6.654±0.785 (N=122)	5.768±0.57 (N=97)
Visit 2	9.611±0.414 (N=190)	9.619±0.542 (N=106)	9.602±0.635 (N=84)
P (Visit2-Visit1)	<0.001	0.002	<0.001
Brief Test of Attention			
Visit 1	6.46±0.282 (N=196)	6.359±0.328 (N=113)	6.554±0.454 (N=83)
Visit 2	6.525±0.223 (N=169)	6.58±0.236 (N=95)	6.465±0.389 (N=74)
P (Visit2-Visit1)	0.857	0.585	0.882
Animal Fluency			
Visit 1	18.133±0.586 (N=218)	17.315±0.87 (N=121)	18.87±0.768 (N=97)
Visit 2	18.21±0.682 (N=190)	17.385±0.971 (N=106)	19.133±0.911 (N=84)

P (Visit2-Visit1)	0.932	0.957	0.825
Digits Span, Forward			
Visit 1	7.092±0.26 (N=212)	6.95±0.312 (N=118)	7.222±0.41 (N=94)
Visit 2	7.115±0.233 (N=176)	6.979±0.342 (N=97)	7.264±0.306 (N=79)
P (Visit2-Visit1)	0.949	0.950	0.935
Digits Span, Backward			
Visit 1	5.455±0.257 (N=212)	5.642±0.407 (N=118)	5.286±0.318 (N=94)
Visit 2	5.765±0.27 (N=175)	5.793±0.403 (N=97)	5.733±0.356 (N=78)
P (Visit2-Visit1)	0.407	0.791	0.349
Clock, command			
Visit 1	8.859±0.146 (N=219)	8.607±0.23 (N=122)	9.088±0.163 (N=97)
Visit 2	8.821±0.12 (N=188)	8.816±0.16 (N=106)	8.825±0.182 (N=82)
P (Visit2-Visit1)	0.838	0.455	0.282
Trail making test, Part A			
Visit 1[a]	41.529±2.321 (N=216)	46.575±4.022 (N=121)	36.879±1.886 (N=95)
Visit 2	45.809±4.209 (N=189)	47.305±6.977 (N=105)	44.164±4.357 (N=84)
P (Visit2-Visit1)	0.373	0.928	0.126
Trail making test, Part B			
Visit 1	215.473±21.447 (N=216)	231.259±27.539 (N=121)	200.925±32.384 (N=95)
Visit 2	183.191±14.678 (N=189)	189.627±22.398 (N=105)	176.115±18.721 (N=84)
P (Visit2-Visit1)	0.214	0.241	0.507

Key: CES-D=Center for Epidemiologic Studies-Depression; MMSE=Mini-Mental State Examination; PIR=poverty income ratio; WRAT=Wide Range Achievement Test.

[a] $p<0.05$ for null hypothesis of no difference in means of cognitive test scores by sex (referent category: Women) within each visit. Wald test from svy:reg command.

Table S2: Seventy SNPs from AlzGene Database genotyped and/or imputed in the HANDLS African American subjects

Single Nucleotide Polymorphisms (SNPs)	**Genes**	Al1 (Major)	Al2 (Minor)	Frequency
TF*	rs1049296	C	T	0.91758
BLMH	rs1050565	T	C	0.79546
CST3*	rs1064039	C	T	0.7903
IL1B	rs1143634	G	A	0.87227
LDLR	rs11669576	G	A	0.81711
OLR1	rs12316150	A	T	0.9716
APBB2	rs13133980	G	C	0.76012
MAPT	rs1467967	A	G	0.63136
PSEN1*	rs165932	T	G	0.74596
CTSD	rs17571	G	A	0.96512
TNF	rs1799724	C	T	0.9671
CCR2	rs1799864	G	A	0.84532
DLST	rs1799900	A	G	0.9126
HFE	rs1799945	C	G	0.97464
NOS3	rs1799983	G	T	0.90184
LRP1	rs1799986	C	T	0.93883
PRNP*	rs1799990	A	G	0.66874
TGFB1	rs1800469	G	A	0.75953
HFE	rs1800562	G	A	0.99267
IL1A	rs1800587	G	A	0.60793
TNF	rs1800629	G	A	0.87327
FAS	rs1800682	G	A	0.70754
IL6	rs1800795	G	C	0.92192
IL10	rs1800871	G	A	0.59249

