

## **Supplementary Material**

Table 1. Summary of linear mixed models examining global and tract-specific MD on cognitive change (controlling for modified global MD)

Table 2. Summary of linear mixed models examining global and tract-specific RD on cognitive change (controlling for modified global RD)

Table 3. Summary of linear mixed models examining global and tract-specific AxD on cognitive change (controlling for modified global AxD)

Table 4. Summary of linear regression models examining global FA and tract-specific FA on baseline cognition (controlling for modified global FA)

Table 5. Summary of linear regression models examining global and tract-specific MD on baseline cognition (controlling for modified global MD)

Table 6. Summary of linear regression models examining global and tract-specific RD on baseline cognition (controlling for modified global RD)

Table 7. Summary of linear regression models examining global and tract-specific AxD on baseline cognition (controlling for modified global AxD)

Table 8. Summary of linear mixed models examining each modified measure of global FA on cognitive change

Table 9. Summary of linear mixed models examining tract-specific FA on cognitive change (not controlling for modified global FA)

## Methods

Confirmatory factor analyses of the neuropsychological measures were conducted on the Harvard Aging Brain baseline cohort. This includes 277 participants with at least one neuropsychological follow-up visit, without respect to the availability of diffusion-weighted imaging data. Neuropsychological data were available for 277 participants at baseline and first follow-up, 265 at second follow-up, 255 at third follow-up, 182 at fourth follow-up, 117 at fifth follow-up, and 36 at sixth follow-up. Initial separate models for the first three time-points had fit statistics as follows:  $\chi^2(17) = 13.4$ ,  $p = 0.71$ , TLI = 1.0, RMSEA = 0.0 at baseline;  $\chi^2(17) = 23.3$ ,  $p = 0.14$ , TLI = 0.978, RMSEA = 0.037 at first follow-up;  $\chi^2(17) = 24.6$ ,  $p = 0.71$ , TLI = 0.976, RMSEA = 0.041 at second follow-up. The average loadings of the first three time-points were computed and applied to all time-points to avoid biasing to a single time-point while enabling consistency of the measurement to be maintained even as new time-points are added. The loadings of each task on executive function were: .622 for phonemic fluency, .533 for Letter-Number Sequencing, and .666 for the Trail Making Test (Form B minus Form A). For episodic memory, the loadings were: .534 for Logical Memory, .605 for the Free and Cued Selective Reminding Test, and .739 for Six-Trial Selective Reminding. For processing speed, the loadings were: .942 for Digit Symbol Coding, and .637 for the Trail Making Test (Form A). Imposing these loadings on each time-point with available data from greater than 150 participants resulted in the following fit statistics:  $\chi^2(25) = 16.7$ ,  $p = 0.89$ , TLI = 1.0, RMSEA = 0.0 at baseline;  $\chi^2(25) = 25.2$ ,  $p = 0.45$ , TLI = 0.999, RMSEA = 0.006 at first follow-up;  $\chi^2(25) = 28.2$ ,  $p = 0.30$ , TLI = 0.993, RMSEA = 0.022 at second follow-up;  $\chi^2(25) = 43.7$ ,  $p = 0.01$ , TLI = 0.957, RMSEA = 0.054 at third follow-

up;  $\chi^2(25) = 25.9$ ,  $p = 0.41$ , TLI = 0.997, RMSEA = 0.014 at fourth follow-up.

Comparisons between the freely estimated models and the models with constrained loadings found no significant differences after correction for multiple comparisons. These findings suggest that application of the estimated loadings to all time-points provides acceptable model fit.

All neuropsychological tests were z-transformed using the mean and standard deviation from the baseline time-point ( $n = 277$ ) and scaled such that higher scores indicated better performance. The natural log of each timed measure from the Trail Making Test was computed prior to z-transformation.

In the present study, individual factor scores were removed from analyses if missing data caused the factor weight to be less than 50%. This resulted in exclusion of eight executive function scores, two episodic memory scores, and five processing speed scores across all time-points.

