Supplementary Table 1 Cross-sectional studies on the association between plasma/serum NfL and neuroimaging markers of neurodegeneration

Authors	Citation in the main text	NfL Source	Sample source	Sample characteristics (No. of individuals; age)	Neuroimaging modality	Neuroimaging measures associated with higher baseline NfL	Variables statistically controlled for
Mattsson et al. (2017)	9	Plasma	ADNI	CU (n = 193; 75.9 ± 4.9 y) MCI (n = 197; 74.7 ± 7.5 y) AD (n = 180; 75.3 ± 7.3 y)	Hippocampal volume Cortical thickness (temporal composite[b]) FDG-PET (mean uptake in ROIs[c])	Entire sample: smaller hippocampus (β = -0.124, p < .001) and lower composite temporal cortical thickness (β = -0.162, p < .001); no association with the mean FDG uptake (β = -0.085, p = 0.10) (The statistics represent the standardized coefficient for the term 'NfL' estimating the cross-sectional association between NfL and an imaging measure in a linear mixed model that has the imaging measure as the outcome variable and includes the 'NfL×time' interaction term estimating the association between baseline NfL and the rate of change in the imaging measure.)	Age, sex, education, diagnosis, APOE ε4
Barker et al. (2021)	17	Plasma	1Florida ADRC	CU (n = 51; 70.8 ± 5.9 y) AD (n = 156; 74.8 ± 8.2 y)	Hippocampal volume MTL atrophy: presence or absence by visual inspection	CU: No association with either the binary (Pearson r = -0.10, p > 0.05) or continuous (Pearson r = 0.02, p > 0.05) measure of hippocampal atrophy AD: lower hippocampal volume (Pearson r = -0.36, p < 0.0001)	N/A
Mattsson et al. (2019)	18	Plasma	ADNI	CU (n = 401; 74.6 ± 5.6 y) MCI (n = 855; 72.4 ± 7.4 y) AD (n = 327; 74.9 ± 7.8 y)	GM volume (hippocampus, entorhinal cortex) Cortical thickness (temporal composite[b]) FDG-PET (mean uptake in ROIs[d])	Entire sample: smaller hippocampus (β = -4.56, p < .001); thinner entorhinal cortex (β = -3.79, p < .001) and composite temporal cortical thickness (β = -4.35, p < .001); lower mean FDG uptake (β = -3.79, p < .001) (The statistics represent the standardized coefficient for each imaging measure estimating the cross-sectional association between NfL and the imaging measure and in a linear mixed model that has NfL as the outcome variable and includes the 'imaging measure×time' interaction term estimating the association between baseline imaging measure and the rate of change in NfL.)	Age, sex
Andersson et al. (2020)	21	Plasma	BioFINDER study; Malmö Diet and Cancer Study	CU (n = 478; 72.1 ± 5.5 y) MCI (n = 227; 70.6 ± 5.4 y)	DTI (TBSS, tract-based spatial statistics)	CU: no association MCI: lower FA in widespread WM regions (The statistics were presented as a voxel-wise statistical map.)	Age, sex

Weston et al. (2017)	24	Serum	Dementia Research Centre, University College London	Noncarriers (n = 11; 38.9 ± 9.5 y) Presymptomatic mutation[a] carriers (n = 19; 36.0 ± 5.7 y) Symptomatic mutation[a] carriers (n = 18; 46.6 ± 9.3 y)	Hippocampal volume	All mutation carriers: smaller hippocampus (Spearman ρ = -0.54, p = 0.003) Presymptomatic carriers: no association with hippocampal volume (statistics not reported)	N/A
Shahid et al. (2022)	41	Plasma	Indiana Memory and Aging Study (IMAS)	CU (n = 47; 70.8 ± 4.8 y) MCI (n = 52; 73.0 ± 6.6 y) AD (n = 19; 72.8 ± 8.4 y)	NODDI metrics(VF_{IC}: intraneurite density, VF_{EC}: extracellular hindered water components, V_{ISO}: CSF compartment) in hippocampal subfields (CA1-3, subiculum, CA4-DG (dentate gyrus))	Entire sample: higher V_{ISO} (r = 0.36; p < 0.05) and lower VF_{EC} (r = -0.30; p < 0.05) in CA4-DG CU: higher V_{ISO} in CA4-DG (r = 0.47; p < 0.05) MCI: no association (all ps > 0.05) AD: no association (all ps > 0.05)	Age, sex, education, APOE ε4, ICV
