Original research

Adherence to the MIND diet and longitudinal brain structural changes over a decade: evidence from the Framingham heart study offspring cohort

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ABSTRACT

Background The MIND diet was favourably linked to lower risk of neurodegenerative diseases. While previous cross-sectional studies implied its beneficial associations with brain imaging markers, its associations with long-term brain structural changes remained unclear.

Methods We included 1647 middle-aged and older individuals from the Framingham Heart Study Offspring cohort (FOS). MIND diet score was calculated from a validated FFQ, repeatedly administered at Exams 5, 6, and 7. Brain imaging markers were acquired between 1999 and 2019, with a median repetition (interquartile range, IQR) of 3 (2-3) times. We used linear mixed models to assess the associations of the MIND diet score and its components with longitudinal brain structural changes.

Results Over a median follow-up of 12.3 years (IQR 6.8–13.8 years), greater adherence to the MIND diet was associated with slower decline in total grey matter volume. Specifically, each three-unit increase in the MIND diet score was linked to a 0.279 cm³/year (95% CI 0.089 to 0.469) slower decline in total grey matter volume, corresponding to a 20.1% attenuation in age-related change that was equivalent to 2.5 years of reduced brain ageing during the 12.3-year follow-up. Additionally, higher MIND diet score was associated with slower increases in lateral ventricular volume (−0.071 cm³/year, 95% CI −0.125 to −0.017), notably in the left lateral ventricle (−0.041 cm³/year, 95% CI −0.070 to −0.013), reflecting approximately 8.0% and 8.8% attenuation of age-related changes, equivalent to roughly 1.0 year of delayed brain ageing during follow-up.

Conclusions In this prospective cohort study, greater adherence to the MIND diet was associated with slower brain structural atrophy, particularly regarding grey matter loss and ventricular enlargement. These findings support the potential of the MIND diet as a strategy to support brain health and delay structural brain ageing.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Mediterranean–Dietary Approaches to Stop Hypertension Diet Intervention for Neurodegenerative Delay (MIND) diet has been linked to better cognitive outcomes, but evidence regarding its relationship with long-term brain structural changes remains limited.

WHAT THIS STUDY ADDS

⇒ In this prospective cohort study that included 1647 middle-aged and older individuals from the Framingham Heart Study Offspring cohort, greater adherence to the MIND diet was associated with slower progression of brain structural atrophy.

⇒ The MIND diet was associated with less grey matter loss and ventricular enlargement, which corresponds to an 8.0%–20.1% attenuation in age-related changes during follow-up.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This study provides evidence for the longitudinal association of a healthy dietary pattern with brain structural changes, thereby strengthening the scientific foundation for developing evidence-based dietary interventions to promote brain health and mitigate neurodegenerative risks in ageing populations.

⇒ While the findings underscore the translational potential of the MIND diet as a public health strategy, they also highlight the necessity for high-quality, long-term intervention studies to further validate and refine these dietary approaches for broader clinical and policy applications.

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INTRODUCTION

Brain ageing and neurodegenerative diseases, such as Alzheimer's disease (AD)[1] and Parkinson's disease (PD),[2] represent significant public health challenges globally,[3–5] with the burden expected to grow as populations continue to age.[6] Given the scarcity of curative treatments, preventive strategies targeting modifiable risk factors are essential to slow brain ageing and reduce the risk of neurodegeneration.[7] Growing evidence highlights the importance of lifestyle factors in maintaining brain health,[8 9] and emerging population-based evidence suggests that healthy dietary patterns may help slow cognitive decline[10 11] and reduce the risks of AD[12] and PD.[13] Specifically, the Mediterranean–Dietary Approaches to Stop Hypertension Diet Intervention for Neurodegenerative Delay (MIND) diet, which combines elements from the Mediterranean and Dietary Approaches to Stop Hypertension diets and incorporates specific food groups for brain health,[10] has attracted considerable attention.[14 15]

The MIND diet was proposed for its focus on cognitive and brain health and its clear recommendations for each food group with prespecified cut-offs, although its generalisability to non-Western populations remains to be assessed.

Brain MRI offers a precise method for assessing brain structure and atrophy,[16–18] which could occur years to decades before clinical symptoms emerge, a period when dietary factors could play a key preventive role.[19] In a cross-sectional analysis based on the Framingham Heart Study (FHS), we observed that higher adherence to the MIND diet was associated with greater total brain volume (TBV).[20] In our subsequent study based on the UK Biobank, MIND diet adherence was not significantly associated with 2-year changes in the overall brain volumetric measures. However, it was related to less putamen and pallidum atrophy among individuals without the *Apolipoprotein E (APOE)* ε4 allele.[21] Evidence from randomised controlled trials is also mixed: one reported beneficial effects on the surface area of the inferior frontal gyrus,[22] while another showed no significant effects,[23] with both limited by relatively short follow-up durations. Overall, understanding the relationship between dietary adherence and long-term brain structural changes remained challenging, and the lack of repeated long-term dietary intake measures complicates the inference on the sustained impacts of diet on brain health.

