Supplementary Material: Longitudinal progression of grey matter atrophy in non-amnestic Alzheimer's disease

February 13, 2019

Patient selection details

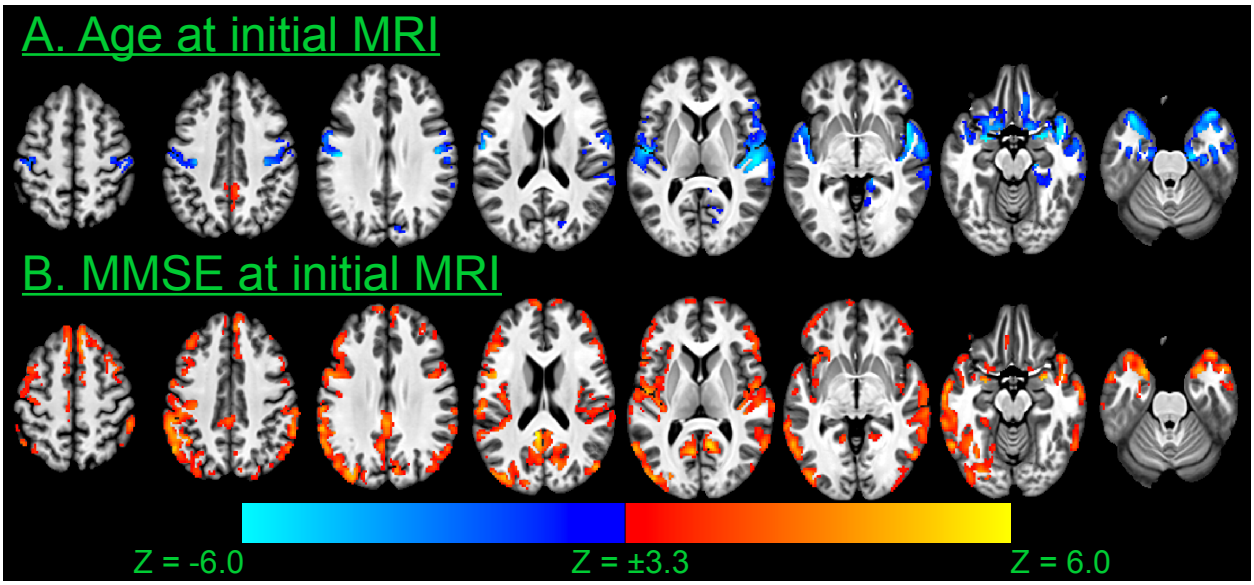
Frontal-variant AD is clinically similar to behavioral-variant frontotemporal dementia (bvFTD) due to underlying frontotemporal lobar degeneration (Mendez *et al.*, 2013), making clinical inference regarding the underlying pathology difficult. In contrast, logopenic-variant primary progressive aphasia and posterior cortical atrophy are associated with AD pathology in up to 70% of cases (Crutch *et al.*, 2017; Giannini *et al.*, 2017). While cerebrospinal fluid (CSF) biomarkers increase the certainty of inferences about pathology (Shaw *et al.*, 2009), they are not infallible, since patients may have co-occurring AD and FTLD pathology. To minimize the odds of including patients with FTLD pathology, we performed additional biomarker screening on the fvAD sample. Clinical diagnosis of fvAD used the bvFTD diagnostic criteria of Rascovsky et al. (2011); individual patients' symptoms supporting the fvAD diagnosis are shown in Supplementary Table 2. Two fvAD patients (P06 and P11) went to autopsy and were confirmed as having primary AD pathology with no co-morbid pathology. Three additional patients (P03, P09, and P10) had ^{18}F-florbetaben amyloid PET scans; all were visually read as positive by a neuroradiologist expert in molecular PET imaging (Dr. Ilya Nasrallah). Patients P02, P09, and P10 all had ^{18}F-flortaucipir PET scans acquired and processed according to methods described in Phillips et al. (2018). Research continues on establishing diagnostic protocols for multi-site flortaucipir data; however, Schwarz et al. (2016) determined regional SUVR thresholds ranging from 1.22 to 1.36 in lateral and ventral temporal cortex to distinguish AD patients from controls; and Ossenkoppele et al. determined an SUVR threshold of 1.27 in medial-basal and lateral temporal cortex for differentiating AD from other neurodegenerative conditions. We calculated an average SUVR for each of our fvAD patients across bilateral parahippocampal, fusiform, and inferior temporal gyri; those means were 1.6 for P02, 2.2 for P09, and 2.3 for P10. Mean cortical SUVRs were 1.33 for P02, 1.91 for P09, and 1.88 for P10. Finally, ten of 12 cases had positive CSF amyloid values (<192 pg/mL) (Shaw *et al.*, 2009), while the remaining two had borderline values (P01 and P07, 197 and 209 pg/mL, respectively). While these borderline values fall within a normal range of variability observed on the Luminex platform (based on pathologically-confirmed AD without secondary neuropathologies from Penn's Integrative Neurodegenerative Disease Database), we performed additional screening to decide the inclusion of the 2 patients. Specifically, we applied a logistic regression classification model published by (Toledo *et al.*, 2012) for discrimination of neuropathological AD vs. FTLD based on Luminex Aβ_{42} and phosphorylated-tau values. This model, which achieved 95.8% accuracy in differentiating FTLD and AD patients, classified all 12 fvAD cases as likely AD; we thus decided to retain all cases in the current analysis.

Supplementary Table 1. Overview of patient selection procedure. Numbers indicate unique individuals at each step from a query of the Integrative Neurodegenerative Disease Database (INDD) at the University of Pennsylvania. FTDC: Penn Frontotemporal Degeneration Center; PMC: Penn Memory Center; CSF: cerebrospinal fluid. Numbers in parentheses indicate the source of evidence for underlying AD pathology.

Criterion	N
Has MRI data	6485
PMC or FTDC participant	6128
Scanned on HUP6	1897
Has autopsy or CSF data	955
Autopsy or CSF data indicates underlying AD pathology	360 (79 autopsy, 281 CSF)
No co-morbid pathologies or exclusionary conditions	302 (22 autopsy, 280 CSF)
PET data (if available) consistent with AD	301 (22 autopsy, 279 CSF)
Has longitudinal MRI at intervals between 0.5 and 3.5 years	142 (10 autopsy, 132 CSF)
Clinical phenotype of interest	90 (8 autopsy, 82 CSF)
Passed MRI QC	74 (7 autopsy, 67 CSF)

Supplementary Table 2. Clinical diagnostic features of the frontal-variant AD group, following the criteria of Rascovsky et al. (2011) for behavioral-variant frontotemporal dementia. Patients were required to meet 3 of 5 criteria to fulfill a behavioral/dysexecutive phenotype. Ones indicate presence of a symptom; zeros indicate its absence.

	P01	P02	P03	P04	P05	P06	P07	P08	P09	P10	P11	P12	Frequency
Age of onset, sex	73 y, F	60 y, M	53 y, F	54 y, M	66 y, M	52 y, M	56 y, F	71 y, M	63 y, F	73 y, M	66 y, M	53 y, F	
Aβ 42 (pg/ml)	197	97	149	166	169.5	81	209	160	159	107	65	104	
Phosphorylated tau (pg/ml)	53	18	28	25	23.5	27	19	59	66	26	24	7	
Total tau/Aβ 42 ratio	1.24	0.34	0.91	0.68	0.528	1.37	0.455	0.41	0.96	0.56	1.431	0.39	
A. Early behavioral disinhibition – 1 must be present	1	1	1	1	1	1	1	1	1	1	1	0	11
Socially inappropriate behavior	1	0	1	1	1	0	1	1	1	1	1	0	9
Loss of manners or decorum	1	1	0	0	1	0	1	1	1	0	0	0	6
Impulsive, rash, or careless actions	1	1	0	0	1	1	0	1	1	1	1	0	8
B. Early apathy or inertia – 1 must be present	1	1	1	1	1	1	1	0	1	1	1	1	11
Apathy - loss of interest, drive, or motivation	0	0	0	0	1	1	1	0	1	1	1	1	7
Inertia - decreased initiation of behavior	1	1	1	1	1	1	1	0	1	1	1	1	11
C. Early loss of sympathy or empathy – 1 must be present	1	1	1	1	1	1	1	1	1	1	0	1	11
Diminished response to others' needs or feelings	1	1	1	1	1	1	1	1	1	0	0	0	9
Diminished social interest, interrelatedness, or warmth	0	0	0	1	1	0	1	1	1	1	0	1	7
D. Early perseverative, stereotyped, or compulsive/ritualistic behavior – 1 must be present	1	0	1	1	1	1	1	1	1	0	1	1	10
Simple repetitive movements	0	0	0	0	0	0	0	0	0	0	0	0	0
Complex, compulsive, or ritualistic behavior	1	0	1	1	1	1	1	1	1	0	1	1	10
Stereotypy of speech - noncommunicative repetition	0	0	0	0	0	0	0	0	0	0	0	0	0
E. Hyperorality and dietary changes – 1 must be present	1	0	0	0	1	0	1	0	0	1	0	1	5
Altered food preferences	1	0	0	0	1	0	1	0	0	1	0	1	5
Binge eating, increased alcohol or cigarettes	0	0	0	0	0	0	1	0	0	0	0	0	1
Oral exploration or consumption of inedible objects	0	0	0	0	0	0	0	0	0	0	0	0	0
F. Exec/generation deficits with relative sparing of memory and visuospatial fn – all must be present	0	1	0	1	1	0	1	0	1	0	0	1	6
Executive task deficits - flexibility, generation, planning, etc.	1	1	1	1	1	1	1	1	1	1	1	1	12
Relative sparing of episodic memory compared to exec	0	1	1	1	1	1	1	1	0	0	0	1	8
Relative sparing of visuospatial skills compared to exec	1	1	0	1	1	0	1	0	0	1	0	1	7