Chen et al. (2021)	42	Plasma	ADNI	CU (n = 67; 75.2 ± 0.6 y) static MCI (n = 52; 73.4 ± 1.1 y) progressive MCI (n = 68; 72.9 ± 0.9 y) AD (n = 57; 74.3 ± 1.1 y)	Hippocampal volume FDG-PET (mean uptake in ROIs[c])	CU and static MCI: lower hippocampal volume (CU: β = -0.283, p = 0.039; sMCI: β = -0.312, p = 0.032) and lower mean FDG uptake (CU: β = -0.246, p = 0.026; sMCI: (β = -0.252, p = 0.021) Progressive MCI and AD: lower hippocampal volume (pMCI: β = -0.267, p = 0.042; AD: (β = -0.279, p = 0.044)	Age, sex, ICV
Chatterjee et al. (2022)	43	Plasma	Kerr Anglican Retirement Village Initiative in Ageing Health	CU Aβ- (n = 67 (52 SMC); 77.8 ± 5.6 y) CU Aβ+ (n = 33 (24 SMC); 79.0 ± 5.4 y)	Hippocampal volume	No association (no statistics reported)	N/A
Rajan et al. (2020)	44	Serum	The Chicago Health and Aging Project (CHAP)	Older adults (n = 1327 (436 AD, 317 MCI; 742 underwent MRI scan); 73.5 ± 6.4 y)	Hippocampal volume Global cortical thickness	No association with hippocampal volume (Estimate = 0.028, 95% CI: -0.119 to 0.175) or global cortical thickness (Estimate = 0.75, 95% CI: -3.25 to 4.76) (The statistics represent the coefficient for the term 'NfL' estimating the cross-sectional association between NfL and an imaging measure in a linear mixed model that has the imaging measure as the outcome variable and includes the 'NfL×time' interaction term estimating the association between baseline NfL and the rate of change in the imaging measure.)	Age, sex, race/ethnicity, education, APOE ε4

Mielke et al. (2019)	45	Plasma	The Mayo Clinic Study of Aging (MCSA)	Middle-aged to older adults without dementia (n = 79 (64 CU, 15 MCI); 76.4 y (IQR: 71.7, 80.7))	Cortical thickness (temporal composite) Hippocampal volume FDG-PET (mean uptake in ROIs[e]) FA of the corpus callosum	No association (all βs < 0.132, all ps > 0.162) (The statistics represent the standardized coefficient for the term 'NfL' estimating the cross-sectional association between NfL and an imaging measure in a linear mixed model that has the imaging measure as the outcome variable and includes the 'NfL×time' interaction term estimating the association between baseline NfL and the rate of change in the imaging measure.)	Age, sex, and education, ICV (in the models examining hippocampal volume)
Chatterjee et al. (2018)	46	Plasma	Kerr Anglican Retirement Village Initiative in Ageing Health	CU with PET Aβ- (n = 65 (51 SMC); 77.6 ± 5.6 y) CU with PET Aβ+ (n = 35 (25 SMC); 79.2 ± 5.4 y)	Hippocampal volume	No significant association with hippocampal volume (left hemisphere, Pearson r = -0.095, p = 0.356; right hemisphere, Pearson r = -0.096, p = 0.352)	N/A
Hu et al. (2019)	47	Plasma	ADNI	CU Aβ- (n = 130; 72.8 ± 5.5 y) CU Aβ+ (n = 113; 73.3 ± 6.2 y)	Hippocampal volume FDG-PET (mean uptake in ROIs[c])	No association with hippocampal volume (CU Aβ+: β = -0.034, p = 0.736; CU Aβ-: β = -0.080, p = 0.318) and FDG uptake (CU Aβ+: β = -0.094, p = 0.382; CU Aβ-: β = -0.045, p = 0.637)	Age, sex, education, APOE ε4