IL10	rs1800872	G	T	0.5916
IL10	rs1800896	T	C	0.65699
MTHFR	rs1801131	T	G	0.82483
MTHFR	rs1801133	G	A	0.91162
TCN2	rs1801198	C	G	0.77133
BCHE	rs1803274	C	T	0.82747
HTR6	rs1805054	C	T	0.8273
IDE	rs1832196	G	A	0.73245
CHAT	rs1880676	G	A	0.95166
IDE*	rs1887922	T	C	0.91934
TFAM*	rs1937	G	C	0.97402
IDE	rs1999764	T	C	0.90194
PLAU	rs2227564	C	T	0.9595
ABCA1	rs2230806	C	T	0.36582
ABCA1	rs2230808	C	T	0.234
IDE	rs2251101	T	C	0.88928
TFAM	rs2306604	G	A	0.80018
MPO	rs2333227	C	T	0.67856
SLC6A4	rs25531	T	C	0.78126
LPL	rs268	A	G	0.9978
LPL	rs328	C	G	0.93071
NOTCH4	rs367398	G	A	0.50259
IDE	rs3758505	A	C	0.70459
CHAT	rs3810950	G	A	0.95166
APOE*	rs405509	G	T	0.72841
PLAU	rs4065	C	T	0.52426
ACE*	rs4291	A	T	0.67994

ACE*	rs4343	A	G	0.76874
APOE*	rs449647	A	T	0.71431
IDE	rs4646953	A	G	0.90724
IDE	rs4646954	G	A	0.70117
GAPDHS*	rs4806173	C	G	0.68382
CHRNB2*	rs4845378	G	T	0.93035
CYP46A1	rs4900442	C	T	0.67679
ICAM1	rs5498	A	G	0.80201
IDE	rs551266	T	C	0.91951
BDNF	rs56164415	G	A	0.94897
BDNF	rs6265	C	T	0.96873
HTR2A	rs6313	G	A	0.60939
BACE1	rs638405	G	C	0.5253
PON1	rs662	C	T	0.64648
TNF	rs673	G	A	0.94328
CETP	rs708272	G	A	0.73507
CYP46A1	rs754203	A	G	0.85181
APOE	rs769446	T	C	0.94834
PSEN2	rs8383	C	T	0.58134

*SNPs used to create AlzScore in HANDLS

SNP details: rs1049296_C "TF (C>T)"; rs1064039_A "CST3 (A>G)" ; rs165932_Tinv "PSEN1 (G>T)"; rs1799990_Ainv "PRNP (G>A)"; rs2251101_T "IDE (T>C)"; rs2306604_C "TFAM (C>T)"; rs405509_A "APOE (A>C)"; rs4291_A "ACE (A>T)"; rs4343_A "ACE (A>G)"; rs449647_Ainv "APOE (T>A)"; rs4806173_Cinv "GAPDHS (G>C)"; rs4845378_Ginv "CHRNB2(T>G)"

Table S3: Coefficient estimates for associations between cognitive test performance and Healthy Aging in Neighborhoods of Diversity across the Life Span (HANDLS) Alzheimer's Risk Score (hAlzScore) by time and diet, for HANDLS participants >50 years of age with complete and reliable cognitive test scores derived from mixed-effects linear regression models (β-Coefficients and standard errors) ‡