Supplementary Figure 1. Voxelwise associations of cortical thickness with age and MMSE score at initial MRI. Image overlays are t-statistic maps from linear mixed effects models, thresholded at voxelwise $p<0.001$ with a minimum cluster volume of 600 µl, corresponding to a corrected cluster-wise threshold of $p<0.05$. Warm colors indicate that cortical thickness over time is positively associated with each variable; cool colors indicate inverse associations.

Voxelwise analysis of cortical thinning

Neuropsychological performance at time of initial MRI

Longitudinal neuropsychological performance

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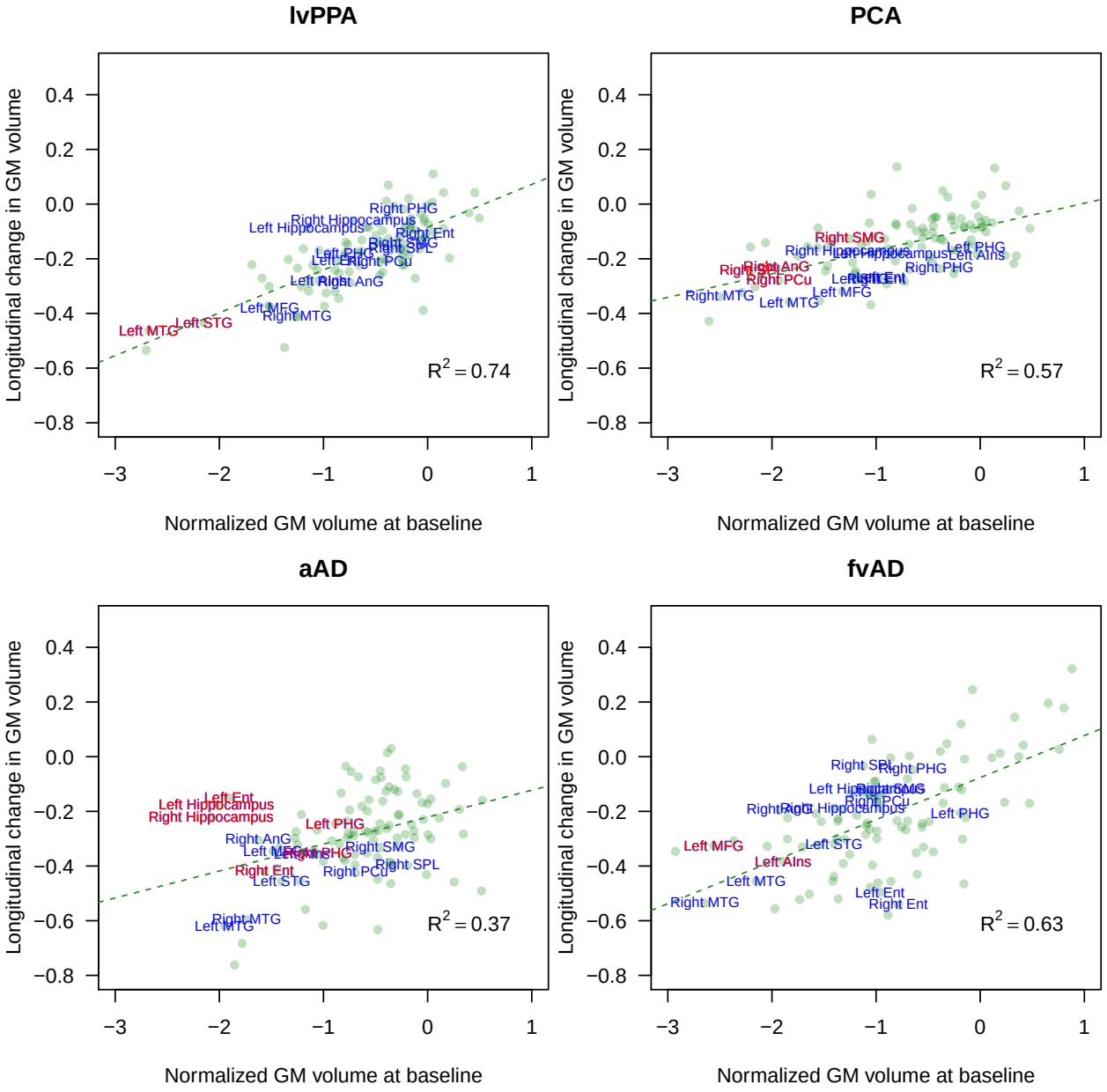
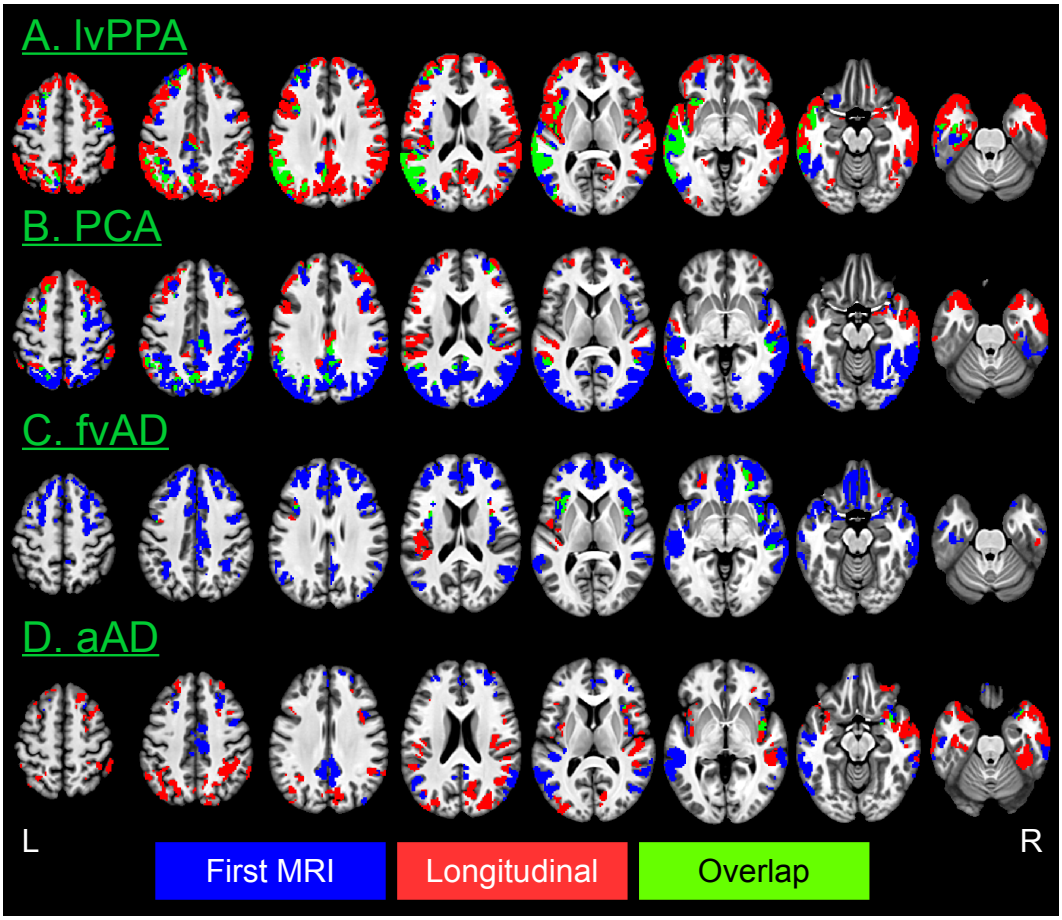
Supplementary Table 3. Post-hoc contrasts of longitudinal change in medial temporal lobe regions after combining lvPPA, PCA, and fvAD patients into a single non-amnestic AD (naAD) group.