Verberk et al. (2020)	49	Plasma	Amsterdam Dementia Cohort	PET Aβ- (n = 76 (52 SCD, 24 MCI); 61 ± 9 y) PET Aβ+ (n = 176 (18 SCD, 26 MCI, 132 AD); 63 ± 7 y)	Visual rating of medial temporal lobe atrophy according to the MTA-scale (0–4)	Entire sample: more advanced MTA atrophy (Spearman ρ = 0.33, p < 0.001)	N/A
Pereira et al. (2017)	50	Plasma	ADNI	CU Aβ- (n=57; 74.8 ± 5.2 y) CU Aβ+ (n=37; 76.5 ± 5.2 y) MCI Aβ- (n=36; 74.5 ± 9.0 y) MCI Aβ+ (n=109; 74.2 ± 6.9 y) AD Aβ- (n=5; 82.2 ± 5.4 y) AD Aβ+ (n=65; 73.7 ± 7.6 y)	Cortical thickness (voxel-wise) Subcortical GM volume[f]	CU: no association MCI Aβ-: thinner PCC, lingual, inferior parietal, inferior temporal, insular, and middle frontal cortices; smaller thalamus (p = 0.043), hippocampus (p = 0.004), amygdala (p = 0.034), and accumbens (p = 0.008) MCI Aβ+: thinner precuneus and superior parietal gyrus; smaller putamen (p = 0.030), pallidum (p = 0.012), hippocampus (p = 0.038), and accumbens (p = 0.033) AD Aβ+: thinner precuneus, superior temporal, supramarginal, and rostral middle frontal cortices (The voxel-wise p-values for the association between NfL and cortical thickness were presented as a voxel-wise statistical map.)	Age, sex

Shi et al. (2019)	51	Plasma	Community-based sample from Nanjing, China	CU (n = 87; 64.8 ± 7.4 y) amnestic MCI (n = 68; 64.5 ± 7.7 y)	Hippocampal volume, cortical volume (voxel-wise)	Smaller hippocampal volume (r = -0.259, p < 0.05) and cortical volume of left inferior and middle temporal gyri (r = -0.515, p < 0.001)	Age, gender, education
Kang et al. (2020)	52	Plasma	ADNI	CU Aβ- (n = 66; 75.7 ± 5.4 y) CU Aβ+ (n = 17; 76.9 ± 6.0 y) MCI Aβ- (n = 48; 75.3 ± 8.0 y) MCI Aβ+ (n = 112; 74.3 ± 7.3 y) AD Aβ+ (n = 73; 74.0 ± 7.6 y)	GM VBM (temporal composite[9]; entorhinal cortex; hippocampus)	MCI Aβ+: lower GM density in the lateral temporal cortex and hippocampus MCI Aβ-: lower GM density in the insular cortex AD Aβ+: lower GM density in the hippocampus, precuneus/PCC, angular, dorsal lateral and medial frontal, and lateral temporal cortices, and cerebellum (The statistics were reported as voxel-wise statistical maps, as well as tables providing statistics at specific coordinates)	Age, sex, APOE ε4, education, CSF p-tau (log), time between the NfL measurements and MRI scan
Parbo et al. (2020)	55	Plasma	Community and Memory clinics in Jutland and Funen, Denmark.	MCI and early AD (n = 27; 73.6 ± 6.1 y)	Cortical thickness (voxel-wise) DTI (cortex; voxel-wise)	Lower cortical thickness in a small area in the superior frontal cortex Higher MD in the temporal and cingulate cortices (The statistics were reported as voxel-wise statistical maps.)	N/A
Benedet et al. (2020)	57	Plasma	ADNI	CU (n = 382; 73.5 ± 6.9 y) CI (n = 767 (420 MCI, 347 AD); 74.4 ± 7.8 y)	GM VBM (voxelwise)	CU with APOE ε4: lower volume of temporal and frontal cortices and PCC CU without APOE ε4: no association with GM atrophy CI: lower volume of frontal and temporal cortices, including medial temporal lobe (The voxel-wise T values for the association between NfL and grey matter VBM were presented as a voxel-wise statistical map.)	Age at initial NfL measurement, sex, scanner field strength (1.5 or 3 T), APOE ε4, time between plasma collection and MRI scan