	All	Women	Men
*Mini-Mental State Exam, MMSE****,†††,‡‡‡	N=225; k=1.82	N=123; k=1.85	N=181; k=1.77
Time	-0.0±0.17	-0.64±0.55	-0.10±0.26
hAlzScore	**-0.12§±0.07**	-0.05±0.09	-0.15±0.11
hAlzScore × Time	0.02±0.02	0.01±0.02	0.02±0.03
Diet Change*	0.06±0.14	-0.09±0.16	0.02±0.26
Diet Change × Time	-0.02±0.04	0.05±0.04	0.02±0.07
hAlzScore × Diet Change	-0.00±0.08	-0.06±0.09	0.19±0.14
hAlzScore × Diet Change × Time	0.03±0.02	**0.04‖±0.02**	-0.04±0.04
Initial Diet†	-0.05±0.11	-0.18±0.13	-0.10±0.22
Initial Diet × Time	0.01±0.03	0.04±0.03	0.06±0.06
hAlzScore × Initial Diet	0.05±0.06	-0.02±0.07	**0.25‖±0.12**
hAlzScore × Initial Diet ×Time	0.02±0.01	0.02±0.01	-0.03±0.03
California Verbal Learning Test CVLT, List A‡‡,¶¶	N=223; k=1.76	N=122; k=1.8	N=173; k=1.71
Time	**-0.80§±0.43**	-2.22±1.52	-0.57±0.53
hAlzScore	**-0.36§±0.20**	**-0.44§±0.24**	-0.24±0.33
hAlzScore × Time	0.05±0.05	0.16‖±0.07	-0.08±0.07
Diet Change	0.36±0.36	0.06±0.42	0.99±0.70
Diet Change × Time	-0.04±0.10	-0.16±0.13	0.24±0.15
hAlzScore × Diet Change	-0.22±0.22	-0.17±0.26	-0.25±0.38

hAlzScore × Diet Change × Time	**0.15¶±0.06**	**0.21¶±0.08**	0.02±0.08
Initial Diet	-0.07±0.31	-0.13±0.36	-0.07±0.57
Initial Diet × Time	-0.04±0.08	-0.06±0.10	0.06±0.13
hAlzScore × Initial Diet	-0.10±0.18	-0.30±0.21	-0.05±0.32
hAlzScore × Initial Diet ×Time	**0.12¶±0.04**	**0.18¶±0.06**	0.03±0.07
California Verbal Learning Test CVLT, Free Recall Long Delay FRLD	N=219; k=1.74	N=121; k=1.78	N=167; k=1.7
Time	**-0.41‖±0.19**	**-1.15§±0.63**	**-0.83‖±0.27**
hAlzScore	**-0.21‖±0.10**	0.02±0.13	**-0.50¶±0.14**
hAlzScore × Time	0.02±0.02	0.02±0.03	0.04±0.04
Diet Change	-0.05±0.18	-0.29±0.23	**0.71‖±0.29**
Diet Change × Time	0.03±0.04	0.08±0.06	-0.05±0.07
hAlzScore × Diet Change	0.11±0.11	0.19±0.14	-0.09±0.16
hAlzScore × Diet Change × Time	0.03±0.02	0.04±0.03	0.03±0.04
Initial Diet	-0.03±0.16	-0.15±0.21	**0.42§±0.24**
Initial Diet × Time	-0.02±0.03	0.02±0.04	**-0.10§±0.06**
hAlzScore × Initial Diet	0.03±0.09	0.02±0.12	-0.14±0.14
hAlzScore × Initial Diet ×Time	**0.04‖±0.02**	**0.05‖±0.03**	0.05±0.04
Benton Visual Retention Test, BVRT ††	N=227; k=1.89	N=123; k=1.92	N=192; k=1.85
Time	**0.80§±0.41**	**-2.84§±1.46**	**1.04‖±0.48**
hAlzScore	0.29±0.19	**0.71¶±0.26**	-0.09±0.27
hAlzScore × Time	-0.07±0.04	-0.10±0.06	0.02±0.06
Diet Change	-0.31±0.37	-0.35±0.46	-0.48±0.67
Diet Change × Time	-0.07±0.10	0.00±0.13	-0.08±0.16