To address these limitations, we investigated the associations of long-term adherence to the MIND diet with longitudinal changes in brain structure over a decade using data from the community-based FHS offspring cohort (FOS).

METHODS

Study population

The FHS was established in 1948 in Framingham, Massachusetts, aimed to investigate the epidemiology and risk factors of coronary heart disease and other cardiovascular conditions in the USA.[24 25] The FOS was launched in 1971 with 5124 men and women, consisting of the children of the original cohort and their spouses. Since enrolment, participants have undergone examinations every 4–8 years, with brain MRI assessments added every 2–6 years beginning in 1999. As of 2022, the study has completed its tenth examination cycle. The FOS has an overall retention rate of 99%, which reflects the high commitment of participants and data quality.[25] Data collection for the FHS was approved by the Institutional Review Board of Boston University (H-24583), and the present analysis was approved by the Ethics Committee of the School of Public Health, Zhejiang University (ZGL202403-2).

For this analysis, we included participants who completed at least one valid food frequency questionnaire (FFQ) at exams 5 (1991–1995), 6 (1995–1998) and/or 7 (1998–2001) to assess dietary intake (total energy intake 600–3999 kcal/d for females or 600–4199 kcal/d for males and ≤13 missing items),[26] underwent at least two brain MRI assessments between 1999 and 2019 and were free of dementia and stroke at their first MRI.[27 28] Among 2952 dementia- and stroke-free participants with valid dietary data, 2233 also participated in the MRI substudy, among whom we further excluded 586 participants (26%) with only one brain MRI scan for the longitudinal analysis, for whom the specific classification as withdrawals or non-respondents during follow-up is not available. In total, 1647 middle-aged and older adults were included, as is shown in the flowchart in figure 1. We defined the study baseline as the date of the most recent FFQ assessment. Participants had a median of 3 MRI scans (IQR 2–3) over a median follow-up of 12.3 years (IQR 6.8–13.8).

Dietary assessment

Dietary intake was assessed using a semiquantitative FFQ administered at exams 5–7. The FFQ contains approximately 140 items and captures habitual intake over the preceding year with response options ranging from 'never' to 'six or more servings per day'. Its validity for nutrient and food group assessment in the US population has been established through repeated validation studies against dietary records and biomarkers.[29–33] Among participants, 1266 (77%) completed all three assessments, and 1568 (95%) completed at least two. The MIND diet score was calculated by summing the scores from nine recommended food groups (leafy green vegetables, other vegetables, nuts, berries, beans, whole grains, fish, poultry and olive oil), five restricted food groups (red meat, butter/margarine, cheese, pastries and sweets and fast fried foods) and moderate intake of wine. Scores of 1, 0.5 or 0 were assigned based on fully, partially or not meeting recommended intake levels, respectively, and the MIND diet score ranged from 0 to 15, with a higher score representing better adherence.[10] For participants who went through >1 dietary assessment, the average MIND diet score was used.

Brain magnetic resonance measures

MRI scans were performed with a Siemens 1.5-T scanner (Siemens Medical Solutions) with standardised T1-weighted coronal spoiled gradient-recalled echo and fluid-attenuated inversion recovery sequences, as detailed previously.[28 34] MRI data processing, including image registration, segmentation and quantification, was performed by a neurologist blinded to participant identity. Imaging-derived phenotypes (IDPs) included TBV, volumes of total grey matter, total white matter, cerebrospinal fluid, lateral ventricles (total, left and right), third ventricle, hippocampus (total, left and right) and white matter hyperintensity (WMH). Central cerebrospinal fluid spaces were divided into the lateral ventricles, excluding the temporal horns of the lateral ventricles as an estimate of hippocampal size.[35] All volumetric measures but WMH were z-transformed to total intracranial volume to adjust for head size differences after the verification of normality, and WMH volumes were log-transformed and then z-transformed due to skewed distribution.[21] The detailed descriptions have been provided in online supplemental Methods. Spearman's correlation indices between the IDPs were presented in online supplemental Figure S1.

Covariates

We included multiple sociodemographic, lifestyle and health-related factors collected concurrently or prior to dietary assessments for confounding adjustments according to previous studies on diet and brain health.[14 36 37] The sociodemographic factors included age at baseline, sex (self-reported) and highest education level (with or without college degree), according to the previous literature.[38] Lifestyle factors included smoking status (never, former or current), physical activity index (PAI, calculated by summing the hours spent in a typical 24-hour day, each weighted according to activity intensity level)[39] and body mass index (BMI) category (<25.0, 25–<30 and ≥30 kg/m^2).[40] Total energy intake was calculated concurrently with the MIND score from FFQ. Health-related factors included depressive status assessed using the Center for Epidemiologic Studies Depression Scale (CES-D) and physician-adjudicated diagnoses of type 2 diabetes, hypertension, hypercholesterolaemia and cardiovascular diseases (CVDs).[25] All covariates were collected at the date of the most recent FFQ assessment or using the most updated value before FFQ assessment, if missing.

