

Supplementary Table 1: Baseline associations between hippocampal volume and diffusion metrics of the tracts of interest

	Estimate	SE	T-test	DOF	p-value	95% CI
Left adjusted hippocampal volume						
Left HCB - FA	0.015	0.004	3.674	251	0.0003***	[0.0071, 0.0233]
Left HCB - MD	-0.002	0.001	-2.269	251	0.026*	[-0.0039, -0.0003]
Left HCB- AxD	-0.001	0.001	-0.684	251	0.504	[-0.0030, 0.0015]
Left HCB - RD	-0.003	0.001	-2.882	251	0.005**	[-0.0043, -0.0008]
Left UF - FA	0.003	0.004	0.673	248	0.500	[-0.0056, 0.0114]
Left UF - MD	-0.002	0.001	-1.389	248	0.174	[-0.0041, 0.0007]
Left UF - AxD	-0.002	0.002	-1.296	248	0.205	[-0.0052, 0.0011]
Left UF - RD	-0.002	0.001	-1.361	248	0.181	[-0.0038, 0.0007]
Right adjusted hippocampal volume						
Right HCB - FA	0.0124	0.006	2.265	251	0.023*	[0.0017, 0.0232]
Right HCB - MD	-0.0024	0.001	-2.167	251	0.030*	[-0.0046, -0.0002]
Right HCB - AxD	-0.0021	0.002	-1.449	251	0.145	[-0.0050, 0.0007]
Right HCB - RD	-0.0027	0.001	-2.393	251	0.016*	[-0.0050, -0.0005]
Right UF - FA	0.0179	0.006	2.922	248	0.004**	[0.0059, 0.0299]
Right UF - MD	-0.0028	0.001	-3.142	248	0.002**	[-0.0046, -0.0011]
Right UF - AxD	-0.0016	0.001	-1.424	248	0.158	[-0.0038, 0.0006]
Right UF - RD	-0.0034	0.001	-3.691	248	0.0003***	[-0.0052, -0.0016]

Robust linear regressions with Huber-M estimator and covaried for age, education and sex. For the UF the tract could not be estimated in 3 cases (n=253, for the HCB: n=256 independent participants). Abbreviations: HCB = Hippocampal cingulum; UF = Uncinate Fasciculus; FA = Fractional Anisotropy; MD = Mean Diffusivity; AxD = Axial Diffusivity; RD = Radial diffusivity, CI= Confidence interval. Estimates for FA were multiplied by 10^3 and for MD, AxD and RD by 10^6 . *: p-value < 0.05; **: p-value < 0.01; ***: p-value < 0.001. All p-values are two-sided.