hAlzScore × Diet Change	-0.20±0.23	-0.29±0.30	0.27±0.35
hAlzScore × Diet Change × Time	0.05±0.06	0.06±0.08	-0.02±0.08
Initial Diet	-0.16±0.31	-0.16±0.37	-0.07±0.55
Initial Diet × Time	0.00±0.07	0.07±0.10	-0.11±0.12
hAlzScore × Initial Diet	0.07±0.17	0.05±0.20	0.36±0.30
hAlzScore × Initial Diet ×Time	**-0.10‖±0.04**	**-0.10‖±0.05**	-0.07±0.07
Brief Test of Attention	N=220; k=1.78	N=121; k=1.81	N=173; k=1.75
Time	0.27±0.24	0.11±0.55	0.21±0.24
hAlzScore	-0.04±0.09	-0.14±0.11	-0.01±0.13
hAlzScore × Time	-0.01±0.03	0.00±0.02	0.01±0.03
Diet Change	**-0.29§±0.18**	-0.32±0.20	-0.19±0.30
Diet Change × Time	0.04±0.06	0.02±0.04	0.10±0.07
hAlzScore × Diet Change	0.08±0.10	0.23§±0.12	-0.10±0.16
hAlzScore × Diet Change × Time	-0.00±0.03	-0.01±0.02	0.04±0.04
Initial Diet	**-0.37‖±0.15**	**-0.50¶±0.17**	0.03±0.26
Initial Diet × Time	0.04±0.04	0.04±0.03	-0.03±0.06
hAlzScore × Initial Diet	0.09±0.09	-0.00±0.09	-0.01±0.15
hAlzScore × Initial Diet ×Time	-0.01±0.02	-0.01±0.02	0.05±0.04
Animal Fluency	N=228; k=1.95	N=124; k=1.95	N=201; k=1.93
Time	0.33±0.26	0.48±1.65	0.63±0.39
hAlzScore	0.05±0.18	0.13±0.25	0.15±0.29
hAlzScore × Time	-0.04±0.03	-0.05±0.07	**-0.09§±0.05**
Diet Change	-0.14±0.35	-0.05±0.44	-0.20±0.71

Diet Change × Time	**0.11§±0.06**	0.16±0.14	0.03±0.12
hAlzScore × Diet Change	0.00±0.21	-0.18±0.26	0.12±0.37
hAlzScore × Diet Change × Time	0.02±0.04	0.01±0.08	0.06±0.06
Initial Diet	0.04±0.29	0.30±0.36	-0.59±0.59
Initial Diet × Time	0.02±0.05	0.02±0.11	-0.00±0.10
hAlzScore × Initial Diet	**0.32‖±0.16**	0.30±0.20	0.32±0.32
hAlzScore × Initial Diet ×Time	-0.03±0.03	-0.05±0.06	0.04±0.05
Digits Span, forward§§§	N=226; k=1.85	N=123; k=1.83	N=192; k=1.86
Time	0.14±0.11	0.25±0.36	**0.31§±0.16**
hAlzScore	0.01±0.07	-0.02±0.09	0.13±0.11
hAlzScore × Time	-0.00±0.01	-0.00±0.02	-0.00±0.02
Diet Change	**0.24§±0.14**	**0.44¶±0.17**	0.06±0.26
Diet Change × Time	-0.00±0.03	0.01±0.03	-0.01±0.05
hAlzScore × Diet Change	-0.01±0.08	0.03±0.10	-0.00±0.14
hAlzScore × Diet Change × Time	0.00±0.02	0.00±0.02	-0.02±0.03
Initial Diet	0.14±0.11	0.20±0.14	0.03±0.21
Initial Diet × Time	-0.01±0.02	-0.02±0.03	0.00±0.04
hAlzScore × Initial Diet	-0.03±0.06	-0.08±0.07	0.10±0.12
hAlzScore × Initial Diet ×Time	-0.00±0.01	0.01±0.01	-0.03±0.02
*Digits Span, backward***	N=226; k=1.84	N=123; k=1.82	N=192; k=1.86
Time	**-0.26§±0.15**	-0.40±0.51	-0.17±0.21
hAlzScore	-0.06±0.07	**-0.19‖±0.09**	0.13±0.10
hAlzScore × Time	0.01±0.02	0.03±0.02	-0.00±0.03

