**Supplementary Table S1**. Cross-sectional and longitudinal studies investigating nutritional intake and cerebral structure in older adults without dementia (or in mixed groups adjusting for dementia diagnosis)

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Study** | **Study Measure\*** | **Reported Target Groups** | | **Age (years)** | | | **Cerebral Structure Outcomes** |
| **Descriptor** | **N** | **Range** | **Mean** | **SD** |  |
| **B Vitamins (or related biomarkers)** | | |  |  |  |  |  |
| Tan et al.(1) | HcY | DF | 768 | ≥60.0 | 69.60 | 6.50 | **Cross sectional (MRI)** ↑ HcY was associated with:  ↓ WMv within FL, PL, & TL  ↓ CT within PL  ↓ Volume of Thalamus, Brainstem & Accumbens |
| Kobe et al.(2) | VIT-B12 | MCI | 100 | 50.0 - 80.0 | 69.0 | 7.80 | **Cross sectional (MRI & DTI)** ↓ VIT-B12 was associated with:  ↓ HC microstructural integrity (HC tail, DG, & CA4 subfield) |
| Hsu et al.(3) | HcY | H | 338 | 25 - 81 | 51.60 | 10.50 | **Cross sectional (DTI)** ↑ HcY was associated with:  ↓ WM microstructural integrity within regions FL &  anterior TL, CC & Midbrain  (corresponding with multiple WM fibre bundles) |
| Madsen et al.(4) | HcY | Mixed† | 225 (CN)  392 (MCI) 186 (AD) | NR | 75.33 (CN) 75.39 (MCI) 75.45 (AD) | 7.67 (CN) 7.60 (MCI) 6.84 (AD) | **Cross sectional (MRI)**  ↑ HcY was associated with:  ↓ CT within FL, PL, & TL  ↓ Cortical GMv within FL, PL, & TL Significant associations only observed for whole group. No significant associations observed for specific subgroups |
| Bettcher et al.(5) | HcY | H | 151 | 62.0 - 87.0 | 71.60 | 5.70 | **Cross sectional (DTI)** ↑ HcY was associated with:  ↓ WM microstructural integrity within CC |
| Feng et al.(6) | VIT-B12, Folate, & HcY | H | 228 | ≥55.0 | 65.40 | 6.20 | **Cross sectional (MRI)**  ↑ HcY was associated with:  ↓ TC-WMv  VIT-B12 or folate were not associated with cerebral structure |
| Ford et al.(7) | HcY | H | 106 (HHcY) 49 (LHcY) | 46.0 - 85.0 | 65.50 (HHcY) 73.70 (LHcY) | 10.10 (HHcY) 7.90 (LHcY) | **Cross sectional (MRI)** HHcY (≥15µmol/L) was associated with:  ↓ Cortical GMv within small regions of FL, OL, & CrB |
| Raz et al.(8) | HcY | H | 144 | 44.0 - 77.0 | 58.89 | 9.09 | **Cross sectional (MRI)** Total HcY interacted with age to predict:  ↑ WMHv within FL, PL, & TL (older adults with↑ HcY) |
| Narayan et al.(9) | VIT-B12, Folate, & HcY | DF | 70 | 74.0 - 91.0 | 79.0 | 3.50 | **Longitudinal (MRI; 2 years)** ↑ HcY was associated with:  ↑ TCar HcY was not associated with WML progression  VIT-B12 or folate were not associated with cerebral structure |
| Rajagopalan et al.(10) | HcY | Mixed† | 203 (CN)  356 (MCI) 173 (AD) | NR | 76.13 (CN)  75.15 (MCI) 75.57 (AD) | 4.99 (CN) 7.26 (MCI) 7.62 (AD) | **Cross sectional (MRI)** ↑ HcY was associated with:  ↓ WMv within FL, PL, & OL Significant associations were observed in whole sample, but only in MCI during subgroup analysis  Hyperhomocysteinemia (HcY ≥ 14.0 µM/L) was associated with:  ↓ WMv within FL & PL |
| Tangney et al.(11) | VIT-B12, MMA & HcY | Mixed‡ | 121 | ≥65.0 | 78.70 | 5.70 | **Cross sectional (MRI)** ↑ HcY was associated with:  ↓ TCv   ↑ WMHv ↑ MMA was associated with:  ↓ TCv All associations remained significant following adjustment for dementia diagnosis |