Table2: Hippocampal volume predicting changes in tract diffusivity over time

Predictor: Hippocampal volume at baseline	Hippocampal cingulum change (observations = 386)			Uncinate fasciculus change (observations = 379)		
	Estimate (SE)	p-value	95% CI	Estimate (SE)	p-value	95% CI
Fractional Anisotropy						
• Left	0.003 (0.002)	0.186	[-0.0013, 0.0068]	0.003 (0.002)	0.232	[-0.0019, 0.0076]
• Right	0.003 (0.002)	0.123	[-0.0009, 0.0076]	0.002 (0.002)	0.243	[-0.0019, 0.0072]
Mean diffusivity						
• Left	-0.0006 (0.0008)	0.417	[-0.0022, 0.0009]	0.001 (0.002)	0.675	[-0.0038, 0.0058]
• Right	-0.002 (0.0009)	0.025*	[-0.0038, -0.0003]	0.0005 (0.0005)	0.283	[-0.0004, 0.0015]
Axial diffusivity						
• Left	-0.0005 (0.0009)	0.558	[-0.0023, 0.0013]	0.002 (0.003)	0.443	[-0.0037, 0.0084]
• Right	-0.0020 (0.001)	0.032*	[-0.0042, -0.0002]	0.0008 (0.0007)	0.251	[-0.0005, 0.0021]
Radial diffusivity						
• Left	-0.0007 (0.0007)	0.360	[-0.0021, 0.0008]	0.0005 (0.002)	0.822	[-0.0037, 0.0047]
• Right	-0.0019 (0.0008)	0.022*	[-0.0036, -0.0003]	0.0003 (0.0005)	0.506	[-0.0006, 0.0012]
Predictor: Hippocampal volume changes	Hippocampal cingulum change (observations = 386)			Uncinate fasciculus change (observations = 379)		
	Estimate (SE)	p-value	95% CI	Estimate (SE)	p-value	95% CI
Fractional Anisotropy						
• Left	0.107 (0.068)	0.122	[-0.020, 0.139]	-0.084 (0.084)	0.318	[-0.251, 0.082]
• Right	0.059 (0.040)	0.143	[-0.020, 0.138]	0.049 (0.042)	0.251	[-0.035, 0.133]
Mean diffusivity						
• Left	-0.029 (0.028)	0.292	[-0.084, 0.029]	-0.041 (0.085)	0.629	[-0.210, 0.127]
• Right	-0.037 (0.017)	0.030*	[-0.070, - 0.004]	0.004 (0.001)	0.620	[-0.013, 0.022]
Axial diffusivity						
• Left	-0.027 (0.033)	0.413	[-0.091, 0.037]	-0.032 (0.106)	0.762	[-0.243, 0.178]
• Right	-0.040 (0.019)	0.038*	[-0.078, - 0.002]	0.008 (0.012)	0.533	[-0.017, 0.032]
Radial diffusivity						
• Left	-0.031 (0.026)	0.245	[-0.083, 0.021]	-0.042 (0.075)	0.573	[-0.191, 0.106]
• Right	-0.035 (0.016)	0.029*	[-0.066, - 0.004]	0.0001 (0.008)	0.936	[-0.016, 0.017]

Linear Mixed effects models modeling random intercepts for each individual and a random slope over time with hippocampal volume at baseline (upper panel) or hippocampal volume change over time (lower panel) as predictor and diffusion values of the tract over time as outcome. All models were covaried for age, sex and education and their interaction with time (if $p < 0.10$). Age was centered at 74.07

years, education at 15.84 and female was the reference for sex. Estimates for FA were multiplied by 10^3 and for MD, AxD and RD 10^5 . *: p-value < 0.05

Supplementary Table 3: Tract diffusivity predicting changes in hippocampal volume over time

Outcome : Hippocampal volume change	Hippocampal cingulum baseline (observations = 466)			Uncinate fasciculus baseline (observations = 462)		
	Estimate (SE)	p-value	95% CI	Estimate (SE)	p-value	95% CI
Fractional Anisotropy						
• Left	-0.033 (0.134)	0.803	[-0.297, 0.231]	-0.022 (0.123)	0.861	[-0.265, 0.221]
• Right	0.130 (0.141)	0.357	[-0.148, 0.409]	0.055 (0.137)	0.689	[-0.214, 0.324]
Mean diffusivity						
• Left	-0.315 (0.613)	0.608	[-1.523, 0.893]	0.282 (0.394)	0.475	[-0.495, 1.058]
• Right	-0.710 (0.465)	0.128	[-1.628, 0.207]	-1.164 (0.755)	0.125	[-2.653, 0.325]
Axial diffusivity						
• Left	-0.345 (0.557)	0.536	[-1.444, 0.754]	0.217 (0.321)	0.496	[-0.415, 0.850]
• Right	-0.624 (0.431)	0.150	[-1.474, 0.227]	-0.913 (0.644)	0.158	[-2.182, 0.357]
Radial diffusivity						
• Left	-0.237 (0.597)	0.691	[-1.422, 0.938]	0.302 (0.423)	0.476	[-0.532, 1.137]
• Right	-0.709 (0.470)	0.132	[-1.635, 0.216]	-1.057 (0.736)	0.153	[-2.507, 0.394]
Outcome : Hippocampal volume change	Hippocampal cingulum change (observations = 466)			Uncinate fasciculus change (observations = 462)		
	Estimate (SE)	p-value	95% CI	Estimate (SE)	p-value	95% CI
Fractional Anisotropy						
• Left	0.126 (0.208)	0.544	[-0.285, 0.538]	-0.040 (0.191)	0.835	[-0.417, 0.337]
• Right	-0.056 (0.230)	0.807	[-0.512, 0.399]	0.134 (0.212)	0.527	[-0.285, 0.553]
Mean diffusivity						
• Left	-0.377 (0.740)	0.611	[-1.842, 1.087]	0.870 (0.642)	0.178	[-0.402, 2.142]
• Right	-0.011 (0.748)	0.988	[-1.491, 1.468]	-1.294 (1.156)	0.266	[-3.583, 0.996]
Axial diffusivity						
• Left	-0.327 (0.667)	0.624	[-1.647, 0.992]	0.308 (0.520)	0.555	[-0.722, 1.337]
• Right	-0.072 (0.654)	0.913	[-1.366, 1.222]	-0.898 (1.027)	0.384	[-2.932, 1.135]
Radial diffusivity						
• Left	-0.421 (0.746)	0.573	[-1.896, 1.055]	1.234 (0.692)	0.077	[-0.137, 2.604]
• Right	-0.178 (0.767)	0.817	[-1.697, 1.341]	-1.278 (1.109)	0.252	[-3.474, 0.919]