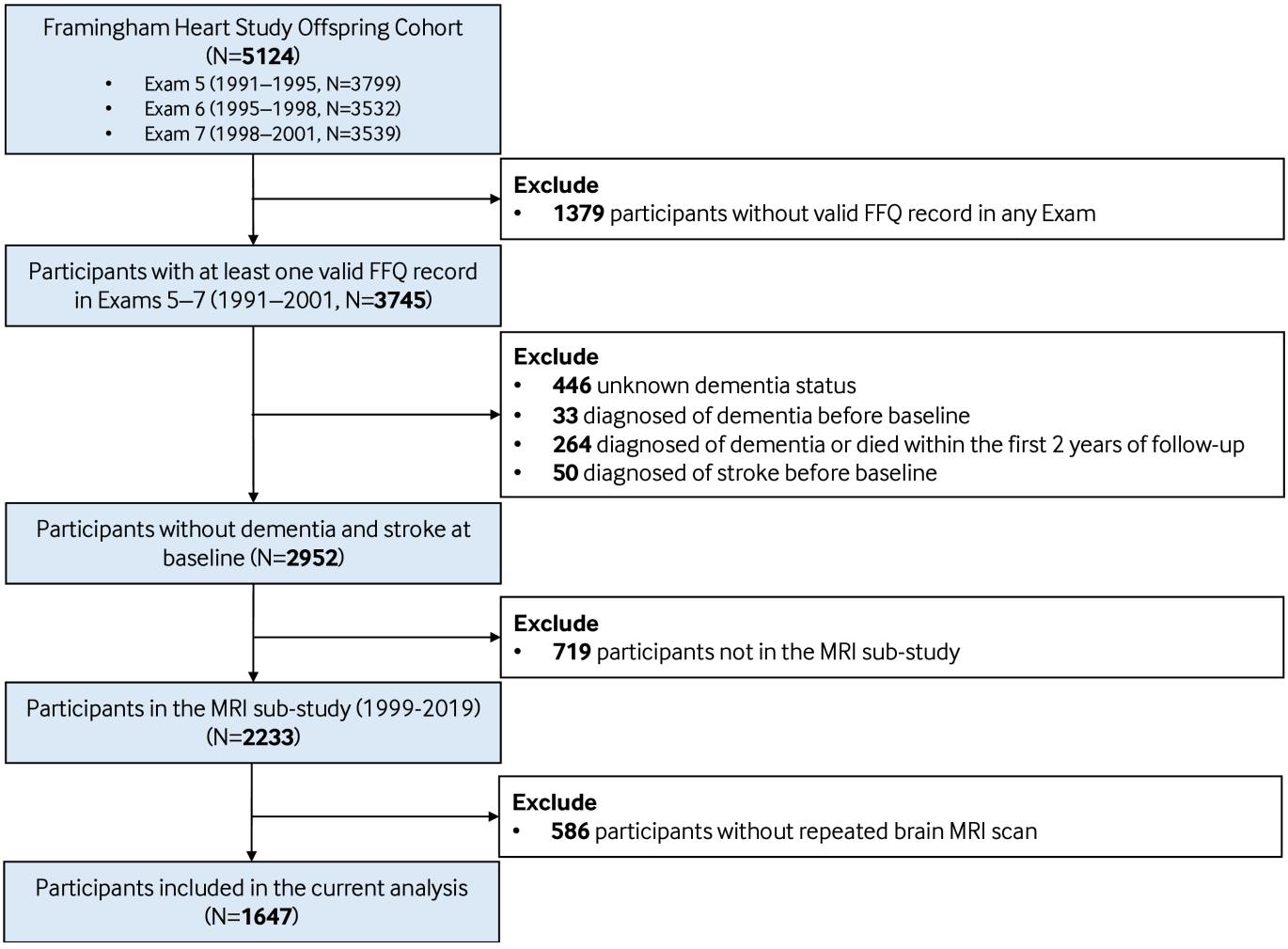

Figure 1 Participant inclusion flowchart. FFQ, food frequency questionnaire.