Mayeli et al. (2019)	68	Plasma	ADNI	MCI (n = 149 (some converted to AD); 75.4 ± 6.6 y)	FDG-PET (44 cortical regions affected by the AD pathology)	MCI: lower uptake in the left fusiform (r = -0.191, p < 0.05), right angular (r = -0.256, p < 0.01), bilateral middle temporal (both rs < -0.176, both ps < 0.05), right inferior parietal (r = -0.241, p < 0.01) cortices AD: lower uptake in the left hippocampal (r = -0.188, p < 0.05), bilateral parahippocampal (both rs < -0.268, both ps < 0.001), bilateral fusiform (both rs < -0.236, both ps < 0.01), right angular (r = -0.249, p < 0.01), bilateral middle temporal (both rs < -0.226, both ps < 0.01), right inferior temporal (r = -0.283, p < 0.001) cortices	Age, sex (Results with the additional adjustment for the Alzheimer's Disease Rating Scale (ADAS) are also reported)

Benedet et al. (2019)	69	Plasma	ADNI	CU (n = 81; 75.6 ± 5.0 y) CI (n = 162; 64.6 ± 7.2 y)	FDG-PET (voxelwise)	CU Aβ+: lower uptake in the PCC, parietal, and temporal areas CU Aβ-: lower uptake in small areas in the parietal cortex CI Aβ+: lower uptake in the PCC/precuneus, and frontal, temporal, and occipital cortices CI Aβ-: lower uptake in small areas in the frontal and temporal cortices (The voxel-wise *T* values for the association between NfL and FDG standard uptake ratio were presented as a voxel-wise statistical map.) The voxel-wise associations between plasma NfL and cortical FDG standard uptake value ratio in the entire CU and entire CI are also reported.	Age, sex, collection time point, time between the plasma measurement and [18F]FDG acquisition
Schultz et al. (2020)	71	Serum	DIAN observational study	Noncarriers (n = 84; 40.5 ± 10.7 y) Mutation[a] carriers (n = 117; 38.6 ± 10.8 y)	DTI (voxel-wise; 12 white matter tract ROIs[h])	Noncarriers: no association with DTI index in the entire WM skeleton Carriers: lower FA and higher MD, RD, and AD (axial diffusivity) across almost the entire WM skeleton and all WM tracts (|0.007| ≤ unstandardized *B*s ≤ |0.344| , all *p*s ≤ 0.040) except the corticospinal tract MD (*B* = 0.032, *p* = 0.069) and AD (*B* = 0.007, *p* = 0.785) (The voxel-wise p-values for the association between NfL and DTI metrics were presented as a voxel-wise statistical map.)	Age, sex, mutation status, NfL×mutation status interaction
Marks et al. (2021)	72	Plasma	The Mayo Clinic Study of Aging (MCSA)	CU (n = 864; age: median = 75.6 y, IQR = 67.0, 80.9) MCI (n = 131; age: median = 81.4 y, IQR = 75.6, 85.3)	Cortical thickness (temporal, frontal, parietal, occipital) Hippocampal volume FA of the corpus callosum	No association (cortical thickness: *β*s ≤ |0.016|, *p*s ≥ 0.156; hippocampal volume: *β* = -0.121, *p* = 0.067; FA of the corpus callosum: *β* = -0.005, *p* = 0.198) (The statistics represent the standardized coefficient for the term 'NfL' estimating the cross-sectional association between NfL and an imaging measure in a linear mixed model that has the imaging measure as the outcome variable and includes the 'NfL×time' interaction term estimating the association between baseline NfL and the rate of change in the imaging measure.)	Age, sex, education
Steinacker et al. (2019)	100	Serum	German FTLD Consortium	CU (n = 15; 64.8 ± 11.3 y) MCI (n = 17; 63.1 ± 9.3 y) AD (n = 26; 67.0 ± 8.1 y)	Brain volume (201 regions)	No association with brain volume in MCI, and AD (*p* > 0.05)	N/A

AD, dementia of Alzheimer's type; ADNI, Alzheimer's disease neuroimaging initiative; Aβ+, elevated amyloid beta; Aβ- normal amyloid beta; CU, cognitively unimpaired; DIAN, Dominantly Inherited Alzheimer Network; DTI, diffusion tensor imaging; f/u, follow up; GM, gray matter; ICV, intracranial volume; MCI, mild cognitive impairment; MD, mean diffusivity; NODDI, neurite orientation dispersion and density imaging; PCC, posterior cingulate cortex; RD, radial diffusivity; SCD, subjective cognitive decline; VBM, voxel-based morphometry; VF_{EC}, extra-cellular volume fraction; V_{ISO}, isotropic volume fraction