Linear Mixed effects models with random intercepts for each individual and random slope for time modeling tract diffusivity at baseline (upper panel) or tract diffusivity change over time (lower panel) as predictor and hippocampal volume over time as outcome. All models were covaried for age, sex and education and their interaction with time (if $p < 0.10$). Age was centered at 74.07 years, education at 15.84 and female was the reference for sex. Estimates for FA were multiplied by 10^3 and for MD, AxD and RD 10^5 .

Supplementary Table 4: Baseline tract diffusivity predicting changes in PCC tau over time

Outcome : PCC tau changes	Hippocampal cingulum at baseline (observations = 212)			Uncinate fasciculus at baseline (observations = 209)		
	Estimate (SE)	p-value	95% CI	Estimate (SE)	p-value	95% CI
Fractional Anisotropy						
• Left	0.0002 (0.0002)	0.318	[-0.0002, 0.0007]	-0.00002 (0.0003)	0.951	[-0.0005, 0.0005]
• Right	-0.0003 (0.0002)	0.099	[-0.0008, 0.00007]	-0.0002 (0.0002)	0.311	[-0.0006, 0.0002]
Mean diffusivity						
• Left	-0.001 (0.001)	0.356	[-0.0038, 0.0014]	0.001 (0.0008)	0.186	[-0.0018, 0.0033]
• Right	0.002 (0.001)	0.012*	[0.0004, 0.0035]	0.0008 (0.0001)	0.544	[-0.0005, 0.0027]
Axial diffusivity						
• Left	-0.001 (0.001)	0.543	[-0.0032, 0.0017]	0.0009 (0.0007)	0.192	[-0.0004, 0.0022]
• Right	0.002 (0.001)	0.028*	[0.0002, 0.0031]	0.0003 (0.001)	0.810	[-0.0019, 0.0024]
Radial diffusivity						
• Left	-0.001 (0.001)	0.331	[-0.0035, 0.0012]	0.001 (0.001)	0.202	[-0.0006, 0.0028]
• Right	0.002 (0.001)	0.011*	[0.0005, 0.0035]	0.0009 (0.001)	0.447	[-0.0015, 0.0034]

Linear Mixed effects models modeling random intercepts for each individual (and random slope for time) with tract diffusivity at baseline as predictor and PCC tau over time as outcome. All models were covaried for age, sex and education and their interaction with time (if $p < 0.10$). Age was centered at 74.07 years, education at 15.84 and female was the reference for sex. Estimates for FA were multiplied by 10^3 and for MD, AxD and RD 10^5 . PCC = Posterior Cingulate Cortex; *: p-value < 0.05

Supplementary Table 5: Baseline tract diffusivity predicting changes in Inferior temporal tau over time