Statistical analysis

We summarised the baseline characteristics using mean (SD) for normally distributed continuous variables and number (percentage) for categorical variables. In the primary analysis, we assessed the associations of the MIND diet score with the IDPs using linear mixed models to account for the individual random intercept.[41] The models sequentially adjusted for basic socio-demographic, lifestyle and health-related factors. Model 1 was adjusted for age at baseline, the squared term of baseline age,[35] sex, and total energy intake; model 2 was based on model 1 and further adjusted for highest education level, smoking status, PAI and BMI category and model 3 was based on model 2 and further adjusted for CES-D score, type 2 diabetes, hypertension, hypercholesterolaemia, CVDs and interval between the latest FFQ and first brain imaging scan. The primary estimand are coefficients for the interaction term crossing follow-up time and MIND diet score (time×MIND), which represent the differences in slope of brain structural changes by MIND diet score.[41] We verified model assumptions by inspecting histograms and Q–Q plots of residuals to evaluate normality and residuals versus fitted value plots to check for homoscedasticity. No major assumption violations were observed. In supplementary analyses, we categorised participants by tertiles of MIND diet adherence and specified the lowest tertile as the reference group. Statistical significance was determined using the Benjamini–Hochberg (B-H) approach to control the false discovery rate (FDR), with FDR-corrected p values<0.05 considered significant.[42 43] We also conducted prespecified subgroup analyses by age (< 60 years and ≥ 60 years), sex, smoking status (former or current, and never), physical activity (higher and lower) and BMI (≥25 kg/m^2 and <25 kg/m^2). Potential modification effect was tested by including a three-way interaction term (MIND diet score×time × stratification variable), and an FDR-corrected p interaction<0.05 as indicative of a significant interaction.

In secondary analyses, we evaluated the associations of the components of the MIND diet score with the IDPs. To allow comparison across food groups, intake levels were energy adjusted using the residual method and modelled as continuous variables standardised by the 90th–10th percentile range.[44] The p values were corrected using the B-H method.

We conducted several sensitivity analyses: (1) we excluded brain MRI data collected after dementia diagnosis because dementia treatment may influence the structural markers; (2) we used the calendar age (time varying by the study examination visits) rather than follow-up time (starting from 0 since baseline) as the time scale for a more direct interpretation for brain ageing; (3) we excluded all prevalent CVD cases at baseline because they may alter their dietary behaviour after diagnosis and (4) we restricted analyses to participants who completed dietary assessments at exam 7 and at least one earlier exam (exam 5 or 6) to account for long-term dietary intake and reduce population heterogeneity from varied baseline assessments.

Table 1 Baseline characteristics of study participants

Variable	Overall	MIND diet score			p-value
		Tertile 1	Tertile 2	Tertile 3	
N	1647	596	552	499	
MIND diet score, median (IQR)	6.8 (5.8, 7.8)	5.5 (4.7, 5.8)	6.8 (6.5, 7.2)	8.3 (8.0, 9.0)	<0.001
Age, y, mean (SD)	60.9 (8.5)	61.5 (8.8)	60.8 (8.7)	60.5 (7.7)	0.121
Female, N (%)	895 (54.3)	293 (49.2)	290 (52.5)	312 (62.5)	<0.001
Total energy intake, kcal/d, mean (SD)	1882.8 (534.1)	1847.7 (546.2)	1910.5 (539.3)	1894.2 (512.2)	0.117
Intracranial capacity, cm^3, mean (SD)	1234.2 (124.7)	1236.6 (131.8)	1238.0 (121.7)	1226.9 (118.9)	0.301
College and above, N (%)	1191 (72.3)	370 (62.1)	405 (73.4)	416 (83.4)	<0.001
Smoking status, N (%)					
Never	612 (37.2)	209 (35.1)	207 (37.5)	196 (39.3)	<0.001
Former	866 (52.6)	299 (50.2)	291 (52.7)	276 (55.3)	
Current	169 (10.3)	88 (14.8)	54 (9.8)	27 (5.4)	
PAI, mean (SD)	37.9 (6.3)	38.3 (7.1)	37.5 (5.7)	38.0 (5.9)	0.102
BMI, N (%)					0.079
<25.0 kg/m^2	507 (30.8)	186 (31.2)	153 (27.7)	168 (33.7)	
25–<30 kg/m^2	708 (43.0)	240 (40.3)	251 (45.5)	217 (43.5)	
≥30 kg/m^2	432 (26.2)	170 (28.5)	148 (26.8)	114 (22.8)	
Type 2 diabetes, N (%)	140 (8.5)	60 (10.1)	43 (7.8)	37 (7.4)	0.224
Hypertension, N (%)	611 (37.1)	232 (38.9)	199 (36.1)	180 (36.1)	0.512
Hypercholesterolaemia, N (%)	1020 (61.9)	352 (59.1)	344 (62.3)	324 (64.9)	0.134
CVD, N (%)	125 (7.6)	56 (9.4)	42 (7.6)	27 (5.4)	0.046

BMI, body mass index; CVD, cardiovascular disease; DASH, dietary approaches to stop hypertension; MIND, Mediterranean–DASH diet intervention for neurodegenerative delay; PAI, physical activity index.

All statistical analyses were implemented using R 4.3.0. Linear mixed models were performed using the 'lmerTest' package[45] and visualised using the 'interactions' package. Missing values in covariates were carried forward from the previous examinations. We reported 95% CIs (unadjusted for multiplicity), and all *p* values were corrected using the B-H method. Data analyses were performed from August 2024 to January 2025.