| Firbank et al.(12) | VIT-B12, Folate, & HcY | H | 80 | 74.0 - 91.0 | 79.0 | 3.50 | **Cross sectional (MRI)** ↑ HcY was associated with:  ↓ HCv VIT-B12 was not associated with cerebral structure  **Longitudinal (MRI; 2 years)** ↑ HcY was associated with:  ↑ WMar  ↑ HCar VIT-B12 or folate were not associated with cerebral atrophy |
| Chee et al.(13) | HcY | H | 248 | ≥55.0 | 65.80 | 6.53 | **Cross sectional (MRI)** ↑ HcY was associated with:  ↓ TC-WMv |
| de Lau et al.(14) | VIT-B12, HoloTC, TCs & MMA | DF | 1,019 | 60.0 - 90.0 | 72.20 | 7.40 | **Cross sectional (MRI)** ↓ VIT-B12 & ↑ MMA was associated with:  ↑Severity of pvWML ↓ HoloTC & ↓ TCs was associated with:  ↑ Severity of pvWML & scWML |
| Erickson et al.(15) | VIT-B6 & VIT-B12 (3DFD) | H | 32 | 59.0 - 79.0 | 68.0 | 6.0 | **Cross sectional (MRI)** ↑ Estimated VIT-B6 intake was associated with:  ↑GMv within SFC, SMA, PL, MPC, MTC, aCingC, &  poCingC  ↑ Estimated VIT-B12 intake was associated with:  ↑GMv within posterior PL  All associations were significant when only considering intake from supplementation, not diet |
| Seshadri et al.(16) | HcY | DF | 1,965 | 26.0 - 81.0 | 54.0 | 10.0 | **Cross sectional (MRI)** ↑ HcY was associated with:  ↓ TCv, particularly FL & TL volumes   ↑ Risk & prevalence of SBI  Strongest associations were observed in adults aged ≥55 |
| Vogiatzoglou et al.(17) | VIT-B12, HoloTC, TCs, MMA & HcY | H | 107 | ≥60.0 | 73.20 | NR | **Longitudinal (MRI; 5 year)** ↑ VIT-B12 & ↑ HoloTC was associated with:  ↓ TCar ↑ TCs was associated with:  ↓ TCar (unadjusted analysis only) ↑ MMA & ↑ HcY was associated with:  ↑ TCar (unadjusted analysis only) |
| Sachdev et al.(18) | HcY | DF§ | 385 | NR | 62.64 (M) 62.59 (F) | 1.43 (M) 1.45 (F) | **Cross sectional (MRI)** ↑ HcY associated with:  ↑ Deep WMHv |
| den Heijer et al.(19) | HcY | DF | 1,031 | 60.0 - 90.0 | 72.0 | 7.0 | **Cross sectional (MRI)** ↑ HcY was associated with:  ↑ Cortical atrophy  ↓ HCv |
| Whalley et al.(20) | HcY | DF | 82 | 77.70 -78.90 | 78.50 | NR | **Cross sectional (MRI)** ↑ HcY was associated with:  ↓ TC-GMv |
| Sachdev et al.(21) | HcY | H | 36 | 59.0 - 85.0 | 71.60 | NR | **Cross sectional (MRI)** ↑ HcY was associated with:  ↑ Ventricle:brain ratio |
| Vermeer et al.(22) | HcY | DF | 1,077 | 60.0 - 90.0 | 72.20 | 7.40 | **Cross sectional (MRI)** ↑ HcY was associated with:  ↑ Severity of WML  ↑ Severity of SBI |
| Williams et al.(23) | HcY | H | 156 | 60.80 - 90.60 | 74.10 | 6.10 | **Cross sectional (MRI)** ↑ HcY was associated with:  ↓ HC width |
| **Choline** |  |  |  |  |  |  |  |
| Poly et al.(24) | Choline (FFQ) | DF | 1,391 | 36.0 - 83.0 | 60.80 | 9.30 | **Cross sectional (MRI)** ↑ Total choline intake was associated with:  ↓ WMHv |
| **Omega-3 Fatty Acids** |  |  |  |  |  |  |  |
| Zamroziewicz et al.(25) | ω3 & ω6-FA | CN | 94 | 65 - 75 | 69.0 | 3.0 | **Cross sectional (MRI)** ↑ LCPUFA score (various ω6 & ω3-FA) was associated with:  ↑ WM microstructure within fornix |
| Daiello et al.(26) | Reported FOS | Mixed† | 229 (CN) 397 (MCI) 193 (AD) | NR | 76.0 (CN) 74.90 (MCI) 75.50 (AD) | 5.0 (CN) 7.50 (MCI) 7.50 (AD) | **Longitudinal (MRI; multiple scans over 3-4 years)** Reported FOS use in whole group was associated with:  ↑Cortical GMv   ↑ HCv  ↓ Vent-v Subgroup analysis reported FOS use was associated with:  ↑ Cortical GMv (CN & MCI)  ↑ HCv (CN & AD) |
| Pottala et al.(27) | ⍵3-FA | Mostly DF**|** | 1,111 | 71.0 - 88.0 | 78.0 | NR | **Cross sectional(MRI)** ↑ ⍵3-FA index (combined DHA & EPA) was associated with:  ↑ TCv  ↑ HCv |