[a.] mutations in the APP, PSEN1, or PSEN2 gene; [b.] entorhinal, inferior and middle temporal, and fusiform gyrus; [c.] lateral and medial frontal, anterior cingulate, posterior cingulate, lateral parietal, and temporal regions; [d.] angular gyrus, temporal lobe, and posterior cingulate cortex; [e.] left and right angular gyri, bilateral posterior cingulate, and left middle/inferior temporal gyrus; [f.] hippocampus, amygdala, thalamus, caudate, putamen, pallidum, accumbens; [g.] bilateral middle and inferior temporal gyri, fusiform gyrus, entorhinal cortex, and hippocampus; [h.] inferior longitudinal fasciculus, superior longitudinal fasciculus, frontal occipital fasciculus, perforant pathway, uncinate fasciculus, cingulum, frontal aslant, corticospinal, anterior corpus callosum, posterior corpus callosum, forceps minor, forceps major

Supplementary Table 2 Longitudinal studies on the association between baseline NfL and change in neuroimaging markers of neurodegeneration

Authors	Citation in the main text	NfL Source	Sample source	Baseline sample characteristics (No. of individuals; age)	MRI F/U (m: month(s); y: year(s))	Neuroimaging modality	Changes in neuroimaging measures associated with higher baseline NfL	Variables statistically controlled for
Mattsson et al. (2017)	9	Plasma	ADNI	CU (n = 193; 75.9 ± 4.9 y) MCI (n = 197; 74.7 ± 7.5 y) AD (n = 180; 75.3 ± 7.3 y)	6, 12, 18, 24, 36, 48 m	Hippocampal volume Cortical thickness (temporal composite[b]) FDG-PET (mean uptake in ROIs[c])	Entire sample: greater rates of hippocampal atrophy (β = -0.0189, p < 0.001), decline of temporal composite cortical thickness (β = -0.0489, p < 0.001), and hypometabolism (β = -0.0474, p < 0.001)	Age, sex, education, diagnosis, APOE ε4
Moscoso et al. (2021)	23	Plasma	ADNI	CU (n = 374 (Aβ+: 32 %); 74.8 ± 6.6 y) CI (n = 734 (Aβ+: 65 %); 73.6 ± 8.0 y)	Median f/u duration CU: - GM volume: 5.0 y - FDG-PET: 2 y CI: - GM volume: 2.1 y - FDG-PET: 2 y	GM volume (voxelwise; temporal composite[b]; hippocampus) FDG-PET (voxelwise; mean uptake in ROIs[d]	*GM volume* CU Aβ-: greater rate of atrophy of small cortical areas in the paracentral lobule and superior frontal gyrus CU Aβ+: greater rate of atrophy of wide areas across precuneus, parietal, temporal, and lateral frontal cortices CI Aβ-: greater rate of atrophy of almost all frontal cortex, precuneus, and lateral temporal cortices CI Aβ+: greater rate of atrophy of PCC, paracentral lobule, temporal, and some frontal cortices *FDG-PET* CU Aβ-: no association CU Aβ+: greater rate of hypometabolism in the temporal and parietal cortices CI Aβ-: No association CI Aβ+: greater rate of hypometabolism in the precuneus/PCC, lateral parietal, and temporal cortices (The voxel-wise *r* values for the association between NfL and an imaging measure were presented as a voxel-wise statistical map.)	Age, sex, (MRI scanner field strength (1.5 or 3 T) and ICV for atrophy measures
Weston et al. (2017)	24	Serum	Dementia Research Centre, University College London	Noncarriers (n = 11; 38.9 ± 9.5 y) Presymptomatic mutation[a] carriers (n = 19; 36.0 ± 5.7 y) Symptomatic mutation[a] carriers (n = 18; 46.6 ± 9.3 y)	33 participants had 1 f/u Mean ± SD interval: 1.3 ± 0.5 y	Hippocampal volume	All carriers: no association with hippocampal volume (Spearman ρ = 0.37, p = 0.09) Presymptomatic carriers: no association with hippocampal volume (statistics not reported)	N/A