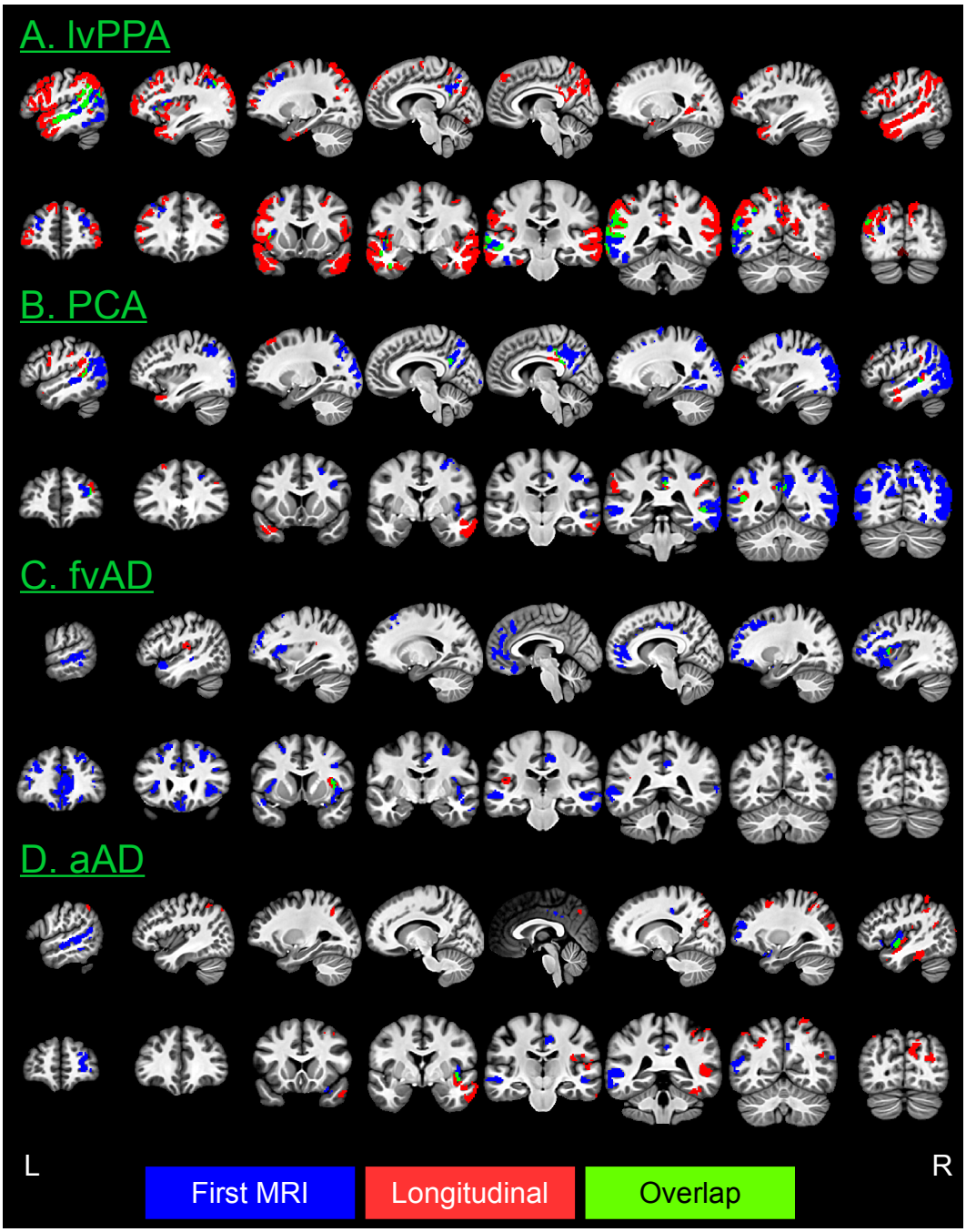
Region	Comp	Z	P
Right Hippocampus	**aAD-Control**	**-3.52**	**0.001**
	naAD-Control	**-3.27**	**0.002**
	naAD-aAD	1.21	0.275
Left Hippocampus	**aAD-Control**	**-4.10**	**0.000**
	naAD-Control	**-3.28**	**0.002**
	naAD-aAD	1.81	0.095
Right Ent entorhinal area	**aAD-Control**	**-4.10**	**0.000**
	naAD-Control	**-4.30**	**0.000**
	naAD-aAD	1.04	0.336
Left Ent entorhinal area	**aAD-Control**	**-2.16**	**0.045**
	naAD-Control	**-4.75**	**0.000**
	naAD-aAD	-1.31	0.238
Right PHG parahippocampal gyrus	**aAD-Control**	**-3.62**	**0.001**
	naAD-Control	**-3.52**	**0.001**
	naAD-aAD	1.13	0.306
Left PHG parahippocampal gyrus	**aAD-Control**	**-3.51**	**0.001**
	naAD-Control	**-4.33**	**0.000**
	naAD-aAD	0.40	0.701



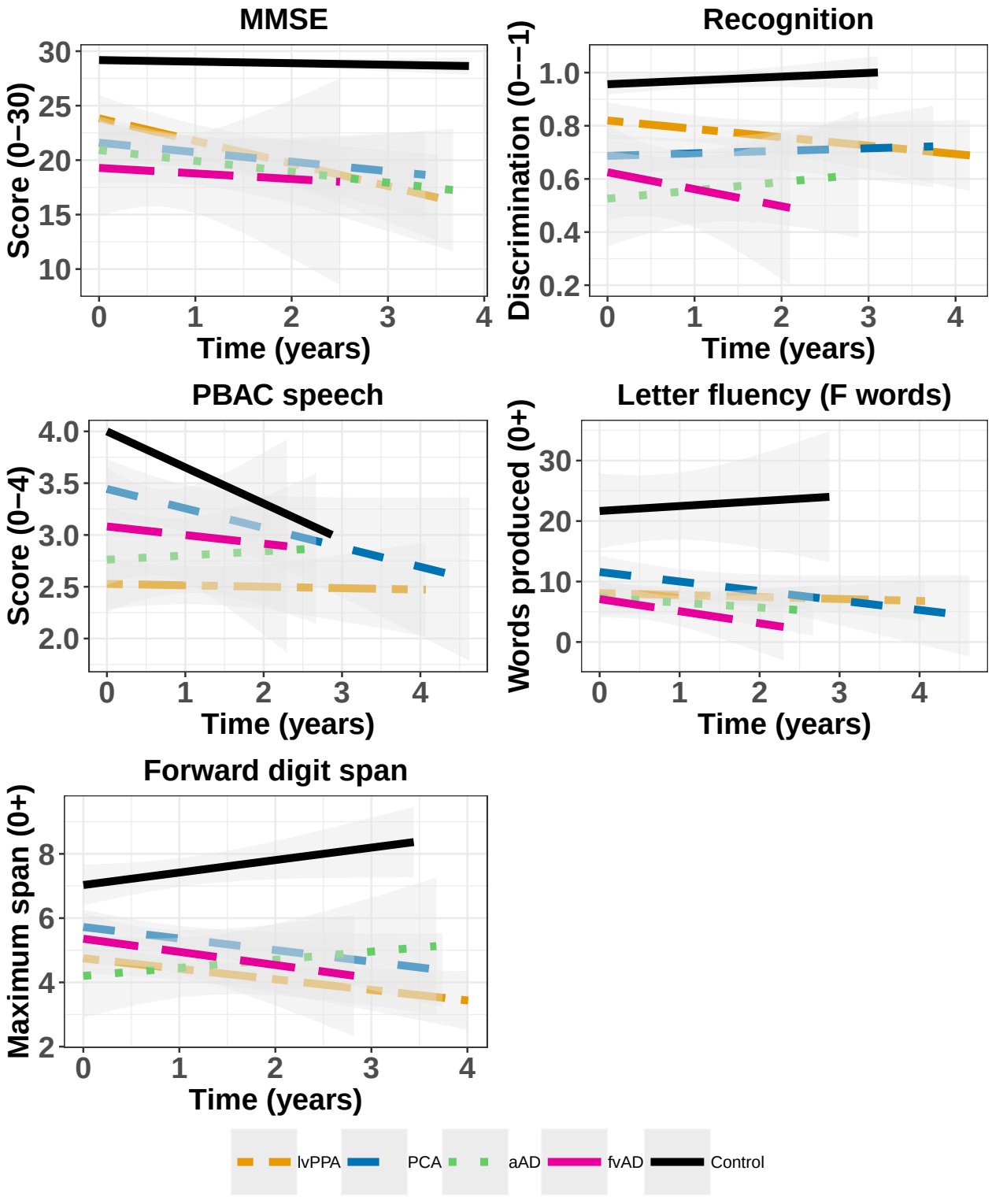
Supplementary Figure 2. Average baseline atrophy vs. annualized change over time for each phenotype in a priori regions of interest. X- and y-axes are plotted in z-score units relative to cognitively normal controls; points represent observed atrophy values, unadjusted for age, sex, and global cognition.



