**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, & TLSignificant 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: ↑ TCarHcY 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, & OLSignificant associations were observed in whole sample, but only in MCI during subgroup analysisHyperhomocysteinemia (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: ↓ TCvAll 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: ↓ HCvVIT-B12 was not associated with cerebral structure**Longitudinal (MRI; 2 years)**↑ HcY was associated with: ↑ WMar ↑ HCarVIT-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 SBIStrongest 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-vSubgroup 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 ↑ WMHvLowest 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 microstructureOnly estimated intake of ω3-FA or VIT-E, was associated with: ↑ WM microstructural integrityAfter 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-FNo association between MeDI score & either TC-GMv or TC-WMv↑ Dairy intake was associated with: ↓ Microstructural integrity within CCModerate alcohol intake was associated with: ↑ Microstructural integrity within CCAssociation 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:  ↓ TCvMeDI 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 modelFollowing 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: ↓ TCvAssociation 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 subregionsAssociations 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 volumeAssociation 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.

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