Simrén et al. (2021)	27	Plasma	AddNeuroMed study	CU (n = 99; 73.0 ± 6.1 y) MCI (n = 107; 74.5 ± 5.9 y) AD (n = 103; 76.4 ± 5.8 y)	3, 12 m	GM VBM	Entire sample: greater rate of atrophy in scattered areas across precuneus, temporal, and medial and superior frontal No association between change in NfL and change in GM VBM (The voxel-wise *T* values for the association between NfL and grey matter VBM were presented as a voxel-wise statistical map.)	Age, sex, education, APOE ε4
Preische et al. (2019)	32	Serum	DIAN observational study	Noncarriers (n = 162; 38.7 (19.5-69.5) y) Mutation[e] Carriers (n = 243; 39.3 (18.0-67.8) y)	196/405 subjects had 1-5 f/u Mean no. of visits: 2.5 Median f/u: 3 y	Precuneus cortical thickness	Carriers: greater rates of decline in the precuneus volume (B = -0.105, p < 0.001) Associations between change in NfL and change in precuneus atrophy rate, as well as FDG uptake are also reported in the original paper.	Age, sex
Rajan et al. (2020)	44	Serum	The Chicago Health and Aging Project (CHAP)	Older adults (n = 1327 (436 AD, 317 MCI; 742 underwent MRI scan; 183 had ≥ 2 scans); 73.5 ± 6.4 y)	≤ 6 f/u for ≤ 19 y	Hippocampal volume Global cortical thickness	Greater rates of decline in the hippocampal volume (Estimate = -0.049, 95% CI: -0.083 to -0.015) and global cortical thickness (Estimate = -1.57, 95% CI: -3.05 to -0.09)	Age, gender, race/ethnicity, education, APOE ε4
Mielke et al. (2019)	45	Plasma	The Mayo Clinic Study of Aging (MCSA)	Middle-aged to older adults without dementia (n =79 (64 CU, 15 MCI); 76.4 (IQR: 71.7, 80.1))	≤ 2 f/u (15, 30 m)	Cortical thickness (temporal composite) FDG-PET (mean uptake in ROIs[e]) FA of the corpus callosum	Greater rates of decline in the hippocampal volume (β = -0.022, p = 0.023), temporal cortical thickness (β = -0.007, p = 0.019), hypometabolism (β = -0.010, p = 0.018), and FA of the corpus callosum (β = -0.002, p = 0.015)	Age, sex, and education, ICV (in the models examining hippocampal volume)
Hu et al. (2019)	47	Plasma	ADNI	CU Aβ- (n = 130; 72.8 ± 5.5 y) CU Aβ+ (n = 113; 73.3 ± 6.2 y)	f/u range: 1-10 y > 75 % of the participants had ≥ 3 y of f/u	Hippocampal volume	CU Aβ-: no association with hippocampal volume (β = -0.001, p = 0.931) CU Aβ+: greater rate of atrophy of the hippocampus (β = -0.035, p = 0.009)	Age, sex, education, APOE ε4
Pereira et al. (2021)	48	Plasma	BioFINDER	Nondemented (n = 159 (52 CU, 44 SCD, 63 MCI); 69.2 (42.4-87.5) y)	Median no. of visits = 2 y (IQR = 1) median f/u time = 1.6 y (IQR = 0.7)	Hippocampal volume Cortical thickness (temporal composite[b])	Greater rate of hippocampal atrophy (t = -5.014, p < 0.001, Cohen's d = -0.79) Greater rate of decline in the temporal cortical thickness (t = -3.043, p = 0.003, Cohen's d = -0.48)	Age, sex, amyloid status, APOE ε4, presence of cognitive impairment, ICV

Benedet et al. (2020)	57	Plasma	ADNI	CU (n = 382; 73.5 ± 6.9 y) CI (n = 767 (420 MCI, 347 AD); 74.4 ± 7.8 y)	≤ 48 m	GM VBM (voxelwise)	CU: greater rate of atrophy of primarily frontal and temporal cortices at 48 months than at the baseline CI: greater rate of atrophy of mainly temporal regions over 12, 24, 36, and 48 months than at the baseline (The voxel-wise *T* values for the association between NfL and grey matter VBM were presented as a voxel-wise statistical map.)	Age at initial NfL measurement, sex, scanner type (1.5 or 3 T), APOE ε4, time between plasma collection and MRI