Diet Change	0.07±0.13	0.14±0.16	-0.04±0.24
Diet Change × Time	0.02±0.04	0.05±0.05	-0.00±0.06
hAlzScore × Diet Change	0.00±0.08	0.05±0.10	-0.08±0.13
hAlzScore × Diet Change × Time	0.02±0.02	**0.05§±0.03**	-0.03±0.03
Initial Diet	-0.13±0.11	-0.21±0.14	0.08±0.19
Initial Diet × Time	0.05±0.03	**0.06§±0.04**	0.00±0.05
hAlzScore × Initial Diet	-0.05±0.06	-0.06±0.07	-0.11±0.11
hAlzScore × Initial Diet ×Time	0.02±0.02	0.01±0.02	0.01±0.03
Clock, Command‡‡	N=228; k=1.93	N=125; k=1.95	N=195; k=1.89
Time	0.06±0.09	0.18±0.32	0.03±0.12
hAlzScore	-0.01±0.04	-0.02±0.06	-0.04±0.07
hAlzScore × Time	0.01±0.01	-0.01±0.01	**0.04¶±0.02**
Diet Change	**0.14§±0.08**	0.03±0.10	**0.26*±0.16**
Diet Change × Time	-0.02±0.02	-0.02±0.03	-0.04±0.04
hAlzScore × Diet Change	-0.02±0.05	0.01±0.06	-0.12±0.08
hAlzScore × Diet Change × Time	-0.00±0.01	0.00±0.02	-0.01±0.02
Initial Diet	0.01±0.07	-0.12±0.08	0.13±0.13
Initial Diet × Time	0.02±0.02	0.02±0.02	-0.00±0.03
hAlzScore × Initial Diet	0.05±0.04	0.05±0.05	0.01±0.07
hAlzScore × Initial Diet ×Time	0.01±0.01	0.01±0.01	0.01±0.02
Trailmaking Test, part A	N=224; k=1.84	N=123; k=1.87	N=101; k=1.81
Time	-0.01±0.04	0.13±0.11	0.02±0.05
hAlzScore	-0.00±0.02	0.02±0.02	0.00±0.02

hAlzScore × Time	0.03±0.03	-0.01±0.01	-0.00±0.00
Diet Change	-0.01±0.01	-0.00±0.04	0.03±0.06
Diet Change × Time	0.01±0.02	-0.01±0.01	-0.03±0.02
hAlzScore × Diet Change	1.07±0.75	0.02±0.03	-0.01±0.03
hAlzScore × Diet Change × Time	-0.00±0.00	-0.01±0.01	0.00±0.00
Initial Diet	-0.01±0.03	-0.05±0.03	-0.00±0.05
Initial Diet × Time	-0.01±0.01	**-0.02¶±0.01**	0.00±0.01
hAlzScore × Initial Diet	-0.00±0.02	-0.02±0.02	0.01±0.03
hAlzScore × Initial Diet ×Time	0.00±0.00	0.00±0.00	0.00±0.01
Trailmaking Test, part B§§,‖‖,‡‡‡	N=222; k=1.77	N=123; k=1.76	N=99; k=1.78
Time	-0.07±0.05	**-0.25§±0.15**	-0.06±0.06
hAlzScore	-0.06±0.02	-0.00±0.04	-0.08±0.03
hAlzScore × Time	0.00±0.01	-0.00±0.01	0.00±0.07
Diet Change	0.06±0.05	**0.12§±0.07**	-0.09±0.08
Diet Change × Time	-0.02±0.01	**-0.03¶±0.01**	0.01±0.01
hAlzScore × Diet Change	0.02±0.03	0.04±0.04	0.02±0.04
hAlzScore × Diet Change × Time	-0.00±0.01	-0.01±0.01	0.06±0.01
Initial Diet	-0.02±0.04	-0.01±0.05	-0.06±0.06
Initial Diet × Time	-0.00±0.01	-0.01±0.01	0.03±0.01
hAlzScore × Initial Diet	0.05±0.02	0.03±0.03	0.06±0.03
hAlzScore × Initial Diet ×Time	-0.00±0.00	-0.00±0.01	-0.00±0.01

Abbreviations: MMSE= Mini-Mental State Examination; CVLT-List A= California Verbal Learning test- List A; CVLT-DFR= California Verbal Learning Test-Long-Delayed Free Recall; BVRT= Benton Visual Retention Test; Attention= Brief Test of Attention; Trails A= Trailmaking Test A; Trails B= Trailmaking Test B; Digit Span Forward= Digits Span Forward Test; Digit Span Backward= Digits Span Backward Test; Clock Command= Clock Command

Test; Identical Pictures= Identical Pictures Test; Card Rotation= Card rotation Test; Animal Fluency= Animal Fluency Test.