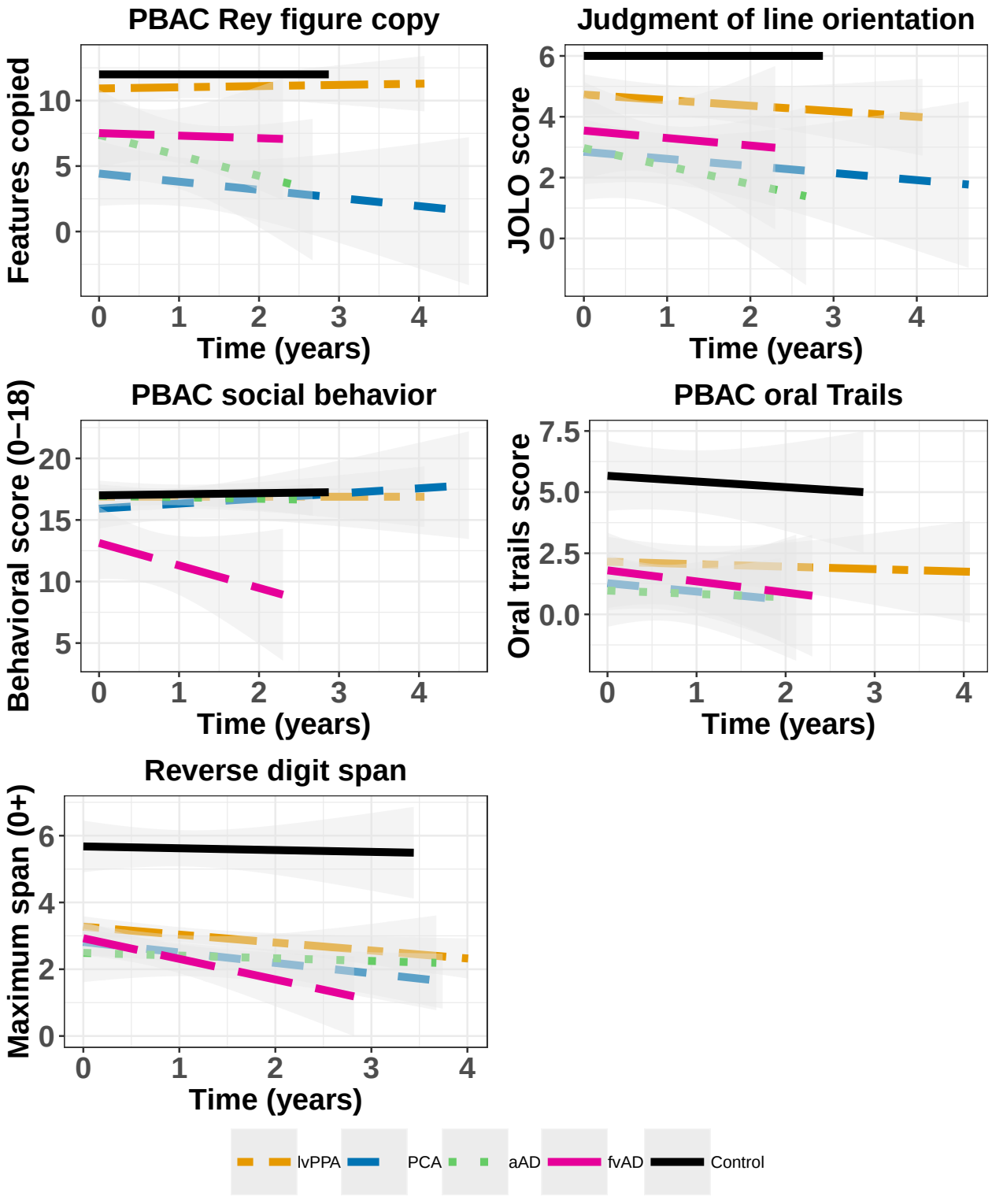
Supplementary Figure 3. Voxelwise differences in cortical thickness relative to matched controls at a threshold of $p<0.01$, uncorrected for multiple comparisons. Image overlays are binarized t-statistic maps for simple contrasts of controls minus each patient group. Blue: simple effect of group (patients<controls) from cross-sectional analysis of participants' initial MRI scans; red: group x time interaction from longitudinal LME models, indicating where patients have more rapid cortical thinning than controls; green: overlap between group and group x time effects. All results are displayed with a minimum cluster volume of 600 µl.



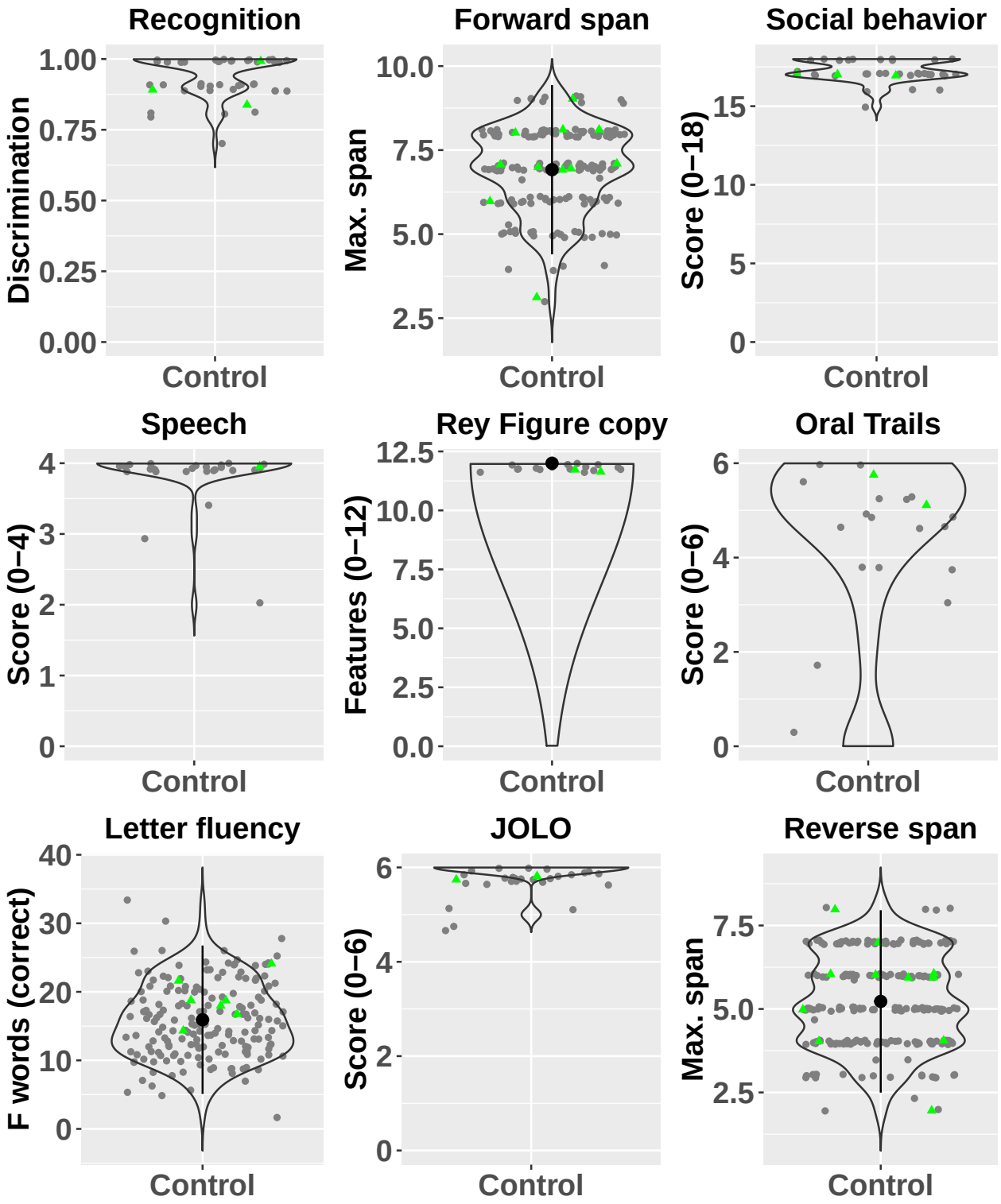
Supplementary Figure 4. Sagittal and coronal views of voxelwise differences in cortical thickness relative to matched controls at a cluster-wise corrected significance threshold of $p<0.05$. Results are the same as those depicted axially in Figure 3. Blue: simple effect of group (patients<controls) from cross-sectional analysis of participants' initial MRI scans; red: group x time interaction from longitudinal LME models, indicating where patients have more rapid cortical thinning than controls; green: overlap between group and group x time effects. All results are displayed with a minimum cluster volume of 600 µl.