Outcome : Inferior temporal tau changes	Hippocampal cingulum at baseline (observations = 212)		
	Estimate (SE)	p-value	95% CI
Fractional Anisotropy			
• Left	-0.00004 (0.0001)	0.823	[-0.0004, 0.0003]
• Right	-0.000001 (0.0002)	0.997	[-0.0004, 0.0004]
Mean diffusivity			
• Left	-0.0004 (0.001)	0.657	[-0.0026, 0.0016]
• Right	0.0004 (0.001)	0.517	[-0.0009, 0.0018]
Axial diffusivity			
• Left	-0.001 (0.001)	0.345	[-0.0031, 0.0011]
• Right	0.0005 (0.001)	0.427	[-0.0008, 0.0018]
Radial diffusivity			
• Left	-0.0002 (0.001)	0.857	[-0.0021, 0.0018]
• Right	0.0004 (0.001)	0.578	[-0.0010, 0.0017]

Linear Mixed effects models modeling random intercepts for each individual with tract diffusivity at baseline as predictor and inferior temporal tau over time as outcome. All models were covaried for age, sex and education and their interaction with time (if $p < 0.10$). Age was centered at 74.07 years, education at 15.84 and female was the reference for sex. Estimates for FA were multiplied by 10^3 and for MD, AxD and RD by 10^5 .

Supplementary Table 6: Baseline tract diffusivity predicting changes in PCC tau over time differently for amyloid positive and amyloid negative individuals

Outcome : PCC tau changes	Hippocampal cingulum at baseline (observations = 210)		
	Estimate (SE)	p-value	95% CI
Fractional Anisotropy x amyloid status			
• Left	-0.0006 (0.0004)	0.233	[-0.0016, 0.0004]
• Right	-0.002 (0.0004)	0.0004**	[-0.0025, -0.00075]
Mean diffusivity x amyloid status			
• Left	0.0009 (0.003)	0.775	[-0.0056, 0.0074]
• Right	0.004 (0.002)	0.012*	[0.0010, 0.0076]
Axial diffusivity x amyloid status			
• Left	-0.002 (0.004)	0.538	[-0.0076, 0.0040]
• Right	0.002 (0.002)	0.118	[-0.0006, 0.0056]
Radial diffusivity x amyloid status			
• Left	0.002 (0.003)	0.491	[-0.0038, 0.0078]
• Right	0.005 (0.002)	0.004*	[0.0016, 0.0081]

Linear Mixed effects models modeling random intercepts for each individual, tract diffusivity at baseline by amyloid status as predictor and PCC tau over time as outcome. All models were covaried for age, sex and education and their interaction with time (if $p < 0.10$). Age was centered at 74.07 years, education at 15.84 and female was the reference for sex. Estimates for FA were multiplied by 10^3 and for MD, AxD and RD by 10^5 . *: p-value < 0.05; **: p-value < 0.01

Supplementary Table 7: Baseline tract diffusivity predicting changes in memory over time

Outcome : Memory change	Hippocampal cingulum			Hippocampal cingulum x PCC Tau status			Hippocampal cingulum x IT Tau status		
	(observations = 1167)			(observations = 714)			(observations = 714)		
	Estimate (SE)	p-value	95% CI	Estimate (SE)	p-value	95% CI	Estimate (SE)	p-value	95% CI
Fractional Anisotropy									
• Left	0.001 (0.0003)	0.003**	[0.0003, 0.0015]	0.0001 (0.0007)	0.837	[-0.0012, 0.0015]	0.002 (0.002)	0.195	[-0.0011, 0.0052]
• Right	0.0009 (0.0003)	0.0005***	[0.0004, 0.0015]	0.0006 (0.0007)	0.345	[-0.0007, 0.0020]	0.0009 (0.001)	0.467	[-0.0015, 0.0034]
Mean diffusivity									
• Left	-0.003 (0.001)	0.011*	[-0.0055, -0.0007]	0.002 (0.003)	0.466	[-0.0039, 0.0085]	0.008 (0.007)	0.241	[-0.0058, 0.0231]
• Right	-0.002 (0.0009)	0.007**	[-0.0042, -0.0006]	-0.006 (0.002)	0.015*	[-0.0103, -0.0011]	-0.005 (0.003)	0.150	[-0.0110, 0.0017]
Axial diffusivity									
• Left	-0.002 (0.001)	0.148	[-0.0037, 0.0006]	0.004 (0.002)	0.184	[-0.0019, 0.0098]	0.011 (0.006)	0.063	[-0.0006, 0.0022]
• Right	-0.001 (0.0008)	0.083	[-0.0030, 0.0002]	-0.005 (0.002)	0.023*	[-0.0093, -0.0007]	-0.005 (0.003)	0.094	[-0.0114, 0.0010]
Radial diffusivity									
• Left	-0.004 (0.001)	0.003**	[-0.0061, -0.0013]	0.001 (0.003)	0.680	[-0.0047, 0.0072]	0.004 (0.007)	0.572	[-0.0105, 0.0189]
• Right	-0.003 (0.0009)	0.002**	[-0.0047, -0.0011]	-0.006 (0.002)	0.017*	[-0.0102, -0.0010]	-0.004 (0.003)	0.185	[-0.0106, 0.0021]