| Walhovd et al.(28) | ⍵3-FA | H | 92 | 44.40 - 86.30 | 63.30 | 8.70 | **Longitudinal (MRI; 2 years)** ↑ DHA was associated with:  ↓ C-thin within MTC & STC |
| Bowman et al.(29) | ω3-FA | DF | 32 | ≥65.0 | 92.40 | 3.50 | **Cross sectional (MRI)** ↑ ω3-FA was associated with:  ↓ WMHv |
| Titova et al.(30) | ⍵3-FA (7DFD) | H | 198 | ≥70.0 | Approx. 70.10 | 0.0 | **Cross sectional (MRI)** ↑ Intake of DHA & EPA was associated with:  ↑ TC-GMv. |
| Samieri et al.(31) | ω3-FA | Mixed**¶** | 281 | ≥65.0 | 72.30 | 3.80 | **Longitudinal (MRI; 4 year)** ↑ EPA was associated with:  ↓ GM atrophy within right Med-TL structures (AMYG,  ParaHC, & HC)  Associations were unchanged following exclusion of dementia cases |
| Tan et al.(32) | ⍵3-FA | DF | 1,575 | NR | 67.0 | 9.0 | **Cross sectional (MRI)** Lowest quartile RBC DHA was associated with:  ↓ TCv  ↑ WMHv Lowest quartile ⍵3-FA index was associated with:  ↓ TCv  ↑ WMHv |
| **Vitamin D** |  |  |  |  |  |  |  |
| Karakis et al.(33) | VIT-D | DF§ | 1,291 | NR | 59.50 | 9.10 | **Cross sectional (MRI)** VIT-D deficiency was associated with:  ↓ HCv. |
| Walhovd et al.(28) | VIT-D | H | 92 | 44.40 - 86.30 | 63.30 | 8.70 | **Longitudinal (MRI; 2 years)** ↑ VIT-D levels were associated with:  ↓ C-thin within rLPFC |
| **Nutrient Patterns** |  |  |  |  |  |  |  |
| Gu et al.(34) | NP (FFQ) | Mixed**\*\*** | 239 | ≥65.0 | 84.10 | 5.10 | **Cross sectional (MRI)** ↑NP (ω3-FA, ω6-FA, & VIT-E) score was associated with:  ↑ Mean cerebral WM microstructure Only estimated intake of ω3-FA or VIT-E, was associated with:  ↑ WM microstructural integrity  After excluding dementia cases, NP (ω3-FA, ω6-FA, & VIT-E) score or ω3-FA intake remained associated with WM microstructure |
| Berti et al.(35) | NP (FFQ) | CN | 52 | 25.0 - 72.0 | 54.0 | 11.0 | **Cross sectional (MRI)** Of the 5 NP identified (3 associated with cerebral structure)  ↑ NP-1 (VIT-B1, VIT-B2, VIT-B3, VIT-B6 & folic acid) score was associated with:  ↑ GMv within FL ↑ NP-4 (VIT-B12, VIT-D & Zinc) score was associated with:  ↑ GMv within FL & TL  ↑ NP-5 (S-Fat, T-Fat, cholesterol & sodium) score was associated with:  ↓ GMv within FL & LL |
| Bowman et al.(36) | NBP | DF | 104 | ≥65.0 | 87.0 | 10.0 | **Cross sectional (MRI)**  8 NBP identified (3 associated with cerebral structure)  ↑NBP-1 (VIT-B1, VIT-B2, VIT-B6, VIT-B12, folate, VIT-C, VIT-D, & VIT-E) score was associated with:   ↑ TCv ↑ NBP-5 (ω3-FA) score was associated with:  ↓ WMHv  ↑ NBP-8 (T-Fat) score was associated with  ↓ TCv |
| **Mediterranean style diet** | |  |  |  |  |  |  |
| Luciano et al.(37) | MeDI (FFQ) | H | 562 | Approx. 70.0 (at FFQ) | 72.65 | 0.72 | **Longitudinal (MRI; 3 years**) ↓ MeDI score was associated with  ↑ 3 year reduction in TCv |
| Staubo et al.(38) | MeDI (FFQ) | CN | 672 | 70.0 - 89.0 | 79.80 | 5.0 | **Cross sectional (MRI)** ↑ MeDI score was associated with:  ↑ CT within FL, PL, TL, & OL ↑ Fish, legume, vegetable, & whole grain/cereal intake was associated with:   ↑ CT within FL, PL, TL & OL ↑ Fruit intake was associated with:  ↓ CT within PL ↑ Red meat intake was associated with:  ↑ CT of ERC |
| Gu et al.(39) | MeDI (FFQ) | DF | 674 | ≥65.0 | 80.10 | 5.60 | **Cross sectional (MRI)** MeDI score (≥5) was associated with:  ↑ TCv  ↑ TC-GMv  ↑ TC-WMv ↑ Fish intake was associated with:  ↑ TC-GMv  ↑ Mean CT ↓ Meat intake was associated with:  ↓ TCv  ↑ TC-GMv |