Supplementary Figure 5a. Longitudinal change in neuropsychological performance. The x-axis indicates time (in years) from the first available assessment.



Supplementary Figure 5b. Longitudinal change in neuropsychological performance (continued). The x-axis indicates time (in years) from the first available assessment.



Supplementary Figure 6. Neuropsychological performance for cognitively normal seniors in the Integrative Neurodegenerative Disease Database (INDD). Green triangles represent observations for control participants in the current study that were available within 1 year of their first MRI scan. The mean of each distribution is represented by a large black dot, and the vertical lines represent 1 SD above and below the mean.

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Supplementary Table 4. Peak effects of initial cortical thinning for each patient group relative to controls. Reported values are t-statistics for the peak voxel (local minimum) within each anatomically-defined region at a cluster-wise significance threshold of $p<0.05$, as well as the volume of statistically significant voxels in microliters. Brain regions are anatomically defined using joint label fusion of the Mindboggle parcellation.

Region	aAD: T_{init}	aAD: Vol_{init}	lvPPA: T_{init}	lvPPA: Vol_{init}	PCA: T_{init}	PCA: Vol_{init}	fvAD: T_{init}	fvAD: Vol_{init}
Right ACgG anterior cingulate gyrus	—	—	—	—	—	—	-5.3	1974
Left ACgG anterior cingulate gyrus	—	—	—	—	—	—	-6.7	2120
Right AIns anterior insula	-4.6	582	—	—	-4.4	179	-5.1	2563
Left AIns anterior insula	—	—	-4.2	360	—	—	-5.6	1242
Right AOrG anterior orbital gyrus	-4.7	110	—	—	-3.7	12	-6.2	677
Left AOrG anterior orbital gyrus	—	—	—	—	—	—	-3.7	39
Right AnG angular gyrus	-4.4	512	—	—	-6.5	6275	-4.7	770
Left AnG angular gyrus	-4.4	281	-6.9	2960	-7.2	4146	—	—
Right Calc calcarine cortex	—	—	—	—	-5.0	198	—	—
Left Calc calcarine cortex	—	—	—	—	-3.9	27	—	—
Right CO central operculum	-4.2	36	—	—	-4.3	176	-4.7	419
Left CO central operculum	—	—	-4.0	111	—	—	—	—
Right Cun cuneus	—	—	—	—	-5.3	302	—	—
Left Cun cuneus	—	—	—	—	-4.0	68	—	—
Right Ent entorhinal area	-4.1	54	—	—	—	—	-3.8	69
Left Ent entorhinal area	—	—	—	—	—	—	—	—
Right FO frontal operculum	-4.0	8	—	—	—	—	-5.0	634
Left FO frontal operculum	—	—	-4.2	329	—	—	-5.6	428
Right FRP frontal pole	—	—	—	—	—	—	-3.8	11
Left FRP frontal pole	—	—	—	—	—	—	—	—
Right FuG fusiform gyrus	—	—	—	—	-5.9	1398	—	—
Left FuG fusiform gyrus	—	—	-5.6	1126	—	—	—	—
Right GRe gyrus rectus	—	—	—	—	—	—	-5.5	720
Left GRe gyrus rectus	—	—	—	—	—	—	-4.9	801
Right IOG inferior occipital gyrus	—	—	—	—	-6.5	4652	—	—
Left IOG inferior occipital gyrus	—	—	-6.5	876	-5.0	1663	—	—
Right ITG inferior temporal gyrus	—	—	—	—	-6.2	2873	-4.4	53
Left ITG inferior temporal gyrus	-4.4	88	-6.1	2262	-5.4	329	-3.6	11
Right LiG lingual gyrus	—	—	—	—	-5.9	990	—	—
Right LOrG lateral orbital gyrus	-3.4	2	—	—	—	—	-4.5	110
Left LOrG lateral orbital gyrus	—	—	—	—	—	—	-4.0	9
Right MCgG middle cingulate gyrus	-5.7	590	—	—	-5.9	422	-5.9	1345
Left MCgG middle cingulate gyrus	-3.6	27	—	—	—	—	-3.9	16
Right MFC medial frontal cortex	—	—	—	—	—	—	-5.5	1403
Left MFC medial frontal cortex	—	—	—	—	—	—	-5.2	783
Right MFG middle frontal gyrus	-5.4	782	-4.8	402	-5.8	2537	-6.2	4185
Left MFG middle frontal gyrus	—	—	-5.0	1450	—	—	-4.7	2944
Right MOG middle occipital gyrus	—	—	—	—	-7.7	4837	—	—
Left MOG middle occipital gyrus	—	—	-6.5	1574	-7.2	4396	—	—
Right MOrG medial orbital gyrus	—	—	—	—	—	—	-4.5	293
Left MOrG medial orbital gyrus	—	—	—	—	—	—	-4.1	336
Right MPoG postcentral gyrus medial segment	—	—	—	—	—	—	—	—
Right MPrG precentral gyrus medial segment	-5.5	217	—	—	-5.7	378	-5.4	166
Right MSFG superior frontal gyrus medial segment	—	—	—	—	—	—	-5.2	1814
Left MSFG superior frontal gyrus medial segment	—	—	—	—	—	—	-6.2	2116
Right MTG middle temporal gyrus	-4.6	398	—	—	-7.3	7282	-5.4	3014
Left MTG middle temporal gyrus	-6.3	3638	-9.3	7806	-6.7	3739	-5.6	2397
Right OCP occipital pole	—	—	—	—	-5.3	448	—	—
Left OCP occipital pole	—	—	—	—	-5.4	552	—	—
Right OFuG occipital fusiform gyrus	—	—	—	—	-5.9	545	—	—
Left OFuG occipital fusiform gyrus	—	—	-4.5	39	-3.5	3	—	—
Right OpIFG opercular part of the inferior frontal gyrus	—	—	—	—	-5.2	264	-4.8	384
Left OpIFG opercular part of the inferior frontal gyrus	—	—	—	—	—	—	—	—
Right OrIFG orbital part of the inferior frontal gyrus	-4.2	116	—	—	—	—	-4.6	292
Left OrIFG orbital part of the inferior frontal gyrus	—	—	-4.0	97	—	—	-4.3	105
Right PCgG posterior cingulate gyrus	-4.3	405	—	—	-6.5	1628	-4.7	514
Left PCgG posterior cingulate gyrus	-3.8	58	-4.6	379	-4.5	379	—	—
Right PCu precuneus	-4.3	400	—	—	-6.2	4664	-4.1	68
Left PCu precuneus	—	—	-4.6	1044	-4.8	2751	—	—
Right PHG parahippocampal gyrus	—	—	—	—	—	—	—	—
Left PHG parahippocampal gyrus	—	—	—	—	—	—	—	—
Right PIns posterior insula	-4.5	383	—	—	-4.3	245	-4.7	503
Left PIns posterior insula	—	—	-4.7	75	—	—	—	—
Right PO parietal operculum	—	—	—	—	—	—	—	—
Left PO parietal operculum	—	—	-5.3	404	-3.9	7	—	—
Right PoG postcentral gyrus	—	—	—	—	-5.0	649	—	—
Left PoG postcentral gyrus	—	—	—	—	—	—	—	—
Right POrG posterior orbital gyrus	-5.0	126	—	—	—	—	-4.7	664
Left POrG posterior orbital gyrus	—	—	—	—	—	—	-3.4	8
Right PP planum polare	-4.2	42	—	—	-4.2	81	-4.7	211
Left PP planum polare	—	—	-4.0	80	—	—	-4.4	55
Right PrG precentral gyrus	—	—	—	—	-5.9	1497	-5.0	174
Left PrG precentral gyrus	—	—	—	—	—	—	—	—
Right PT planum temporale	—	—	—	—	—	—	—	—
Left PT planum temporale	—	—	-5.4	1062	—	—	—	—
Right SCA subcallosal area	—	—	—	—	—	—	-4.2	88
Left SCA subcallosal area	—	—	—	—	—	—	-4.2	90
Right SFG superior frontal gyrus	-5.4	591	-4.9	502	-5.7	1609	-6.2	3794
Left SFG superior frontal gyrus	—	—	-5.0	852	—	—	-5.2	1891
Right SMC supplementary motor cortex	-4.7	18	—	—	-4.9	21	-5.0	411
Left SMC supplementary motor cortex	—	—	—	—	—	—	-4.1	107
Right SMG supramarginal gyrus	-4.1	123	—	—	-5.8	2305	—	—
Left SMG supramarginal gyrus	-4.1	59	-6.7	1631	-5.0	741	—	—
Right SOG superior occipital gyrus	—	—	—	—	-7.5	2371	—	—
Left SOG superior occipital gyrus	—	—	-5.1	328	-6.6	1660	—	—
Right SPL superior parietal lobule	—	—	—	—	-6.9	3857	—	—
Left SPL superior parietal lobule	—	—	-4.8	366	-6.6	3222	—	—
Right STG superior temporal gyrus	-4.7	507	—	—	-6.0	2672	-5.5	929
Left STG superior temporal gyrus	-6.6	2355	-9.3	4816	-6.5	1608	-5.7	1611
Right TMP temporal pole	-4.3	109	—	—	—	—	-3.7	65
Left TMP temporal pole	—	—	—	—	—	—	-5.0	601
Right TrIFG triangular part of the inferior frontal gyrus	—	—	—	—	—	—	-4.5	211
Left TrIFG triangular part of the inferior frontal gyrus	—	—	—	—	—	—	-4.2	84
Right TTG transverse temporal gyrus	—	—	—	—	—	—	—	—
Left TTG transverse temporal gyrus	—	—	-5.3	126	—	—	—	—