#### *MRI diffusion-weighted imaging*

In supplemental analyses, we examined additional diffusivity metrics including mean diffusivity (MD), radial diffusivity (RD), and axial diffusivity (AxD) using the same procedures as described for FA. These additional metrics describe the rate of diffusion; MD describes the average rate of diffusion along all 3 axes; RD describes the rate of diffusion perpendicular to the main axis (computed as the average of the 2 perpendicular axes), and AxD describes the rate of diffusion along the main axis of diffusion.

#### *Statistical analyses*

First, we examined the relationship between the diffusivity metrics and

longitudinal cognition using linear mixed models, as described in the main text. Next, we used linear regression models to address whether baseline global diffusion characteristics predicted baseline cognition independently (Model 1) or synergistically (Model 2) with amyloid status.

Model 1: Cognition ~ global + amyloid status + covariates

Model 2: Cognition ~ global x amyloid status + covariates

Cognition = executive function, episodic memory, or processing speed

Covariates = age at baseline, sex, years of education, and motion in the scanner

Time = time from baseline (years)

Note that Model 2 includes lower order effects

The second set of cross-sectional analyses examined whether the effects of diffusion characteristics on baseline cognition are tract-specific or global in nature. We examined both independent (Model 3) and synergistic effects (Model 4) of tract-specific white matter and amyloid status on cognition.

Model 3: Cognition ~ tract-specific + modified global + amyloid status + covariates

Model 4: Cognition ~ tract-specific x amyloid status + modified global x amyloid status + covariates

Cognition = executive function, episodic memory, or processing speed

Covariates = age at baseline, sex, years of education, and motion in the scanner

Time = time from baseline (years)

Note that Model 4 includes lower order effects

## Results

Results from the linear mixed models using MD, RD, and AxD are presented in Tables 1 – 3. Results from the linear regression models using FA, MD, RD, and AxD are presented in Tables 4 – 7.

Linear regression analyses on only the baseline data (Table 4) demonstrated a different pattern of results than did the longitudinal linear mixed models for global FA

presented in the main text. Here, we found that lower global FA predicted worse performance in executive function and processing speed but not in episodic memory. Removing amyloid status from these models did not alter the impact of global FA on cognition. In these cross-sectional models, amyloid status was not associated with any of the cognitive domains (all  $p > 0.128$ ) nor was the interaction of global FA with amyloid status (all  $p > 0.235$ ). A similar pattern of results was observed in the cross-sectional analyses that examined the other global diffusion measures (MD, RD, and AxD).

Table 1. Summary of linear mixed models examining global and tract-specific MD on cognitive change (controlling for modified global MD)

Region	Estimate	Std Error	<i>t</i> -value	<i>p</i> value
<b>Executive function</b>				
Global	0.012	0.008	1.522	0.564
ATR	-0.009	0.010	-0.883	0.189
CB	-0.008	0.012	-0.674	0.250
PHC	0.012	0.008	1.526	0.564
CST	0.007	0.011	0.669	0.752
Fma	0.007	0.010	0.684	0.747
Fmi	-0.001	0.011	-0.092	0.464
IFOF	-0.014	0.019	-0.774	0.220
ILF	0.009	0.011	0.884	0.689
SLF	0.031	0.012	2.487	0.507
<b>Episodic memory</b>				
Global	-0.021	0.012	-1.786	0.037
ATR	-0.020	0.014	-1.389	0.083
CB	-0.008	0.018	-0.445	0.328
PHC	0.014	0.012	1.220	0.611
CST	0.010	0.015	0.627	0.765
Fma	0.011	0.014	0.741	0.730
Fmi	0.008	0.016	0.485	0.814
IFOF	0.006	0.027	0.227	0.910
ILF	-0.013	0.016	-0.841	0.200
SLF	0.001	0.018	0.047	0.981
<b>Processing speed</b>				
Global	-0.020	0.009	-2.068	0.019
ATR	<b>-0.031</b>	<b>0.012</b>	<b>-2.695</b>	<b>0.004</b>
CB	0.016	0.014	1.160	0.623
PHC	0.006	0.009	0.631	0.764
CST	-0.002	0.012	-0.177	0.430
Fma	0.004	0.012	0.332	0.870
Fmi	0.002	0.013	0.164	0.935
IFOF	-0.026	0.021	-1.224	0.110
ILF	-0.003	0.012	-0.249	0.402
SLF	0.021	0.014	1.513	0.565