* Represents change in diet quality over time (~5 years from baseline)

† Represents diet quality at baseline (Time 0)

‡ Continuous covariates were mean-centered.

k= the total number of observations/total number of groups per test

§ $p<0.10$, || $p<0.05$, ¶ $p<0.01$; ** indicates significant interaction between sex and hAlzScore at the $p<0.05$ level; †† indicates significant interaction between sex and hAlzScore at the $p<0.10$ level; ‡‡ indicates significant interaction between sex and hAlzScore and time at the $p<0.05$ level; §§ indicates significant interaction between sex and diet (change) at the $p<0.05$ level; |||| indicates significant interaction between sex and diet (change) and time at the $p<0.05$ level; ¶¶ indicates significant interaction between sex and diet (change) and time at the $p<0.10$ level; *** indicates significant interaction between sex and diet (change) and hAlzScore at the $p<0.10$ level; ††† indicates significant interaction between sex and diet (change) and hAlzScore and time at the $p<0.05$ level; ‡‡‡ indicates significant interaction between sex and diet and time at the $p<0.05$ level; ‡‡‡ indicates significant interaction between sex and diet and hAlzScore at the $p<0.05$ level; §§§ indicates significant interaction between sex and diet and hAlzScore at the $p<0.10$ level;

Table S4: Coefficient estimate (β±SE) comparison for components of diet quality (HEI-2010, DASH and MAR) and change in each component over time for Trailmaking test B^^

	Women
Trailmaking Test, Part B[a1,c2,d1,d2,e2]	N=123
HEI-2010	
Time	36.88±15.73
Diet Change	-11.60±6.59
Diet Change × Time	**3.63±1.38*** **
Initial Diet	-0.17±1.48
Initial Diet × Time	0.52±0.29
Trailmaking Test, Part B[a1,c2,d1,d2,e2]	N=123
DASH	
Time	37.98±15.68
Diet Change	-7.78±49.19
Diet Change × Time	**21.16±10.87***
Initial Diet	22.62±12.93
Initial Diet × Time	2.96±2.70
Trailmaking Test, Part B[a1,c2,d1,d2,e2]	N=123
MAR	
Time	45.03±15.99
Diet Change	-8.21±4.80
Diet Change × Time	**1.86±0.96***
Initial Diet	-0.13±1.15
Initial Diet × Time	0.19±0.25

Abbreviations: HANDLS= Healthy Aging in Neighborhoods of Diversity Across the Lifespan; hAlzScore= HANDLS Alzheimer's Risk Score; MMSE= Mini-Mental State Examination; CVLT-List A= California Verbal Learning test- List A; CVLT-DFR= California Verbal Learning Test-Delayed Free Recall; BVRT= Benton Visual Retention Test; Attention= Brief Test of Attention; Trails A= Trailmaking Test A; Trails B= Trailmaking Test B; Digit Span Forward= Digits Span Forward Test; Digit Span Backward= Digits Span Backward Test; Clock Command= Clock Command Test; Identical Pictures= Identical Pictures Test; Card Rotation= Card rotation Test; Animal Fluency= Animal Fluency Test.

[#]Represents change in diet quality over time (~5 years from baseline)

[^] Represents diet quality at baseline (Time 0)

[a×] Continuous covariates were mean-centered.

*** p<0.01, ** p<0.05, * p<0.10; [a1] indicates significant interaction between time and se× at the p<0.05 level; [a2] indicates significant interaction between time and se× at the p<0.10 level; [b1] indicates significant interaction between se× and diet at the p<0.05 level; [b2] indicates significant interaction between se× and diet at the p<0.10 level; [c1] indicates significant interaction between se× and diet (change) at the p<0.05 level; [c2] indicates significant interaction between se× and diet (change) at the p<0.10 level; [d1] indicates significant interaction between se× and diet (change) and time at the p<0.05 level; [d2] indicates significant interaction between se× and diet (change) and time at the p<0.10 level; [e1] indicates significant interaction between se× and diet and time at the p<0.05 level; [e2] indicates significant interaction between se× and diet and time at the p<0.10 level;

^^ All results are presented based on the primary PCA analysis.