RESULTS

Baseline characteristics of the study population

We included 1647 participants in this study, among whom the mean (SD) age at baseline was 60.9 (8.5), 54.3% were female and the median MIND diet score was 6.8 out of 15 (table 1). Compared with those in the lowest tertile (T1), participants in the highest tertile (T3) of MIND diet score were more likely to be female (62.5% vs 49.2%), college educated (83.4% vs 62.1%) and less likely to be current smokers (5.4% vs 14.8%) or with obesity (22.8% vs 28.5%). They also had a lower prevalence of type 2 diabetes (7.4% vs 10.1%), hypertension (36.1% vs 38.9%) and CVD (5.4% vs 9.4%). At baseline, participants with higher MIND scores had lower volumes of lateral ventricles and WMHs (online supplemental Table S1).

Associations of the MIND diet with brain structural changes

Over a median follow-up of 12.3 years, participants experienced declines in total brain, grey matter, white matter and hippocampal volumes, alongside increased cerebrospinal fluid, ventricular volumes and WMH (online supplemental Table S2). As shown in table 2, higher MIND diet scores were associated with slower grey matter atrophy, with each 3-unit increase linked to a 0.279 cm^3/year slower decline (95% CI 0.089 to 0.469, p=0.004; B-H adjusted p=0.027), representing a 20.1% attenuation of the aging-related decline (1.40 cm^3/year) and equivalent to 2.5 years of reduced brain ageing during follow-up. Similarly, each 3-point increase in MIND score was associated with slower expansion of total ventricular volume by −0.071 cm^3/year (95% CI −0.125 to −0.017; B-H adjusted p=0.043) and of the left lateral ventricle by −0.041 cm^3/year (95% CI −0.070 to −0.013; B-H adjusted p=0.027), reflecting 8.0% and 8.8% of the corresponding time effects and ~1.0 year of delayed brain ageing during follow-up, respectively. A statistically significant association was also observed for the right lateral ventricle (−0.030 cm^3/year, 95% CI −0.056 to −0.003), although not surviving multiple testing correction.

The associations were further supported by the analyses comparing the participants at the top versus bottom tertiles (figure 2 and online supplemental Table S3). Compared with the lowest tertile, participants in the highest tertile showed a significantly slower decline in grey matter volume (0.380 cm^3/year, 95% CI 0.150 to 0.609) and slower increases in total lateral ventricle volume (−0.087 cm^3/year, 95% CI −0.152 to −0.021), left ventricle volume (−0.052 cm^3/year, 95% CI −0.086 to −0.017) and right ventricle volume (−0.036 cm^3/year, 95% CI −0.068 to −0.003). A smaller annual increase in WMH volume was also observed (−0.009 cm^3/year, 95% CI −0.017 to −0.000).

The associations of the food groups in the MIND diet with brain structural changes were shown in online supplemental Figure S2 and Table S4. The primary contributors to the beneficial associations included the berries, associated with slower increment in the ventricle volumes, and poultry, associated with slower increment in the ventricle volumes and slower decline in grey matter. Among the restricted food groups, higher intake of sweets was associated with faster ventricular expansion and hippocampal atrophy, while fast fried foods were also linked to greater hippocampal volume decline. Unexpectedly, higher whole grain intake was associated with unfavourable changes of several indicators, including faster declines in grey matter

Table 2 Associations of MIND diet score (per three-unit increment) with longitudinal brain structural changes (cm^3/year)

Outcome	Difference (95% CI)			P value	FDR-corrected p value
	Model 1	Model 2	Model 3		
TBV	0.102 (−0.087 to 0.291)	0.102 (−0.087 to 0.292)	0.104 (−0.086 to 0.293)	0.283	0.425
Total grey matter volume	0.277 (0.087 to 0.467)	0.278 (0.088 to 0.468)	0.279 (0.089 to 0.469)	0.004	0.027
Total white matter volume	−0.190 (−0.376 to −0.003)	−0.189 (−0.376 to −0.002)	−0.189 (−0.375 to −0.002)	0.048	0.115
Total cerebrospinal fluid volume	0.017 (−0.135 to 0.170)	0.017 (−0.136 to 0.169)	0.016 (−0.137 to 0.168)	0.839	0.875
Lateral ventricle volume	−0.071 (−0.125 to −0.017)	−0.071 (−0.125 to −0.016)	−0.071 (−0.125 to −0.017)	0.011	0.043
Left lateral ventricle volume	−0.041 (−0.070 to −0.013)	−0.041 (−0.070 to −0.013)	−0.041 (−0.070 to −0.013)	0.004	0.027
Right lateral ventricle volume	−0.030 (−0.056 to −0.003)	−0.030 (−0.056 to −0.003)	−0.030 (−0.056 to −0.003)	0.030	0.089
Third ventricle volume	−0.001 (−0.003 to 0.000)	−0.002 (−0.003 to 0.000)	−0.002 (−0.003 to 0.000)	0.085	0.167
Left hippocampus volume	−0.000 (−0.001 to 0.001)	−0.000 (−0.001 to 0.001)	−0.000 (−0.001 to 0.001)	0.875	0.875
Right hippocampus volume	−0.001 (−0.002 to 0.001)	−0.001 (−0.002 to 0.001)	−0.001 (−0.002 to 0.001)	0.351	0.468
Hippocampus volume	−0.001 (−0.003 to 0.002)	−0.001 (−0.003 to 0.002)	−0.001 (−0.003 to 0.002)	0.563	0.676
WMH volume	−0.006 (−0.013 to 0.001)	−0.006 (−0.013 to 0.001)	−0.006 (−0.013 to 0.001)	0.097	0.167