Each row summarizes the results from a separate linear mixed model. All models control for age, sex, education, motion in the scanner, amyloid status, and their interactions with time. In tract-specific analyses, the modified measure of global MD in each model does not include the specific tract under investigation. Abbreviations: MD = mean diffusivity; ATR = anterior thalamic radiation; CB = cingulum bundle; PHC = parahippocampal cingulum; CST = corticospinal tract; IFOF = inferior frontal occipital fasciculus; ILF = inferior longitudinal fasciculus; Fma = forceps major; Fmi = forceps minor; SLF = superior longitudinal fasciculus. Bolded values are significant at  $p < 0.017$  for global effects and  $p < 0.006$  for tract-specific effects.

Table 2. Summary of linear mixed models examining global and tract-specific RD on cognitive change (controlling for modified global RD)

Region	Estimate	Std Error	<i>t</i> -value	<i>p</i> value
<b>Executive function</b>				
Global	0.005	0.008	0.621	0.767
ATR	-0.010	0.010	-0.953	0.171
CB	-0.024	0.012	-1.948	0.026
PHC	0.008	0.009	0.954	0.670
CST	0.004	0.011	0.320	0.875
Fma	-0.002	0.011	-0.143	0.443
Fmi	-0.002	0.012	-0.130	0.448
IFOF	-0.011	0.018	-0.587	0.279
ILF	0.017	0.011	1.554	0.560
SLF	0.021	0.013	1.575	0.558
<b>Episodic memory</b>				
Global	<b>-0.030</b>	<b>0.012</b>	<b>-2.552</b>	<b>0.005</b>
ATR	-0.016	0.015	-1.087	0.139
CB	-0.027	0.018	-1.517	0.065
PHC	0.006	0.012	0.492	0.812
CST	0.007	0.016	0.468	0.820
Fma	0.001	0.016	0.085	0.967
Fmi	-0.003	0.017	-0.204	0.420
IFOF	0.020	0.026	0.798	0.713
ILF	-0.007	0.016	-0.442	0.329
SLF	-0.006	0.019	-0.332	0.370
<b>Processing speed</b>				
Global	<b>-0.023</b>	<b>0.009</b>	<b>-2.490</b>	<b>0.006</b>
ATR	-0.028	0.012	-2.407	0.008
CB	0.004	0.014	0.271	0.894
PHC	0.002	0.010	0.170	0.933
CST	0.007	0.013	0.538	0.796
Fma	-0.010	0.013	-0.819	0.207
Fmi	-0.002	0.014	-0.146	0.442
IFOF	-0.035	0.021	-1.678	0.047
ILF	-0.004	0.013	-0.328	0.372
SLF	0.027	0.015	1.814	0.535

Each row summarizes the results from a separate linear mixed model. All models control for age, sex, education, motion in the scanner, amyloid status, and their interactions with time. In tract-specific analyses, the modified measure of global RD does not include the specific tract under investigation. Abbreviations: RD = radial diffusivity; ATR = anterior thalamic radiation; CB = cingulum bundle; PHC = parahippocampal cingulum; CST = corticospinal tract; IFOF = inferior frontal occipital fasciculus; ILF = inferior longitudinal fasciculus; Fma = forceps major; Fmi = forceps minor; SLF = superior longitudinal fasciculus. Bolded values are significant at  $p < 0.017$  for global effects and  $p < 0.006$  for tract-specific effects.