Supplementary Table 5. Peak effects for contrasts of longitudinal change over time for each patient group relative to controls. Reported values are t-statistics for the peak voxel (local maximum) within each anatomically-defined region at a cluster-wise significance threshold of $p<0.05$, as well as the volume of statistically significant voxels in microliters. Brain regions are anatomically defined using joint label fusion of the Mindboggle parcellation.

Region	aAD: T_{long}	aAD: Vol_{long}	lvPPA: T_{long}	lvPPA: Vol_{long}	PCA: T_{long}	PCA: Vol_{long}	fvAD: T_{long}	fvAD: Vol_{long}
Right ACgG anterior cingulate gyrus	—	—	—	—	—	—	—	—
Left ACgG anterior cingulate gyrus	—	—	—	—	—	—	—	—
Right AIns anterior insula	4.4	239	3.6	45	—	—	4.8	317
Left AIns anterior insula	—	—	4.8	1901	—	—	—	—
Right AOrG anterior orbital gyrus	—	—	—	—	—	—	—	—
Left AOrG anterior orbital gyrus	—	—	4.4	147	—	—	—	—
Right AnG angular gyrus	5.1	706	6.3	2552	—	—	—	—
Left AnG angular gyrus	5.6	372	5.9	6894	3.8	30	—	—
Right Calc calcarine cortex	—	—	4.0	29	—	—	—	—
Left Calc calcarine cortex	—	—	—	—	—	—	—	—
Right CO central operculum	5.1	419	4.9	755	—	—	4.1	89
Left CO central operculum	—	—	5.0	1289	4.2	102	5.0	317
Right Cun cuneus	5.2	438	5.1	1024	—	—	—	—
Left Cun cuneus	—	—	4.0	134	—	—	—	—
Right Ent entorhinal area	—	—	4.3	516	—	—	—	—
Left Ent entorhinal area	—	—	5.4	396	3.7	49	—	—
Right FO frontal operculum	—	—	3.9	93	—	—	4.4	145
Left FO frontal operculum	—	—	6.2	1186	—	—	—	—
Right FRP frontal pole	—	—	—	—	—	—	—	—
Left FRP frontal pole	—	—	4.3	243	—	—	—	—
Right FuG fusiform gyrus	4.8	1151	4.5	299	—	—	—	—
Left FuG fusiform gyrus	—	—	5.4	607	—	—	—	—
Right GRe gyrus rectus	—	—	—	—	—	—	—	—
Left GRe gyrus rectus	—	—	—	—	—	—	—	—
Right IOG inferior occipital gyrus	—	—	—	—	—	—	—	—
Left IOG inferior occipital gyrus	—	—	4.0	126	—	—	—	—
Right ITG inferior temporal gyrus	5.2	369	6.6	1851	6.2	776	—	—
Left ITG inferior temporal gyrus	—	—	5.5	1398	—	—	—	—
Right LiG lingual gyrus	—	—	5.2	164	—	—	—	—
Right LOrG lateral orbital gyrus	—	—	5.0	640	—	—	—	—
Left LOrG lateral orbital gyrus	—	—	4.7	531	—	—	—	—
Right MCgG middle cingulate gyrus	—	—	3.4	16	4.8	296	—	—
Left MCgG middle cingulate gyrus	—	—	—	—	3.6	12	—	—
Right MFC medial frontal cortex	—	—	—	—	—	—	—	—
Left MFC medial frontal cortex	—	—	—	—	—	—	—	—
Right MFG middle frontal gyrus	5.2	521	5.3	2550	5.0	1159	—	—
Left MFG middle frontal gyrus	—	—	5.8	4787	—	—	—	—
Right MOG middle occipital gyrus	4.6	557	—	—	—	—	—	—
Left MOG middle occipital gyrus	—	—	5.5	3586	—	—	—	—
Right MOrG medial orbital gyrus	—	—	3.3	3	—	—	—	—
Left MOrG medial orbital gyrus	—	—	—	—	—	—	—	—
Right MPoG postcentral gyrus medial segment	—	—	3.7	26	—	—	—	—
Right MPrG precentral gyrus medial segment	—	—	—	—	—	—	—	—
Right MSFG superior frontal gyrus medial segment	—	—	4.1	258	—	—	—	—
Left MSFG superior frontal gyrus medial segment	—	—	4.2	142	—	—	—	—
Right MTG middle temporal gyrus	6.3	3163	7.0	10918	6.2	3346	—	—
Left MTG middle temporal gyrus	—	—	6.0	8247	5.8	312	—	—
Right OCP occipital pole	—	—	—	—	—	—	—	—
Left OCP occipital pole	—	—	—	—	—	—	—	—
Right OFuG occipital fusiform gyrus	—	—	4.5	53	—	—	—	—
Left OFuG occipital fusiform gyrus	—	—	—	—	—	—	—	—
Right OpIFG opercular part of the inferior frontal gyrus	—	—	4.9	1693	—	—	—	—
Left OpIFG opercular part of the inferior frontal gyrus	—	—	6.0	1728	4.0	135	—	—
Right OrIFG orbital part of the inferior frontal gyrus	—	—	4.3	50	—	—	—	—
Left OrIFG orbital part of the inferior frontal gyrus	—	—	4.4	222	—	—	—	—
Right PCgG posterior cingulate gyrus	—	—	5.3	1202	5.0	767	—	—
Left PCgG posterior cingulate gyrus	—	—	4.8	518	5.2	229	—	—
Right PCu precuneus	5.0	991	6.2	4540	3.3	9	—	—
Left PCu precuneus	3.9	36	6.2	2951	5.2	177	—	—
Right PHG parahippocampal gyrus	—	—	3.8	120	—	—	—	—
Left PHG parahippocampal gyrus	—	—	6.0	827	—	—	—	—
Right PIns posterior insula	5.3	1047	5.3	843	—	—	—	—
Left PIns posterior insula	—	—	4.7	1204	—	—	—	—
Right PO parietal operculum	4.0	187	5.5	321	4.4	103	—	—
Left PO parietal operculum	—	—	6.0	941	4.7	734	4.4	175
Right PoG postcentral gyrus	4.6	232	3.3	9	—	—	—	—
Left PoG postcentral gyrus	—	—	4.8	442	4.0	25	—	—
Right POrG posterior orbital gyrus	—	—	3.8	32	—	—	—	—
Left POrG posterior orbital gyrus	—	—	4.4	1	—	—	—	—
Right PP planum polare	4.8	230	5.3	744	3.4	1	—	—
Left PP planum polare	—	—	4.8	744	—	—	—	—
Right PrG precentral gyrus	—	—	4.8	1258	—	—	—	—
Left PrG precentral gyrus	—	—	5.5	1737	4.1	355	—	—
Right PT planum temporale	4.5	414	5.5	1474	4.2	64	—	—
Left PT planum temporale	—	—	5.7	1004	4.5	375	4.0	38
Right SCA subcallosal area	—	—	—	—	—	—	—	—
Left SCA subcallosal area	—	—	—	—	—	—	—	—
Right SFG superior frontal gyrus	4.7	37	4.6	531	—	—	—	—
Left SFG superior frontal gyrus	—	—	5.0	2475	4.9	804	—	—
Right SMC supplementary motor cortex	—	—	—	—	—	—	—	—
Left SMC supplementary motor cortex	—	—	4.0	386	—	—	—	—
Right SMG supramarginal gyrus	5.0	684	5.9	4242	4.6	346	—	—
Left SMG supramarginal gyrus	5.9	409	6.2	7248	5.3	880	—	—
Right SOG superior occipital gyrus	4.6	479	5.3	42	—	—	—	—
Left SOG superior occipital gyrus	—	—	4.1	231	—	—	—	—
Right SPL superior parietal lobule	5.4	1707	6.0	840	—	—	—	—
Left SPL superior parietal lobule	4.5	590	5.1	3549	—	—	—	—
Right STG superior temporal gyrus	5.4	1004	6.8	7056	4.3	506	—	—
Left STG superior temporal gyrus	—	—	5.8	4765	5.9	497	—	—
Right TMP temporal pole	6.2	655	5.8	3869	4.2	22	—	—
Left TMP temporal pole	—	—	5.6	4764	4.5	979	—	—
Right TrIFG triangular part of the inferior frontal gyrus	—	—	4.8	415	—	—	—	—
Left TrIFG triangular part of the inferior frontal gyrus	—	—	5.7	1210	—	—	—	—
Right TTG transverse temporal gyrus	4.6	159	4.6	204	—	—	—	—
Left TTG transverse temporal gyrus	—	—	4.1	111	3.4	7	4.4	295