Table S5: Coefficient estimates (β±SE) for associations between California Verbal Learning Test (CVLT)^^ performance and hAlzScore by time and each diet quality component (HEI-2010, DASH and MAR), for HANDLS participants >50y of age

	All	Women
HEI-2010		
California Verbal Learning Test CVLT, List A[b1, d2]	N=223; k=1.8	N=122; k=1.8
Time	-0.82*±0.43	-2.22±1.52
hAlzScore	-0.39**±0.20	-0.40±0.24
hAlzScore × Time	0.05±0.05	0.14*±0.07
Change in HEI	0.23*±0.14	0.13±0.18
Change in HEI × Time	-0.03±0.04	-0.09±0.06
hAlzScore × Change in HEI	-0.05±0.09	-0.04±0.11
hAlzScore × Change in HEI × Time	**0.06**±0.02**	**0.10***±0.03**
HEI-2010	0.01±0.03	0.02±0.04
HEI-2010 × Time	-0.01±0.01	-0.01±0.01
hAlzScore × HEI-2010	0.01±0.02	-0.02±0.03
hAlzScore × HEI-2010 ×Time	**0.01**±0.01**	**0.02***±0.007**
DASH		
California Verbal Learning Test CVLT, List A[b1, d2]	N=223; k=1.8	N=122; k=1.8
Time	-0.78*±0.43	-2.23±1.47
hAlzScore	-0.36*±0.19	-0.48**±0.24
hAlzScore × Time	0.06±0.05	0.17**±0.07
Change in DASH	-1.51±1.17	-1.23±1.30
Change in DASH × Time	0.03±0.32	-0.58±0.40
hAlzScore × Change in DASH	-0.40±0.75	-0.30±0.96
hAlzScore × Change in DASH × Time	**0.45**±0.20**	**0.84***±0.28**
DASH	-0.44±0.31	-0.51±0.36
DASH × Time	0.03±0.08	-0.03±0.10
hAlzScore × DASH	-0.29*±0.16	-0.41**±0.20
hAlzScore × DASH ×Time	**0.15***±0.04**	**0.24***±0.06**
MAR		
California Verbal Learning Test CVLT, List A[b1, d2]	N=223; k=1.8	N=122; k=1.8
Time	-0.62±0.44	-2.47±1.61
hAlzScore	-0.34*±0.20	-0.44*±0.26
hAlzScore × Time	0.04±0.05	0.13±0.08
Change in MAR	0.14±0.11	0.06±0.13
Change in MAR × Time	0.01±0.03	0.04±0.04
hAlzScore × Change in MAR	-0.05±0.06	-0.11±0.07
hAlzScore × Change in MAR × Time	0.01±0.02	0.03±0.02
MAR	0.01±0.03	0.005±0.03
MAR × Time	-0.005±0.01	-0.001±0.01
hAlzScore × MAR	0.003±0.01	-0.01±0.01
hAlzScore × MAR ×Time	-0.001±0.004	0.003±0.005
HEI-2010		
California Verbal Learning Test CVLT, Free Recall Long Delay FRLD	N=219; k=1.7	N=121; k=1.8