Table 3. Summary of linear mixed models examining global and tract-specific AxD on cognitive change (controlling for modified global AxD)

Region	Estimate	Std Error	<i>t</i> -value	<i>p</i> value
<b>Executive function</b>				
Global	0.027	0.008	3.413	0.500
ATR	-0.003	0.009	-0.269	0.394
CB	0.009	0.009	1.032	0.652
PHC	0.012	0.008	1.652	0.550
CST	0.010	0.008	1.191	0.617
Fma	0.011	0.008	1.363	0.587
Fmi	0.001	0.009	0.173	0.932
IFOF	-0.004	0.013	-0.352	0.363
ILF	-0.001	0.009	-0.160	0.437
SLF	0.030	0.009	3.320	0.500
<b>Episodic memory</b>				
Global	0.005	0.011	0.398	0.845
ATR	-0.021	0.014	-1.542	0.062
CB	0.015	0.013	1.153	0.625
PHC	0.020	0.011	1.778	0.538
CST	0.008	0.012	0.651	0.758
Fma	0.016	0.011	1.421	0.578
Fmi	0.019	0.013	1.468	0.571
IFOF	-0.015	0.019	-0.813	0.208
ILF	-0.018	0.013	-1.371	0.086
SLF	0.008	0.013	0.647	0.759
<b>Processing speed</b>				
Global	-0.006	0.009	-0.664	0.253
ATR	<b>-0.030</b>	<b>0.011</b>	<b>-2.650</b>	<b>0.004</b>
CB	0.017	0.011	1.603	0.555
PHC	0.009	0.009	1.041	0.649
CST	-0.009	0.010	-0.943	0.173
Fma	0.016	0.009	1.696	0.545
Fmi	0.007	0.010	0.669	0.752
IFOF	0.000	0.015	0.010	0.996
ILF	-0.002	0.011	-0.215	0.415
SLF	0.006	0.010	0.557	0.789

Each row summarizes the results from a separate linear mixed model. All models control for age, sex, education, motion in the scanner, amyloid status, and their interactions with time. In tract-specific analyses, the modified measure of global AxD does not include the specific tract under investigation. Abbreviations: AxD = axial diffusivity; ATR = anterior thalamic radiation; CB = cingulum bundle; PHC = parahippocampal cingulum; CST = corticospinal tract; IFOF = inferior frontal occipital fasciculus; ILF = inferior longitudinal fasciculus; Fma = forceps major; Fmi = forceps minor; SLF = superior longitudinal fasciculus. Bolded values are significant at  $p < 0.017$  for global effects and  $p < 0.006$  for tract-specific effects.



Table 4. Summary of linear regression models examining global FA and tract-specific FA on baseline cognition (controlling for modified global FA)

Region	Estimate	Std Error	<i>t</i> -value	<i>p</i> value
<b>Executive function</b>				
Global	<b>0.116</b>	<b>0.048</b>	<b>2.414</b>	<b>0.008</b>
ATR	-0.038	0.062	-0.621	0.768
CB	-0.082	0.068	-1.214	0.613
PHC	0.015	0.053	0.286	0.388
CST	0.020	0.061	0.337	0.369
Fma	-0.040	0.061	-0.654	0.757
Fmi	0.143	0.070	2.061	0.020
IFOF	-0.093	0.091	-1.026	0.652
ILF	0.083	0.069	1.210	0.114
SLF	0.011	0.082	0.130	0.448
<b>Episodic memory</b>				
Global	-0.041	0.048	-0.849	0.698
ATR	-0.031	0.063	-0.498	0.810
CB	0.097	0.068	1.413	0.080
PHC	-0.007	0.054	-0.131	0.948
CST	-0.073	0.061	-1.194	0.617
Fma	-0.066	0.062	-1.066	0.644
Fmi	0.113	0.070	1.620	0.054
IFOF	0.055	0.091	0.602	0.274
ILF	-0.005	0.070	-0.067	0.973
SLF	-0.080	0.082	-0.970	0.667
<b>Processing speed</b>				
Global	<b>0.128</b>	<b>0.055</b>	<b>2.351</b>	<b>0.010</b>
ATR	-0.131	0.070	-1.858	0.532
CB	0.120	0.077	1.561	0.060
PHC	0.024	0.061	0.402	0.344
CST	-0.064	0.069	-0.933	0.676
Fma	0.040	0.070	0.572	0.284
Fmi	0.125	0.079	1.582	0.058
IFOF	-0.105	0.103	-1.015	0.656
ILF	0.188	0.078	2.417	0.008
SLF	0.029	0.092	0.317	0.376