| Pelletier et al.(40) | MeDI (FFQ & 24-diet recall) | Mixed**††** | 146 | ≥65.0 | 73.0 | NR | **Cross sectional (MRI & DTI)** ↑ MeDI score was associated with:  ↑ Microstructural integrity within CC, aThR, pThR,  pCingG, & ParaHC-F No association between MeDI score & either TC-GMv or TC-WMv  ↑ Dairy intake was associated with:  ↓ Microstructural integrity within CC Moderate alcohol intake was associated with:  ↑ Microstructural integrity within CC  Association between MeDI score & WM microstructural integrity remained significant following exclusion of dementia cases |
| Mosconi et al.(41) | MeDI (FFQ) | CN | 20 (HMeDI) 32 (LMeDI) | 25.0 - 72.0 | 55.0 (HMeDI) 53.0 (LMeDI) | 12.0 (HMeDI) 13.0 (LMeDI) | **Cross sectional (MRI)** HMeDI score (≥5) associated with:  ↑ CT of OFC, ERC, & poCingC |
| Titova, Ax et al.(42) | MeDI (7DFD) | CN | 194 | ≥70.0 | 70.10 | 0.01 | **Cross sectional (MRI)** ↑ Meat or meat product intake associated with:   ↓ TCv MeDI score not associated with TCv, TC-GMv, or TC-WMv. |
| **‘Prudent’ & Western style diets** |  |  |  |  |  |  |  |
| Croll et al.(43) | Diet Quality (Adherence to Dutch Dietary Guidelines) | DF | 4,213 | 45.50-97.50 | 65.70 | 10.80 | **Cross Sectional (MRI)**  ↑ Diet Quality (Adherence to Dutch Dietary Guidelines) was associated with:  ↑ TCv  ↑ TC-GMv  ↑ TC-WMv  ↑ HCv |
| Jacka et al.(44) | P-Diet & WeDi (FFQ) | DF§ | 118 | 60.0 - 64.0 | 62.60 | 1.42 | **Cross sectional (MRI)** ↑ P-Diet score was associated with:  ↑ HCv ↑ WeDi score was associated with:  ↓ HCv  **Longitudinal (MRI; 4 years)** P-Diet or WeDi scores not associated with differential rates of HC atrophy during followup |
| **Alcohol Intake** |  |  |  |  |  |  |  |
| Topiwala et al.(45) | Alcohol Intake (Self Report) | DF§ | 527 | NR | 69.60 | 5.30 | **Cross sectional (MRI & DTI)** ↑ Mean alcohol intake (units/week) was associated with:  ↓ GM-d within HC  ↑ risk of abnormal HC atrophy  ↓ Microstructural integrity in CC |
| Gu et al.(46) | Alcohol Intake (FFQ) | DF | 589 | ≥65 | 80.10 | 5.50 | **Cross sectional (MRI)** Light-to-moderate alcohol intake associated with  ↑ TCv (relative to abstinence) Association was limited to wine intake & only in basic model  Following exclusion of past heavy drinkers or alcoholics, moderate wine intake was associated with:  ↑ TCv (relative to abstinence) |
| Paul et al.(47) | Alcohol Intake (Self Report) | DF | 1,839 | 33.0 - 88.0 | 60.64 | 9.42 | **Cross sectional (MRI)** ↑ Self-reported alcohol intake associated with:  ↓ TCv Association was stronger in females |
| Sachdev et al.(48) | Alcohol Intake (SQ) | H | 383 | 60.0 - 64.0 | 62.66 | 1.43 | **Cross sectional (MRI)** ↑ Alcohol intake was associated with  ↑ GMv within FL, PL, & OL subregions  ↓ WMv within TL & med-TL subregions Associations only significant in males |
| den Heijer et al.(49) | Alcohol Intake (SQ) | DF | 1,074 | 60.0 -90.0 | 72.0 | 7.0 | **Cross sectional (MRI)** Light alcohol intake (compared to abstinence or heavy consumption) associated with:  ↓ Severity of pvWML (relative to abstinence or heavy  intake) ↑ Alcohol intake associated with:  ↑HCv  ↑ AMYG volume Association with HC & AMYG volumes only evident in APOE ε4 allele carriers |
| **Fish Intake** |  |  |  |  |  |  |  |
| Raji et al.(50) | Fish Intake (FFQ) | CN | 163 (FFC) 97 (inf-FC) | NR | 78.30 (FFC) 78.40 (inf-FC) | 3.54 (FFC) 3.31 (inf-FC) | **Cross sectional (MRI)** ↑ Weekly fish intake associated with:  ↑ GMv in HC, preC, poCingC, & OFC. |