Model 1 was adjusted for age, age-square, sex and total energy intake; model 2 was based on model 1 and further adjusted for highest education level, smoking status, PAI, BMI category and model 3 was based on model 2 and further adjusted for CES-D score, type 2 diabetes, hypertension, hypercholesterolaemia, CVDs and interval between the latest FFQ and first brain imaging scan. The coefficient of interest was time×MIND diet score. We presented the *p* values from model 3 as the primary model for interpretation.
BMI, body mass index; CES-D, Center for Epidemiologic Studies Depression Scale; CVDs, cardiovascular diseases; DASH, dietary approaches to stop hypertension; FDR, false discovery rate; FFQ, food frequency questionnaire; MIND, Mediterranean–DASH diet intervention for neurodegenerative delay; PAI, physical activity index; TBV, total brain volume; WMH, white matter hyperintensity.

and hippocampal volumes and increased ventricular, while higher cheese intake was associated with slower declines in grey matter and hippocampal volumes and less ventricular and WMH volume increase.

Subgroup and sensitivity analyses

In the subgroup analyses, as presented in figure 3 and online supplemental Table S5, the association of MIND score with lateral ventricle volume and left lateral ventricle volume was significantly stronger in older participants (B-H adjusted *p* interactions=0.047 and 0.042, respectively). The association of MIND score with lower third ventricle volume was only significant in more physically active participants (B-H adjusted *p* interaction=0.029). Moreover, the association between MIND score and total cerebrospinal fluid volume was significant for participants with a BMI<25 kg/m^2 (0.366 cm^3/year, 95% CI 0.109 to 0.623), but not for BMI≥25 kg/m^2 (−0.160 cm^3/year, 95% CI −0.347 to 0.027; B-H adjusted *p* interaction=0.017).

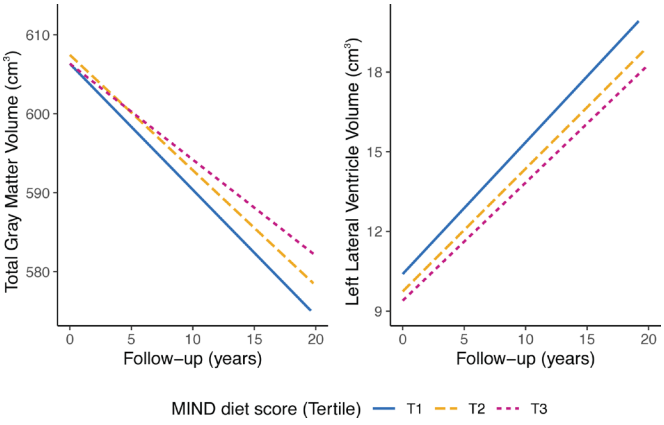

Figure 2 Fitted longitudinal brain structural changes (cm^3/year) according to MIND diet score (tertiles). The models were adjusted for age, age-square, sex, total energy intake, highest education level, smoking status, PAI, BMI category, CES-D score, type 2 diabetes, hypertension, hypercholesterolaemia, CVDs and interval between the latest FFQ and first brain imaging scan. The coefficient of interest was time×MIND diet score. BMI, body mass index; CES-D, Center for Epidemiologic Studies Depression Scale; CVDs, cardiovascular diseases; DASH, dietary approaches to stop hypertension; FFQ, food frequency questionnaire; MIND, Mediterranean–DASH diet intervention for neurodegenerative delay; PAI, physical activity index.

The results in the sensitivity analysis further confirmed the robustness of the primary findings (online supplemental Table S6). When we stopped follow-up at dementia diagnosis, used age as a time scale, excluded all prevalent CVD cases at baseline and restricted analyses to participants who completed dietary assessments at exam 7 and at least one earlier exam, the associations for total grey matter volume and lateral ventricle volumes remained significant. Stopping follow-up at dementia diagnosis, excluding prevalent CVD cases, strengthened the associations with faster decline in white matter volume, and using age as time scale magnified the association with slower decline in TBV.