Each row summarizes the results from a separate linear regression model. All models control for age, sex, education, motion in the scanner, and amyloid status. In tract-specific analyses, the modified measure of global FA does not include the specific tract under investigation. Abbreviations: FA = fractional anisotropy; ATR = anterior thalamic radiation; CB = cingulum bundle; PHC = parahippocampal cingulum; CST = corticospinal tract; IFOF = inferior frontal occipital fasciculus; ILF = inferior longitudinal fasciculus; Fma = forceps major; Fmi = forceps minor; SLF = superior longitudinal fasciculus. Bolded values are significant at  $p < 0.017$  for global effects and  $p < 0.006$  for tract-specific effects.

Table 5. Summary of linear regression models examining global and tract-specific MD on baseline cognition (controlling for modified global MD)

Region	Estimate	Std Error	<i>t</i> -value	<i>p</i> value
<b>Executive function</b>				
Global	<b>-0.135</b>	<b>0.048</b>	<b>-2.811</b>	<b>0.003</b>
ATR	-0.010	0.062	-0.157	0.438
CB	0.019	0.073	0.259	0.898
PHC	0.018	0.050	0.365	0.858
CST	0.028	0.066	0.423	0.837
Fma	0.039	0.061	0.639	0.762
Fmi	-0.125	0.067	-1.866	0.032
IFOF	0.083	0.112	0.741	0.730
ILF	-0.110	0.066	-1.682	0.047
SLF	-0.040	0.075	-0.534	0.297
<b>Episodic memory</b>				
Global	0.017	0.049	0.354	0.862
ATR	0.025	0.062	0.401	0.845
CB	-0.035	0.074	-0.481	0.312
PHC	0.037	0.050	0.738	0.731
CST	0.085	0.067	1.273	0.601
Fma	-0.011	0.062	-0.172	0.432
Fmi	-0.150	0.067	-2.235	0.013
IFOF	-0.028	0.113	-0.248	0.402
ILF	-0.021	0.067	-0.309	0.379
SLF	0.068	0.075	0.897	0.686
<b>Processing speed</b>				
Global	<b>-0.125</b>	<b>0.055</b>	<b>-2.280</b>	<b>0.012</b>
ATR	0.099	0.070	1.417	0.579
CB	0.098	0.083	1.180	0.620
PHC	0.044	0.056	0.785	0.717
CST	0.065	0.075	0.870	0.692
Fma	-0.066	0.070	-0.944	0.173
Fmi	-0.149	0.077	-1.945	0.027
IFOF	0.162	0.127	1.280	0.601
ILF	-0.126	0.075	-1.689	0.046
SLF	-0.067	0.085	-0.784	0.217

Each row summarizes the results from a separate linear regression model. All models control for age, sex, education, motion in the scanner, and amyloid status at baseline. In tract-specific analyses, the modified measure of global MD does not include the specific tract under investigation. Abbreviations: MD = mean diffusivity; ATR = anterior thalamic radiation; CB = cingulum bundle; PHC = parahippocampal cingulum; CST = corticospinal tract; IFOF = inferior frontal occipital fasciculus; ILF = inferior longitudinal fasciculus; Fma = forceps major; Fmi = forceps minor; SLF = superior longitudinal fasciculus. Bolded values are significant at  $p < 0.017$  for global effects and  $p < 0.006$  for tract-specific effects.