**Note:** Studies presented in reverse chronological order and organised by nutrient or diet type. **Abbreviations**: **HcY**, Homocysteine; **DF**, dementia free; **MRI**, magnetic resonance imaging; **WMv**, white matter volume; **FL**, frontal lobe; **PL**, parietal lobe; **TL**, temporal lobe; **CT**, cortical thickness; **VIT-B12**, vitamin B12; **MCI**, mild cognitive impairment; **DTI**, diffusion tensor imaging; **HC**, hippocampus; **DG**, dentate gyrus; **CA4**, cornu ammonis subfield 4; **H**, healthy; **WM**, white matter; **CC**, corpus callosum; **CN**, cognitively normal; **AD**, alzheimer’s dementia; **NR**, not reported; **GMv**, grey matter volume; **TC-WMv**, total cerebral white matter volume; **HHcy**, high homocysteine; **LHcY**, low homocysteine; **OL**, occipital lobe; **CrB**, cerebellum, **WMHv**, white matter hyperintensity volume; **TCar**, total cerebral atrophy rate; **WML**, white matter lesion; **MMA**, methylmalonic acid; **TCv**, total cerebral volume; **HCv**; hippocampal volume; **WMar**, white matter atrophy rate; **HCar**, hippocampal atrophy rate; **HoloTC**, holotranscobalamin; **TCs**, transcobalamin saturation; **pvWML**, periventricular white matter lesion; **scWML**, subcortical white matter lesion; **VIT-B6**, vitamin B6; **3DFD**, 3-day food diary; **SFC**, superior frontal cortex; **SMA**, supplementary motor area; **MPC**, medial parietal cortex; **MTC**, middle temporal cortex; **aCingC**; anterior cingulate cortex; **poCingC**, posterior cingulate cortex; **SBI**, silent brain infarct; **M**, males; **F**, females; **TC-GMv**, total cerebral grey matter volume; **FFQ**, food frequency questionnaire; **ω3-FA**, omega-3 fatty acid; **ω6-FA**, omega-6 fatty acid; **LCPUFA**, long-chain polyunsaturated fatty acid; **FOS**, fish oil supplementation; **Vent-V**, ventricle volume; **DHA**, docosahexaenoic acid; **EPA**, eicosapentaenoic acid; **C-thin**, cortical thinning; **STC**, superior temporal cortex; **7DFD**, 7-day food diary; **med-TL**, medial temporal lobe; **AMYG**, amygdala; **ParaHC**, parahippocampus; **RBC**, red blood cell; **VIT-D**, vitamin D; **rLPFC**, right lateral prefrontal cortex; **NP**, nutrient pattern; **VIT-E**, vitamin E; **VIT-B1**; vitamin B1; **VIT-B2**, vitamin B2; **VIT-B3**, vitamin B3; **S-Fat**, saturated fat; **T-Fat**, trans-saturated fats; **LL**, limbic lobe; **NBP**, nutrient biomarker pattern; **VIT-C**, vitamin C; **MeDI**, mediterranean style diet score; **ERC**, entorhinal cortex; **aThR**, anterior thalamic radiation; **pThR**, posterior thalamic radiation; **pCingG**, paracingulate gyrus; **ParaHC-F**, parahippocampal fornix; **HMeDI**, high mediterranean style diet score; **LMeDI**, low mediterranean style diet score; **OFC**, orbito frontal cortex; **P-Diet**, prudent diet score; **WeDI**, Western style diet score; **GM-d**, grey matter density; **SQ**, structured questionnaire; **APOE** **ϵ4**, apolipoprotein ϵ4; **FFC**, frequent fish consumers; **inf-FC**, infrequent fish consumers; **preC**, precuneus. **Symbols:** **\*** All studies examined blood biomarkers unless otherwise specified;**†** Study included participants with CN, MCI, or AD (baseline diagnosis were controlled for during analysis); **‡** Study included participants (3% of whole sample) with dementia (secondary analysis adjusted for dementia diagnosis); **§** Confirmation of dementia free status was received through correspondence with original authors;**|** Study included one participant (< 0.1% of whole sample) who developed dementia during interval between diet assessment & MRI scan; **¶** Study included 4 participants with dementia (analysis was repeated following exclusion of dementia cases in supplementary analysis); **\*\*** Study included 28 dementia cases (analysis was repeated following exclusion of dementia cases in sensitivity analysis); **††** Study included 22 dementia or suspected dementia cases (analysis was repeated following exclusion of dementia & suspected dementia cases in supplementary analysis); **↑** Greater/Increased; **↓** Lower/Decreased.