DISCUSSION

In this community-based study, greater adherence to the MIND diet was associated with slower grey matter decline and reduced ventricular enlargement over a median follow-up of 12 years. The associations were consistent across a series of sensitivity analyses and were stronger in older, heavier and more physically active individuals. Our findings suggest that the MIND diet could offer potential benefits for brain health, with varying effects across different population subgroups.

Adherence to the MIND diet has been associated with multiple cognitive and neurodegenerative outcomes, such as slower cognitive decline[10] and lower risks of AD[12] and PD.[13] Emerging evidence also supports its associations with favourable brain MRI markers.[20 21 46] For example, a cross-sectional study in the three-city cohort reported that a higher MIND diet score was associated with lower diffusivity values in the splenium of the corpus callosum.[46] In our previous cross-sectional analysis of 1904 FOS participants, a higher MIND diet score was related to larger TBV.[20] Similarly, our earlier UK Biobank analysis found that greater MIND adherence was linked to larger volumes of several subcortical regions and less WMHs.[21] Building on these

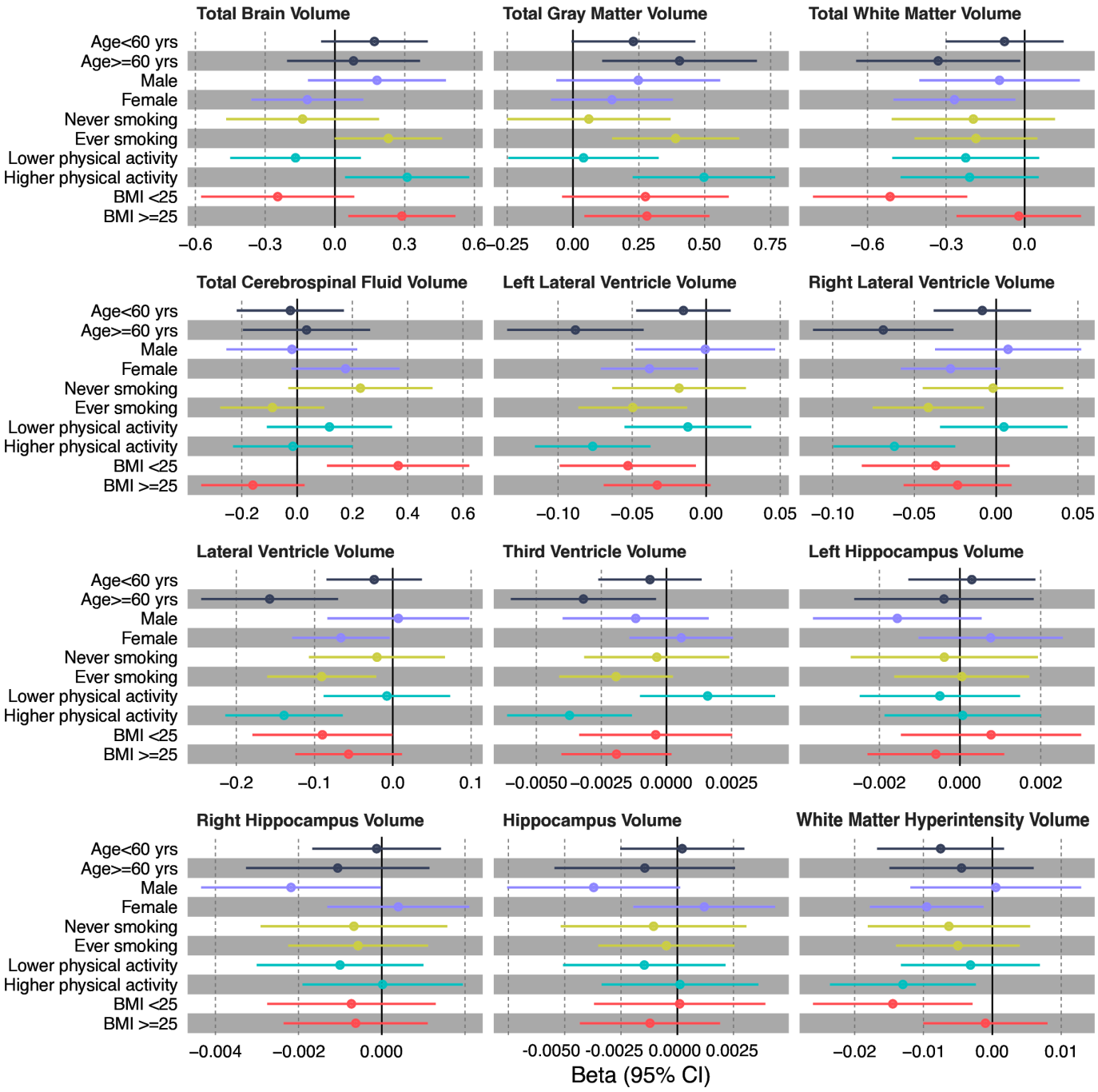

Figure 3 Associations of MIND diet score (per three-unit increment) with longitudinal brain structural changes (cm^3/year) in subgroups of participants. The models were adjusted for age, age-square, sex, total energy intake, highest education level, smoking status, PAI, BMI category, CES-D score, type 2 diabetes, hypertension, hypercholesterolaemia, CVDs and interval between the latest FFQ and first brain imaging scan. The coefficient of interest was time × MIND diet score. The interaction terms reaching statistical significance after FDR correction include: MIND diet score × age × time for lateral ventricle volume and left lateral ventricle volume (p interaction=0.047 and 0.042). BMI, body mass index; CES-D, Center for Epidemiologic Studies Depression Scale; CVDs, cardiovascular diseases; DASH, dietary approaches to stop hypertension; FDR, false discovery rate; FFQ, food frequency questionnaire; MIND, Mediterranean–DASH diet intervention for neurodegenerative delay; PAI, physical activity index.

findings, the current study extended that a higher MIND diet score was related to slower grey matter decline and slower increment of ventricles, using a longitudinal design with repeated measurements of brain MRI markers over a long-term period.

This study advances our understanding of diet-brain associations by addressing the challenge of reverse causality.[47] Early neurodegeneration can alter sensory functions and eating behaviours, which may bias the observed associations between diet and brain health. With a longitudinal follow-up of over a decade of follow-up, our study strengthens the evidence for the brain health benefits of the MIND diet. While overall adherence to the MIND diet appears protective, the associations of individual food components may vary. Unexpected findings, such as the associations of whole grain and cheese with several brain imaging markers, highlight the need for further research to clarify specific food recommendations. Subgroup analyses

showed stronger associations in older individuals, suggesting that the benefits of a healthy diet may be more pronounced among those who are at a higher risk for accelerated brain ageing or who exhibit a larger variation in the rate of brain atrophy. In addition, the stronger associations in more physically active individuals and those without overweight or obesity suggested the potential value of combined lifestyle strategies in mitigating neurodegeneration.[48]