Table 6. Summary of linear regression models examining global and tract-specific RD on baseline cognition (controlling for modified global RD)

Region	Estimate	Std Error	<i>t</i> -value	<i>p</i> value
<b>Executive function</b>				
Global	<b>-0.130</b>	<b>0.048</b>	<b>-2.704</b>	<b>0.004</b>
ATR	0.002	0.063	0.033	0.987
CB	0.063	0.075	0.850	0.698
PHC	-0.009	0.052	-0.174	0.431
CST	0.016	0.066	0.245	0.903
Fma	0.052	0.065	0.807	0.710
Fmi	-0.159	0.071	-2.222	0.014
IFOF	0.103	0.110	0.942	0.674
ILF	-0.108	0.070	-1.558	0.061
SLF	-0.015	0.080	-0.190	0.425
<b>Episodic memory</b>				
Global	0.029	0.049	0.603	0.774
ATR	0.035	0.064	0.549	0.792
CB	-0.078	0.076	-1.029	0.152
PHC	0.017	0.053	0.326	0.872
CST	0.093	0.067	1.397	0.582
Fma	0.044	0.065	0.667	0.753
Fmi	-0.167	0.072	-2.320	0.011
IFOF	-0.065	0.111	-0.582	0.281
ILF	-0.021	0.071	-0.293	0.385
SLF	0.097	0.813	1.192	0.617
<b>Processing speed</b>				
Global	<b>-0.136</b>	<b>0.055</b>	<b>-2.479</b>	<b>0.007</b>
ATR	0.117	0.072	1.637	0.552
CB	-0.060	0.085	-0.702	0.242
PHC	0.014	0.059	0.230	0.909
CST	0.081	0.075	1.080	0.641
Fma	-0.059	0.074	-0.806	0.211
Fmi	-0.164	0.081	-2.011	0.023
IFOF	0.175	0.124	1.408	0.580
ILF	-0.160	0.079	-2.023	0.022
SLF	-0.064	0.092	-0.704	0.241

Each row summarizes the results from a separate linear regression model. All models control for age, sex, education, motion in the scanner, and amyloid status. In tract-specific analyses, the modified measure of global RD does not include the specific tract under investigation. Abbreviations: RD = radial diffusivity; ATR = anterior thalamic radiation; CB = cingulum bundle; PHC = parahippocampal cingulum; CST = corticospinal tract; IFOF = inferior frontal occipital fasciculus; ILF = inferior longitudinal fasciculus; Fma = forceps major; Fmi = forceps minor; SLF = superior longitudinal fasciculus. Bolded values are significant at  $p < 0.017$  for global effects and  $p < 0.006$  for tract-specific effects.

Table 7. Summary of linear regression models examining global and tract-specific AxD on baseline cognition (controlling for modified global AxD)

Region	Estimate	Std Error	<i>t</i> -value	<i>p</i> value
<b>Executive function</b>				
Global	<b>-0.116</b>	<b>0.047</b>	<b>-2.464</b>	<b>0.007</b>
ATR	-0.032	0.059	-0.536	0.296
CB	-0.019	0.052	-0.354	0.362
PHC	0.050	0.047	1.072	0.643
CST	0.009	0.050	0.175	0.931
Fma	0.009	0.049	0.186	0.927
Fmi	-0.047	0.055	-0.867	0.194
IFOF	-0.029	0.079	-0.362	0.359
ILF	-0.097	0.055	-1.750	0.041
SLF	-0.049	0.054	-0.904	0.184
<b>Episodic memory</b>				
Global	-0.011	0.048	-0.225	0.411
ATR	0.006	0.060	0.108	0.957
CB	0.021	0.053	0.404	0.843
PHC	0.054	0.048	1.132	0.629
CST	0.018	0.051	0.362	0.859
Fma	-0.055	0.049	-1.119	0.132
Fmi	-0.083	0.055	-1.520	0.065
IFOF	0.030	0.080	0.381	0.852
ILF	-0.011	0.056	-0.194	0.423
SLF	0.008	0.055	0.145	0.943
<b>Processing speed</b>				
Global	-0.071	0.054	-1.322	0.094
ATR	0.051	0.676	0.756	0.725
CB	0.167	0.059	2.845	0.502
PHC	0.073	0.054	1.353	0.589
CST	0.001	0.057	0.022	0.991
Fma	-0.019	0.056	-0.342	0.367
Fmi	-0.088	0.063	-1.409	0.080
IFOF	0.028	0.091	0.308	0.880
ILF	-0.067	0.062	-1.059	0.146
SLF	-0.040	0.062	-0.653	0.257