References

1. Tan B, Venketasubramanian N, Vrooman H, et al. (2018) Homocysteine and Cerebral Atrophy: The Epidemiology of Dementia in Singapore Study. *J. Alzheimer’s Dis.* **62**, 877–885.

2. Kobe T, Witte AV, Schnelle A, et al. (2016) Vitamin B-12 concentration, memory performance, and hippocampal structure in patients with mild cognitive impairment. *Am. J. Clin. Nutr.* **103**, 1045–1054.

3. Hsu J-L, Chen W-H, Bai C-H, et al. (2015) Microstructural white matter tissue characteristics are modulated by homocysteine: a diffusion tensor imaging study. *PLoS One* **10**, e0116330.

4. Madsen SK, Rajagopalan P, Joshi SH, et al. (2015) Higher homocysteine associated with thinner cortical gray matter in 803 participants from the Alzheimer’s Disease Neuroimaging Initiative. *Neurobiol. Aging* **36**, S203–S210.

5. Bettcher BM, Watson CL, Walsh CM, et al. (2014) Interleukin-6, age, and corpus callosum integrity. *PLoS One* **9**, e106521.

6. Feng L, Isaac V, Sim S, et al. (2013) Associations Between Elevated Homocysteine, Cognitive Impairment, and Reduced White Matter Volume in Healthy Old Adults. *Am. J. Geriatr. Psychiatry* **21**, 164–172.

7. Ford AH, Garrido GJ, Beer C, et al. (2012) Homocysteine, grey matter and cognitive function in adults with cardiovascular disease. *PLoS One* **7**, e33345.

8. Raz N, Yang Y, Dahle CL, et al. (2012) Volume of white matter hyperintensities in healthy adults: contribution of age, vascular risk factors, and inflammation-related genetic variants. *Biochim. Biophys. Acta* **1822**, 361–369.

9. Narayan SK, Firbank MJ, Saxby BK, et al. (2011) Elevated plasma homocysteine is associated with increased brain atrophy rates in older subjects with mild hypertension. *Dement. Geriatr. Cogn. Disord.* **31**, 341–348.

10. Rajagopalan P, Hua X, Toga AW, et al. (2011) Homocysteine effects on brain volumes mapped in 732 elderly individuals. *Neuroreport* **22**, 391–395.