Mayeli et al. (2019)	68	Plasma	ADNI	MCI (n = 149 (some progressed to AD); 75.4 ± 6.6 y)	6, 12 m	FDG-PET (44 cortical regions affected by the AD pathology)	MCI: lower uptake in the right hippocampus (r = -0.213, p < 0.05) at follow-up AD: lower uptake in the right angular (r = -0.265, p < 0.05), bilateral inferior temporal (r ≤ -0.245, p ≤ 0.05), posterior cingulate (r = 0.510, p < 0.05) cortices at follow-up	Age, sex (Results with the additional adjustment for the Alzheimer's Disease Rating Scale (ADAS) are also reported)
Benedet et al. (2019)	69	Plasma	ADNI	CU (n = 302; 73.6 ± 7.2 y) CI (n = 713; 74.1 ± 7.7 y)	≤ 24 m Average: 9.2 m	FDG-PET (voxelwise)	CI Aβ+: greater rate of hypometabolism in the PCC and frontal and temporal cortices over 24 months than at the baseline No associations in the other subgroups (The voxel-wise *T* values for the association between NfL and FDG-uptake were presented as a voxel-wise statistical map.)	Age, sex, collection time point, time between the plasma measurement and [18F]FDG acquisition
Marks et al. (2021)	72	Plasma	The Mayo Clinic Study of Aging (MCSA)	CU (n = 864; age: median = 75.6 y, IQR = 67.0, 80.9) MCI (n = 131; age: median = 81.4 y, IQR = 75.6, 85.3)	Median f/u duration CU: 6.2y MCI: 5.0 y	Cortical thickness (temporal, frontal, parietal, occipital) Hippocampal volume FA of the corpus callosum	Entire sample: greater rate of hippocampal atrophy (β = -0.046, p < 0.001) and corpus callosum FA decline (β = -0.003, p < 0.001)	Age, sex, education
Steinacker et al. (2018)	100	Serum	German FTLD consortium	CU (n = 15; 64.8 ± 11.3 y) MCI (n = 17; 63.1 ± 9.3 y) AD (n = 26; 67 ± 8.1 y)	13 AD, 13 MCI, 12 CU had ≥ 1 f/u MRI scan Intervals: approximately 1 y	Brain volume (201 regions)	No association with the regional cortical volume at follow-up in either the AD or MCI group (p > 0.05)	N/A
Cavedo et al. (2020)	113	Plasma	INSIGHT-preAD cohort	CU with subjective memory complaints (n = 276 (4 converted to AD after 24m, 1 to AD after 36m); 75.7 ± 3.4 y)	1 f/u with an interval of 24 m	Volume of basal forebrain cholinergic system (whole, Ch1/2, Ch4)	No association with the atrophy rate of the whole basal forebrain cholinergic system and the subdivision volumes (Estimate = 0.002, p = 0.753, Cohen's f < 0.001)	Age, sex, education, amyloid status, APOE ε4, tau, tau×NfL

AD, dementia of Alzheimer's type; ADNI, Alzheimer's disease neuroimaging initiative; Aβ+, elevated amyloid beta; Aβ- normal amyloid beta; CU, cognitively unimpaired; DIAN, Dominantly Inherited Alzheimer Network; DTI, diffusion tensor imaging; f/u, follow up; GM, gray matter; ICV, intracranial volume; INSIGHT-preAD, Investigation of Alzheimer's Predictors in Subjective Memory Complainers; MCI, mild cognitive impairment; PCC, posterior cingulate cortex; SCD, subjective cognitive decline; SMC, subjective memory complainers; VBM, voxel-based morphometry
[a.] mutations in the APP, PSEN1, or PSEN2 gene; [b.] entorhinal, inferior and middle temporal, and fusiform gyrus; [c.] lateral and medial frontal, anterior cingulate, posterior cingulate, lateral parietal, and temporal regions; [d.] PCC, and angular and inferior temporal gyrus; [e.] left and right angular gyri, bilateral posterior cingulate, and left middle/inferior temporal gyrus