Supplementary Table 6. Population-average structural connectivity between a priori regions of interest, as assessed by Yeh et al. (2018, NeuroImage). L: left; R: right; Fmid: middle frontal gyrus; TMd: middle temporal gyrus; TSp: superior temporal gyrus; Hipp: hippocampus; SpMar: supramarginal gyrus; Ag: angular gyrus; PreCun: precuneus: PSp: superior parietal lobule.

Association	Region	L_Fmid	L_Insula	L_TMd	L_TSp	L_Hipp	R_Hipp	R_TMd	R_SpMar	R_Ag	R_PreCun	R_PSp
fvAD	L_Fmid	0.00	0.00	0.82	0.45	0.00	0.00	0.00	0.00	0.00	0.00	0.00
fvAD	L_Insula	0.00	0.00	0.66	0.46	0.00	0.00	0.00	0.63	0.00	0.00	0.00
lvPPA	L_TMd	0.82	0.66	0.00	0.55	0.44	0.81	0.77	0.84	0.89	1.06	0.88
lvPPA	L_TSp	0.45	0.46	0.55	0.00	0.38	0.84	0.89	0.75	0.95	1.05	0.90
aAD	L_Hipp	0.00	0.00	0.44	0.38	0.00	0.45	0.00	0.69	0.80	0.00	0.71
aAD	R_Hipp	0.00	0.00	0.81	0.84	0.45	0.00	0.51	0.00	0.00	0.00	0.00
PCA	R_TMd	0.00	0.00	0.77	0.89	0.00	0.51	0.00	0.95	0.78	0.00	0.00
PCA	R_SpMar	0.00	0.63	0.84	0.75	0.69	0.00	0.95	0.00	0.00	0.00	0.00
PCA	R_Ag	0.00	0.00	0.89	0.95	0.80	0.00	0.78	0.00	0.00	0.00	0.83
PCA	R_PreCun	0.00	0.00	1.06	1.05	0.00	0.00	0.00	0.00	0.00	0.00	0.00
PCA	R_PSp	0.00	0.00	0.88	0.90	0.71	0.00	0.00	0.00	0.83	0.00	0.00

Supplementary Table 7. Mixed effect model of longitudinal atrophy in right inferior occipital gyrus.

Effect	Coefficient	Std. error	DF	T	P
(Intercept)	-0.15	1.10	150	-0.13	0.89
Groupg1lvPPA	-0.45	0.30	103	-1.47	0.14
Groupg2PCA	-1.83	0.34	103	-5.36	0.00
Groupg3aAD	-0.51	0.36	103	-1.41	0.16
Groupg4fvAD	-0.56	0.42	103	-1.33	0.18
timediff	-0.09	0.04	150	-2.09	0.04
baseMMSETotal	0.06	0.02	103	2.74	0.01
SexMale	0.08	0.21	103	0.39	0.70
baseageatMRI	-0.02	0.02	103	-1.66	0.10
Groupg1lvPPA:timediff	-0.05	0.06	150	-0.78	0.44
Groupg2PCA:timediff	-0.10	0.08	150	-1.38	0.17
Groupg3aAD:timediff	-0.12	0.08	150	-1.61	0.11
Groupg4fvAD:timediff	-0.02	0.12	150	-0.20	0.84

Supplementary Table 8. Post-hoc between-group contrasts of mean and longitudinal atrophy in right inferior occipital gyrus.

Contrast	Estimate	Std. error	Z	P
mean_PCA-lvPPA	-0.42	0.32	-1.32	0.19
mean_aAD-lvPPA	-0.62	0.41	-1.50	0.13
mean_fvAD-lvPPA	-0.53	0.38	-1.40	0.16
mean_Controls-lvPPA	2.21	0.37	5.90	0.00
mean_aAD-PCA	-0.20	0.42	-0.47	0.64
mean_fvAD-PCA	-0.11	0.40	-0.27	0.79
mean_Controls-PCA	2.63	0.40	6.63	0.00
mean_fvAD-aAD	0.09	0.50	0.19	0.85
mean_Controls-aAD	2.83	0.48	5.91	0.00
mean_Controls-fvAD	2.74	0.45	6.14	0.00
time_PCA-lvPPA	-0.03	0.15	-0.22	0.83
time_aAD-lvPPA	0.06	0.18	0.36	0.72
time_fvAD-lvPPA	-0.26	0.23	-1.14	0.25
time_Controls-lvPPA	0.31	0.17	1.79	0.07
time_aAD-PCA	0.10	0.19	0.50	0.62
time_fvAD-PCA	-0.23	0.24	-0.95	0.34
time_Controls-PCA	0.34	0.19	1.79	0.07
time_fvAD-aAD	-0.33	0.26	-1.26	0.21
time_Controls-aAD	0.25	0.21	1.16	0.25
time_Controls-fvAD	0.57	0.26	2.21	0.03

Supplementary Table 9. Mixed effect model of longitudinal atrophy in left inferior occipital gyrus.

Effect	Coefficient	Std. error	DF	T	P
(Intercept)	-2.33	0.94	150	-2.47	0.01
Groupg1lvPPA	-0.72	0.26	103	-2.79	0.01
Groupg2PCA	-1.05	0.29	103	-3.62	0.00
Groupg3aAD	-0.75	0.31	103	-2.44	0.02
Groupg4fvAD	-0.22	0.36	103	-0.61	0.54
timediff	-0.10	0.03	150	-3.03	0.00
baseMMSETotal	0.08	0.02	103	4.11	0.00
SexMale	0.06	0.18	103	0.33	0.74
baseageatMRI	0.00	0.01	103	0.11	0.91
Groupg1lvPPA:timediff	-0.12	0.05	150	-2.47	0.01
Groupg2PCA:timediff	-0.06	0.06	150	-0.94	0.35
Groupg3aAD:timediff	0.01	0.06	150	0.16	0.88
Groupg4fvAD:timediff	0.08	0.10	150	0.87	0.39

Supplementary Table 10. Post-hoc between-group contrasts of mean and longitudinal atrophy in left inferior occipital gyrus.