Linear Mixed effects models modeling random intercepts for each individual, tract diffusivity at baseline as predictor and memory as outcome. All models were covaried for age, sex and education and their interaction with time (if $p < 0.10$). Age was centered at 74.07 years, education at 15.84 and female was the reference for sex. Estimates for FA were multiplied by 10^3 and for MD, AxD and RD by 10^5 . *: p-value < 0.05 ; **: p-value < 0.01 ; ***: p-value < 0.001

Supplementary Table 8: Baseline tract diffusivity predicting changes in executive functions over time

Outcome : Executive function change	Hippocampal cingulum (observations = 1157)			Hippocampal cingulum x PCC Tau status (observations = 711)			Hippocampal cingulum x IT Tau status (observations = 711)		
	Estimate (SE)	p-value	95% CI	Estimate (SE)	p-value	95% CI	Estimate (SE)	p-value	95% CI
Fractional Anisotropy									
• Left	0.0002 (0.0002)	0.306	[-0.0002, 0.0007]	-0.001 (0.001)	0.383	[-0.0016, 0.0006]	-0.0007 (0.001)	0.580	[-0.0033, 0.0019]
• Right	0.0001 (0.0002)	0.611	[-0.0003, 0.0005]	0.0004 (0.001)	0.431	[-0.0007, 0.0016]	0.0005 (0.001)	0.636	[-0.0016, 0.0025]
Mean diffusivity									
• Left	-0.0008 (0.001)	0.424	[-0.0026, 0.0011]	0.0004 (0.003)	0.882	[-0.0045, 0.0053]	0.0017 (0.006)	0.781	[-0.0101, 0.0135]
• Right	-0.0004 (0.001)	0.580	[-0.0018, 0.0010]	0.001 (0.002)	0.532	[-0.0025, 0.0048]	0.0001 (0.003)	0.974	[-0.0051, 0.0053]
Axial diffusivity									
• Left	-0.0004 (0.001)	0.622	[-0.0021, 0.0013]	-0.001 (0.002)	0.764	[-0.0053, 0.0039]	0.0007 (0.005)	0.877	[-0.0084, 0.0098]
• Right	-0.0002 (0.001)	0.707	[-0.0015, 0.0010]	0.002 (0.002)	0.287	[-0.0016, 0.0053]	0.0003 (0.002)	0.898	[-0.0047, 0.0053]
Radial diffusivity									
• Left	-0.0008 (0.001)	0.358	[-0.0028, 0.0010]	0.001 (0.002)	0.696	[-0.0038, 0.0057]	0.0023 (0.006)	0.701	[-0.0096, 0.0144]
• Right	-0.0005 (0.001)	0.523	[-0.0019, 0.0010]	0.001 (0.002)	0.708	[-0.0030, 0.0044]	-0.0001 (0.003)	0.979	[-0.0053, 0.0051]

Linear Mixed effects models modeling random intercepts for each individual, tract diffusivity at baseline as predictor and executive function as outcome. All models were covaried for age, sex and education and their interaction with time (if $p < 0.10$). Age was centered at 74.07 years, education at 15.84 and female was the reference for sex. Estimates for FA were multiplied by 10^3 and for MD, AxD and RD by 10^5 .