Each row summarizes the results from a separate linear regression model. All models control for age, sex, education, motion in the scanner, and amyloid status. In tract-specific analyses, the modified measure of global AxD does not include the specific tract under investigation. Abbreviations: AxD = axial diffusivity; ATR = anterior thalamic radiation; CB = cingulum bundle; PHC = parahippocampal cingulum; CST = corticospinal tract; IFOF = inferior frontal occipital fasciculus; ILF = inferior longitudinal fasciculus; Fma = forceps major; Fmi = forceps minor; SLF = superior longitudinal fasciculus. Bolded values are significant at  $p < 0.017$  for global effects and  $p < 0.006$  for tract-specific effects.

Table 8. Summary of linear mixed models examining each modified measure of global FA on cognitive change

	Estimate	Std Error	<i>t</i> -value	<i>p</i> value
<b>Executive function</b>				
All tracts except ATR	0.000	0.008	-0.054	0.979
All tracts except CB	0.000	0.008	-0.045	0.982
All tracts except PHC	0.000	0.008	0.090	0.464
All tracts except CST	0.000	0.008	0.061	0.476
All tracts except Fma	0.000	0.008	0.004	0.499
All tracts except Fmi	0.000	0.008	-0.041	0.984
All tracts except IFOF	0.000	0.008	-0.031	0.988
All tracts except ILF	0.002	0.008	0.209	0.417
All tracts except SLF	0.001	0.008	0.181	0.428
<b>Episodic memory</b>				
All tracts except ATR	<b>0.032</b>	<b>0.011</b>	<b>2.805</b>	<b>0.003</b>
All tracts except CB	<b>0.032</b>	<b>0.011</b>	<b>2.810</b>	<b>0.003</b>
All tracts except PHC	<b>0.033</b>	<b>0.011</b>	<b>2.912</b>	<b>0.002</b>
All tracts except CST	<b>0.033</b>	<b>0.011</b>	<b>2.918</b>	<b>0.002</b>
All tracts except Fma	<b>0.032</b>	<b>0.011</b>	<b>2.849</b>	<b>0.003</b>
All tracts except Fmi	<b>0.030</b>	<b>0.011</b>	<b>2.696</b>	<b>0.004</b>
All tracts except IFOF	<b>0.033</b>	<b>0.011</b>	<b>2.937</b>	<b>0.002</b>
All tracts except ILF	<b>0.033</b>	<b>0.011</b>	<b>2.908</b>	<b>0.002</b>
All tracts except SLF	<b>0.033</b>	<b>0.012</b>	<b>2.650</b>	<b>0.004</b>
<b>Processing speed</b>				
All tracts except ATR	<b>0.021</b>	<b>0.009</b>	<b>2.266</b>	<b>0.012</b>
All tracts except CB	<b>0.022</b>	<b>0.009</b>	<b>2.429</b>	<b>0.008</b>
All tracts except PHC	<b>0.023</b>	<b>0.009</b>	<b>2.480</b>	<b>0.007</b>
All tracts except CST	<b>0.023</b>	<b>0.009</b>	<b>2.554</b>	<b>0.006</b>
All tracts except Fma	<b>0.022</b>	<b>0.009</b>	<b>2.366</b>	<b>0.009</b>
All tracts except Fmi	<b>0.021</b>	<b>0.009</b>	<b>2.343</b>	<b>0.010</b>
All tracts except IFOF	<b>0.021</b>	<b>0.009</b>	<b>2.240</b>	<b>0.013</b>
All tracts except ILF	<b>0.022</b>	<b>0.009</b>	<b>2.424</b>	<b>0.008</b>
All tracts except SLF	<b>0.026</b>	<b>0.009</b>	<b>2.845</b>	<b>0.003</b>