Time	-0.39**±0.19	-1.04*±0.63
hAlzScore	-0.22**±0.10	0.03±0.13
hAlzScore × Time	0.03±0.02	0.01±0.03
Change in HEI	0.06±0.07	-0.06±0.10
Change in HEI × Time	-0.004±0.02	0.02±0.02
hAlzScore × Change in HEI	0.01±0.01	0.10±0.06
hAlzScore × Change in HEI × Time	0.03±0.02	0.19±0.14
HEI-2010	0.00±0.02	-0.01±0.02
HEI-2010 × Time	-0.005±0.004	0.007±0.005
hAlzScore × HEI-2010	0.02±0.01	0.02±0.01
hAlzScore × HEI-2010 ×Time	0.002±0.002	0.003±0.003
DASH		
California Verbal Learning Test CVLT, Free Recall Long Delay FRLD	N=219; k=1.74	N=121; k=1.78
Time	-0.42**±0.19	-0.96±0.61
hAlzScore	-0.19**±0.10	0.03±0.13
hAlzScore × Time	0.02±0.02	0.02±0.03
Change in DASH	-1.56***±0.58	-1.45**±0.74
Change in DASH × Time	0.15±0.14	0.16±0.17
hAlzScore × Change in DASH	0.29±0.37	0.07±0.54
hAlzScore × Change in DASH × Time	0.14±0.09	0.16±0.12
DASH	-0.16±0.16	-0.19±0.21
DASH × Time	-0.01±0.04	0.02±0.04
hAlzScore × DASH	-0.004±0.08	-0.03±0.11
hAlzScore × DASH ×Time	**0.05**±0.02**	**0.06**±0.02**
MAR		
California Verbal Learning Test CVLT, Free Recall Long Delay FRLD	N=219; k=1.74	N=121; k=1.78
Time	-0.40**±0.19	-1.11*±0.65
hAlzScore	-0.23**±0.10	0.02±0.15
hAlzScore × Time	0.03±0.02	0.03±0.03
Change in MAR	0.08±0.05	0.03±0.07
Change in MAR × Time	0.007±0.01	0.01±0.02
hAlzScore × Change in MAR	-0.001±0.03	0.02±0.04
hAlzScore × Change in MAR × Time	0.0003±0.006	0.003±0.01
MAR	0.000±0.02	-0.10±0.02
MAR × Time	0.003±0.003	0.003±0.005
hAlzScore × MAR	-0.007±0.008	-0.002±0.10
hAlzScore × MAR ×Time	0.002±0.02	-0.02±0.02

Abbreviations: HANDLS= Healthy Aging in Neighborhoods of Diversity Across the Lifespan; hAlzScore= HANDLS Alzheimer's Risk Score; MMSE= Mini-Mental State Examination; CVLT-List A= California Verbal Learning test- List A; CVLT-DFR= California Verbal Learning Test-Long-Delayed Free Recall; BVRT= Benton Visual Retention Test; Attention= Brief Test of Attention; Trails A= Trailmaking Test A; Trails B= Trailmaking Test B; Digit Span Forward= Digits Span Forward Test; Digit Span Backward= Digits Span Backward Test; Clock Command= Clock Command Test; Identical Pictures= Identical Pictures Test; Card Rotation= Card rotation Test; Animal Fluency= Animal Fluency Test.

[#]Represents change in diet quality over time (~5 years from baseline)

[^] Represents diet quality at baseline (Time 0)

[a×] Continuous covariates were mean-centered.
k= the total number of observations/total number of groups per test
*** p<0.01, ** p<0.05, * p<0.10; [a1] indicates significant interaction between se× and hAlzScore at the p<0.05 level; [a2] indicates significant interaction between se× and hAlzScore at the p<0.10 level; [b1] indicates significant interaction between se× and hAlzScore and time at the p<0.05 level; [b2] indicates significant interaction between se× and hAlzScore and time at the p<0.10 level; [c1] indicates significant interaction between se× and diet (change) at the p<0.05 level; [c2] indicates significant interaction between se× and diet (change) at the p<0.10 level; [d1] indicates significant interaction between se× and diet (change) and time at the p<0.05 level; [d2] indicates significant interaction between se× and diet (change) and time at the p<0.10 level; [e1] indicates significant interaction between se× and diet (change) and hAlzScore at the p<0.05 level; [e2] indicates significant interaction between se× and diet (change) and hAlzScore at the p<0.10 level; [f1] indicates significant interaction between se× and diet (change) and hAlzScore and time at the p<0.05 level; [f2] indicates significant interaction between se× and diet (change) and hAlzScore and time at the p<0.10 level; [g1] indicates significant interaction between se× and diet and time at the p<0.05 level; [g2] indicates significant interaction between se× and diet and time at the p<0.10 level; [h1] indicates significant interaction between se× and diet and hAlzScore at the p<0.05 level; [h2] indicates significant interaction between se× and diet and hAlzScore at the p<0.10 level;

^^ All results are presented based on the primary PCA analysis.