11. Tangney CC, Aggarwal NT, Li H, et al. (2011) Vitamin B12, cognition, and brain MRI measures: a cross-sectional examination. *Neurology* **77**, 1276–1282.

12. Firbank MJ, Narayan SK, Saxby BK, et al. (2010) Homocysteine is associated with hippocampal and white matter atrophy in older subjects with mild hypertension. *Int. Psychogeriatrics* **22**, 804–811.

13. Chee MWL, Chen KHM, Zheng H, et al. (2009) Cognitive function and brain structure correlations in healthy elderly East Asians. *Neuroimage* **46**, 257–269.

14. de Lau LML, Smith AD, Refsum H, et al. (2009) Plasma vitamin B12 status and cerebral white-matter lesions. *J. Neurol. Neurosurgery, Psychiatry* **80**, 149–157.

15. Erickson KI, Suever BL, Prakash RS, et al. (2008) Greater intake of vitamins B6 and B12 spares gray matter in healthy elderly: a voxel-based morphometry study. *Brain Res.* **1199**, 20–26.

16. Seshadri S, Wolf PA, Beiser AS, et al. (2008) Association of Plasma Total Homocysteine Levels With Subclinical Brain Injury. *Arch. Neurol.* **65**, 642–649.

17. Vogiatzoglou A, Smith SM & Bradley KM (2008) Vitamin B12 status and rate of brain volume loss in community-dwelling elderly. *Neurology* **71**, 826–832.

18. Sachdev P, Parslow R, Salonikas C, et al. (2004) Homocysteine and the brain in midadult life: Evidence for an increased risk of leukoaraiosis in men. *Arch. Neurol.* **61**, 1369–1376.

19. den Heijer T, Vermeer SE, Clarke R, et al. (2003) Homocysteine and brain atrophy on MRI of non-demented elderly. *Brain* **126**, 170–175.

20. Whalley LJ, Staff RT, Murray AD, et al. (2003) Plasma vitamin C, cholesterol and homocysteine are associated with grey matter volume determined by MRI in non-demented old people. *Neurosci. Lett.* **341**, 173–176.

21. Sachdev PS, Valenzuela M, Wang XL, et al. (2002) Relationship between plasma homocysteine levels and brain atrophy in healthy elderly individuals. *Neurology* **58**, 1539–1541.

22. Vermeer SE, van Dijk EJ, Koudstaal PJ, et al. (2002) Homocysteine, silent brain infarcts, and white matter lesions: The Rotterdam Scan Study. *Ann. Neurol.* **51**, 285–289.

23. Williams JH, Periera EAC, Budge MM, et al. (2002) Minimal hippocampal width relates to plasma homocysteine in community-dwelling older people. *Age Ageing* **31**, 440–444.

24. Poly C, Massaro JM, Seshadri S, et al. (2011) The relation of dietary choline to cognitive performance and white-matter hyperintensity in the Framingham Offspring Cohort. *Am. J. Clin. Nutr.* **94**, 1584–1591.

25. Zamroziewicz MK, Paul EJ, Zwilling CE, et al. (2017) Predictors of memory in healthy aging: Polyunsaturated fatty acid balance and fornix white matter integrity. *Aging Dis.* **8**, 372–383.

26. Daiello LA, Gongvatana A, Dunsiger S, et al. (2015) Association of fish oil supplement use with preservation of brain volume and cognitive function. *Alzheimer’s Dement.* **11**, 226–235.

27. Pottala J, Yaffe K, Robinson JG, et al. (2014) Higher RBC EPA + DHA corresponds with larger total brain and hippocampal volumes: WHIMS-MRI study. *Neurology* **82**, 435–442.

28. Walhovd KB, Storsve AB, Westlye LT, et al. (2014) Blood markers of fatty acids and vitamin D, cardiovascular measures, body mass index, and physical activity relate to longitudinal cortical thinning in normal aging. *Neurobiol. Aging* **35**, 1055–1064.

29. Bowman GL, Dodge HH, Mattek N, et al. (2013) Plasma omega-3 PUFA and white matter mediated executive decline in older adults. *Front. Aging Neurosci.* **5**, 92.

30. Titova OE, Sjögren P, Brooks SJ, et al. (2013) Dietary intake of eicosapentaenoic and docosahexaenoic acids is linked to gray matter volume and cognitive function in elderly. *Age* **35**, 1495–1505.