Each row summarizes the results from a separate linear mixed model that examines the contribution of each modified measure of global FA to longitudinal cognitive change. All models control for age, sex, education, motion in the scanner, amyloid status, and their interactions with time. Abbreviations: FA = fractional anisotropy; ATR = anterior thalamic radiation; CB = cingulum bundle; PHC = parahippocampal cingulum; CST = corticospinal tract; IFOF = inferior frontal occipital fasciculus; ILF = inferior longitudinal fasciculus; Fma = forceps major; Fmi = forceps minor; SLF = superior longitudinal fasciculus. Bolded values are significant at  $p < 0.017$ .

Table 9. Summary of linear mixed models examining tract-specific FA on cognitive change (not controlling for modified global FA)

	Estimate	Std Error	<i>t</i> -value	<i>p</i> value
<b>Executive function</b>				
ATR	0.005	0.007	0.689	0.246
CB	0.014	0.008	1.659	0.049
PHC	-0.005	0.008	-0.636	0.762
CST	-0.001	0.008	-0.159	0.937
Fma	0.003	0.008	0.384	0.351
Fmi	0.003	0.008	0.360	0.360
IFOF	0.003	0.008	0.424	0.336
ILF	-0.010	0.008	-1.286	0.599
SLF	-0.003	0.008	-0.367	0.858
<b>Episodic memory</b>				
ATR	0.025	0.011	2.324	0.010
CB	<b>0.036</b>	<b>0.012</b>	<b>3.056</b>	<b>0.001</b>
PHC	0.008	0.011	0.688	0.246
CST	0.017	0.011	1.535	0.063
Fma	0.025	0.012	2.073	0.020
Fmi	<b>0.033</b>	<b>0.011</b>	<b>2.901</b>	<b>0.002</b>
IFOF	0.024	0.011	2.161	0.016
ILF	0.020	0.011	1.835	0.034
SLF	<b>0.029</b>	<b>0.011</b>	<b>2.661</b>	<b>0.004</b>
<b>Processing speed</b>				
ATR	<b>0.025</b>	<b>0.009</b>	<b>2.876</b>	<b>0.002</b>
CB	0.019	0.010	2.028	0.022
PHC	0.005	0.009	0.565	0.286
CST	0.008	0.009	0.932	0.176
Fma	0.023	0.010	2.419	0.008
Fmi	0.022	0.009	2.313	0.011
IFOF	<b>0.027</b>	<b>0.009</b>	<b>3.026</b>	<b>0.001</b>
ILF	0.017	0.009	1.969	0.025
SLF	0.009	0.009	1.005	0.158

Each row summarizes the results from a separate linear mixed model that examines the contribution of each tract to longitudinal cognitive change, not controlling for global FA. All models control for age, sex, education, motion in the scanner, amyloid status, and their interactions with time. Abbreviations: FA = fractional anisotropy; ATR = anterior thalamic radiation; CB = cingulum bundle; PHC = parahippocampal cingulum; CST = corticospinal tract; IFOF = inferior frontal occipital fasciculus; ILF = inferior longitudinal fasciculus; Fma = forceps major; Fmi = forceps minor; SLF = superior longitudinal fasciculus. Bolded values are significant at  $p < 0.006$  for tract-specific effects.