Grey matter atrophy and ventricle volume enlargement are well-established markers of brain ageing. Grey matter, rich in neuronal cell bodies, dendrites and synapses, plays a key role in memory, learning and decision-making.[49] Ventricle volume expansion, in contrast, reflects brain atrophy, where the brain tissue loss is accompanied by the enlargement of cerebrospinal fluid-filled spaces.[50] MIND-recommended foods rich in antioxidants, such as berries,[51] and high-quality protein sources like poultry[52] may reduce oxidative stress and mitigate neuronal damage.[53] Conversely, fast fried foods, often high in unhealthy fats, trans fats and advanced glycation end-products, may contribute to inflammation and vascular damage.[54]

Our findings provide important scientific insights and implications for public health practice. The results highlight the need for additional long-term studies to further reveal how specific dietary patterns influence brain ageing and neurodegeneration, which informs future dietary intervention programmes to improve brain health. Given the global rise in ageing populations and the growing burden of neurodegenerative diseases, such as AD and PD, promoting the MIND diet as a part of dietary guidelines for ageing populations could be an accessible strategy to address this challenge.

The major strengths of this study include a long-term follow-up, a large sample size and validated approaches to measure diet and brain imaging markers. However, several limitations should be accounted for when interpreting our findings. First, although the FFQ was devised to measure long-term dietary intake and has been extensively validated, the possibility of recall bias and measurement error remains. Second, the current study focused on the overall brain structure, and future investigations are needed to reveal region-specific cortical and subcortical changes associated with dietary intake. Additionally, although imaging assessments were conducted years after dietary assessments, and the rate of change was used as the study measure to minimise the possibility of reverse causality, residual and unmeasured confounding could not be fully ruled out. To further reduce the influence of reverse causality, we excluded participants with dementia or stroke at the time of first MRI assessment; however, we could not account for mild cognitive decline at FFQ administration, which may also influence dietary reporting. Also, post-baseline dietary changes may further dilute the associations. As data limitation precluded adjustment for *APOE* genotype or examination of its potential modifying effects, the role of genetic factors in the observed associations warrants detailed investigations by future studies. Finally, because our findings are based on middle-aged and older adults primarily of Caucasian ancestry, the generalisability of the study findings to more diverse populations warrants investigations.

CONCLUSIONS

Greater adherence to the MIND diet is associated with slower brain atrophy, particularly in grey matter volume atrophy and ventricle expansion, over a period of more than a decade. These findings reinforce the potential of the MIND diet as a brain-healthy dietary pattern and support its role in strategies aimed at slowing neurodegeneration in ageing populations. Further research is needed to explore the underlying mechanisms and assess the applicability of these findings in more diverse populations.

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Ethics approval This study involves human participants. Data collection for the Framingham Heart Study was approved by the Institutional Review Board of Boston University (H-24583), and the present analysis was approved by the Ethics Committee of the School of Public Health, Zhejiang University (ZGL202403-2). Participants gave informed consent to participate in the study before taking part.

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