31. Samieri C, Maillard P, Crivello F, et al. (2012) Plasma long-chain omega-3 fatty acids and atrophy of the medial temporal lobe. *Neurology* **79**, 642–650.

32. Tan ZS, Harris WS, Beiser AS, et al. (2012) Red blood cell omega-3 fatty acid levels and markers of accelerated brain aging. *Neurology* **78**, 658–664.

33. Karakis I, Pase MP, Beiser A, et al. (2016) Association of Serum Vitamin D with the Risk of Incident Dementia and Subclinical Indices of Brain Aging: The Framingham Heart Study. *J. Alzheimer’s Dis.* **51**, 451–461.

34. Gu Y, Vorburger RS, Gazes Y, et al. (2016) White Matter Integrity as a Mediator in the Relationship between Dietary Nutrients and Cognition in the Elderly. *Ann. Neurol.* **79**, 1014–1025.

35. Berti V, Murray J, Davies M, et al. (2015) Nutrient patterns and brain biomarkers of Alzheimer’s disease in cognitively normal individuals. *J. Nutr. Health Aging* **19**, 413–423.

36. Bowman GL, Howieson D, Traber MG, et al. (2012) Nutrient biomarker patterns, cognitive function, and MRI measures of brain aging. *Neurology* **78**, 241–249.

37. Luciano M, Corley J, Cox SR, et al. (2017) Mediterranean-type diet and brain structural change from 73 to 76 years in a Scottish cohort. *Neurology* **88**, 449–456.

38. Staubo SC, Aakre JA, Vemuri P, et al. (2017) Mediterranean diet, micronutrients and macronutrients, and MRI measures of cortical thickness. *Alzheimer’s Dement.* **13**, 168–177.

39. Gu Y, Brickman AM, Stern Y, et al. (2015) Mediterranean diet and brain structure in a multiethnic elderly cohort. *Neurology* **85**, 1–8.

40. Pelletier A, Barul C & Catherine F (2015) Mediterranean diet and preserved brain structural connectivity in older subjects. *Alzheimer’s Dement.* **11**, 1023–1031.

41. Mosconi L, Murray J, Tsui WH, et al. (2014) Mediterranean Diet and Magnetic Resonance Imaging-Assessed Brain Atrophy in Cognitively Normal Individuals at Risk for Alzheimer’s Disease. *J. Prev. Alzheimer’s Dis.* **1**, 23–32.

42. Titova OE, Ax E, Brooks SJ, et al. (2013) Mediterranean diet habits in older individuals: associations with cognitive functioning and brain volumes. *Exp. Gerontol.* **48**, 1443–1448.

43. Croll PH, Voortman T, Ikram MA, et al. (2018) Better diet quality relates to larger brain tissue volumes: The Rotterdam Study. *Neurology* **90**, e2166–e2173.

44. Jacka FN, Cherbuin N, Anstey KJ, et al. (2015) Western diet is associated with a smaller hippocampus: a longitudinal investigation. *BMC Med.* **13**, 215.

45. Topiwala A, Allan CL, Valkanova V, et al. (2017) Moderate alcohol consumption as risk factor for adverse brain outcomes and cognitive decline: longitudinal cohort study. *BMJ* **357**, j2353.

46. Gu Y, Scarmeas N, Eaton E, et al. (2014) Alcohol intake and brain structure in a multiethnic elderly cohort. *Clin. Nutr.* **33**, 662–667.

47. Paul CA, Au R, Fredman L, et al. (2008) Association of Alcohol Consumption With Brain Volume in the Framingham Study. *Arch. Neurol.* **65**, 1363–1367.

48. Sachdev PS, Chen X, Wen W, et al. (2008) Light to moderate alcohol use is associated with increased cortical gray matter in middle-aged men: A voxel-based morphometric study. *Psychiatry Res. Neuroimaging* **163**, 61–69.

49. den Heijer T, Vermeer SE, Dijk EJ Van, et al. (2004) Alcohol intake in relation to brain magnetic resonance imaging findings in older persons without dementia. *Am. J. Clin. Nutr.* **80**, 992–997.

50. Raji CA, Erickson KI, Lopez OL, et al. (2014) Regular fish consumption and age-related brain gray matter loss. *Am. J. Prev. Med.* **47**, 444–451.