Contrast	Estimate	Std. error	Z	P
mean_PCA-lvPPA	-0.42	0.32	-1.32	0.19
mean_aAD-lvPPA	-0.62	0.41	-1.50	0.13
mean_fvAD-lvPPA	-0.53	0.38	-1.40	0.16
mean_Controls-lvPPA	2.21	0.37	5.90	0.00
mean_aAD-PCA	-0.20	0.42	-0.47	0.64
mean_fvAD-PCA	-0.11	0.40	-0.27	0.79
mean_Controls-PCA	2.63	0.40	6.63	0.00
mean_fvAD-aAD	0.09	0.50	0.19	0.85
mean_Controls-aAD	2.83	0.48	5.91	0.00
mean_Controls-fvAD	2.74	0.45	6.14	0.00
time_PCA-lvPPA	-0.03	0.15	-0.22	0.83
time_aAD-lvPPA	0.06	0.18	0.36	0.72
time_fvAD-lvPPA	-0.26	0.23	-1.14	0.25
time_Controls-lvPPA	0.31	0.17	1.79	0.07
time_aAD-PCA	0.10	0.19	0.50	0.62
time_fvAD-PCA	-0.23	0.24	-0.95	0.34
time_Controls-PCA	0.34	0.19	1.79	0.07
time_fvAD-aAD	-0.33	0.26	-1.26	0.21
time_Controls-aAD	0.25	0.21	1.16	0.25
time_Controls-fvAD	0.57	0.26	2.21	0.03

Supplementary Table 11. Post-hoc comparisons of between group differences for neuropsychological assessments at time of initial MRI. P-values are given both before and after multiple-comparisons correction using the false discovery rate method.

Measure	Effect	Mann-Whitney U	Estimated difference	Lower bound	Upper bound	P	P_{adj}
Age at initial MRI	Control>lvPPA	534	1.8	-2	4.9	0.31	0.52
	Control>PCA	501	3.6	0.32	7.3	0.028	0.15
	Control>aAD	351	1.5	-4.4	6.2	0.5	0.56
	Control<fvAD	183	-2.7	-7.7	2.6	0.37	0.53
	lvPPA>PCA	301	2	-1.2	5.6	0.25	0.52
	lvPPA<aAD	208	-0.31	-5.1	5	0.92	0.92
	lvPPA<fvAD	98.5	-3.6	-10	0.63	0.098	0.33
	PCA<aAD	146	-1.8	-9.3	3.3	0.47	0.56
	PCA<fvAD	64	-6	-13	-0.95	0.031	0.15
	aAD<fvAD	78	-3.7	-11	3	0.3	0.52
Initial MMSE	**Control>lvPPA**	**809.5**	**4**	**2**	**6**	**4.5e-07**	**1.5e-06**
	Control>PCA	**716.5**	**6**	**4**	**9.2**	**4.6e-09**	**4.6e-08**
	Control>aAD	**611**	**6**	**4.2**	**9**	**2.2e-08**	**1.1e-07**
	Control>fvAD	**428**	**6**	**3.2**	**10**	**1.1e-06**	**2.7e-06**
	lvPPA>PCA	316.5	2	-1	5	0.13	0.21
	lvPPA>aAD	276.5	2	-8.1e-06	5	0.1	0.2
	lvPPA>fvAD	195	2	-1	7	0.15	0.21
	PCA<aAD	167	-3e-05	-3	4	0.94	1
	PCA>fvAD	120	2.9e-05	-4	6	1	1
	aAD>fvAD	103	1.9e-05	-4	5	0.98	1
Recognition	lvPPA>PCA	324	0.1	5.2e-05	0.2	0.039	0.099
	lvPPA>aAD	**200**	**0.3**	**0.1**	**0.43**	**0.0056**	**0.034**
	lvPPA>fvAD	210	0.17	-2e-05	0.3	0.049	0.099
	PCA>aAD	133.5	0.17	-7.9e-06	0.4	0.078	0.12
	PCA>fvAD	123	5.7e-05	-0.1	0.2	0.73	0.73
	aAD<fvAD	40	-0.1	-0.33	0.1	0.19	0.23
PBAC speech	**lvPPA<PCA**	**54.5**	**-1**	**-1**	**-0.5**	**0.0019**	**0.011**
	lvPPA<aAD	81	-2.4e-05	-0.5	0.5	0.84	0.87
	lvPPA<fvAD	64	-0.7	-1.5	1.5e-05	0.081	0.16
	PCA>aAD	104.5	0.5	1.4e-05	1.5	0.025	0.075
	PCA>fvAD	86	4e-05	-0.5	1	0.87	0.87
	aAD<fvAD	35.5	-0.5	-1.5	0.5	0.3	0.44
Letter fluency (F words)	lvPPA<PCA	159	-2	-6	1	0.19	0.54
	lvPPA<aAD	135	-1.3e-05	-4	4	0.8	0.8
	lvPPA>fvAD	153.5	2	-2	5	0.45	0.54
	PCA>aAD	146.5	2	-3	6	0.39	0.54
	PCA>fvAD	159.5	4	-6e-05	8	0.067	0.4
	aAD>fvAD	92.5	2	-3	6	0.44	0.54
Forward digit span	lvPPA<PCA	168	-1	-2	4.8e-05	0.056	0.33
	lvPPA>aAD	118	5.8e-05	-1	2	0.84	0.84
	lvPPA<fvAD	123.5	-5e-06	-1	1	0.38	0.61
	PCA>aAD	113.5	1	-1	3	0.27	0.61
	PCA>fvAD	137	3.9e-05	-1	1	0.51	0.61
	aAD<fvAD	43.5	-1	-3	1	0.47	0.61
Rey figure copy	**lvPPA>PCA**	**192.5**	**9**	**3**	**11**	**0.00073**	**0.0044**
	lvPPA>aAD	122.5	1	-3.2e-05	8	0.045	0.09
	lvPPA>fvAD	**150.5**	**2**	**4.3e-05**	**6**	**0.0063**	**0.019**
	PCA<aAD	37	-3	-10	1	0.23	0.27
	PCA<fvAD	34.5	-4	-9	1	0.096	0.14
	aAD>fvAD	46	5.8e-05	-6	3	0.97	0.97
Judgment of line orientation	**lvPPA>PCA**	**199**	**3**	**1**	**4**	**0.0034**	**0.021**
	lvPPA>aAD	116	1	2.8e-05	4	0.032	0.095
	lvPPA>fvAD	116.5	1	-1.7e-05	3	0.12	0.25
	PCA<aAD	46	-4.9e-05	-3	2	0.68	0.68
	PCA<fvAD	42	-1	-3	1	0.28	0.42
	aAD<fvAD	30.5	-1	-3	2	0.62	0.68
PBAC social behavior	lvPPA>PCA	184	1	-2e-05	2	0.13	0.2
	lvPPA>aAD	88	7.8e-05	-0.5	1	0.51	0.52
	lvPPA>fvAD	**181**	**4**	**1**	**6**	**0.00079**	**0.0047**
	PCA<aAD	50	-3.8e-05	-2	1	0.52	0.52
	PCA>fvAD	**128**	**3**	**1**	**6**	**0.018**	**0.035**
	aAD>fvAD	**78**	**4**	**1**	**7.7**	**0.005**	**0.015**
Oral Trails	lvPPA>PCA	60	2e-05	-1	2	0.46	0.69
	lvPPA>aAD	31.5	0.88	-1	3	0.44	0.69
	lvPPA<fvAD	28.5	-2e-05	-3	2	0.91	0.91
	PCA>aAD	27.5	7.5e-05	-3	3	0.79	0.91
	PCA<fvAD	23	-0.53	-3	1	0.46	0.69
	aAD<fvAD	10	-1	-4	3	0.38	0.69
Reverse digit span	lvPPA>PCA	317	1	-5.3e-05	1	0.043	0.26
	lvPPA>aAD	136.5	5e-05	-2.5e-05	1	0.3	0.6
	lvPPA>fvAD	188.5	6.5e-05	-9.7e-05	1	0.17	0.52
	PCA<aAD	76.5	-8.4e-06	-1	1	0.66	0.86
	PCA<fvAD	105	-3.6e-05	-1	1	0.71	0.86
	aAD>fvAD	55.5	2.7e-05	-1	1	0.94	0.94

Supplementary Table 12. Associations between neuropsychological performance and grey matter volume change in task-specific ROIs. P-values are corrected for multiple comparisons using the false discovery rate method; values<0.05 are considered statistically significant and shown in bold.

Task	Region	T	P
Recognition memory	**L entorhinal**	**t(69)=2.7**	**0.02**
	L hippocampus	**t(69)=4.8**	**0.0003**
	L parahippocampal	t(69)=2.0	0.08
	R entorhinal	t(69)=1.9	0.2
	R hippocampus	**t(69)=3.3**	**0.006**
	R parahippocampal	t(69)=1.3	0.3
Speech	L middle temporal	t(46)=1.0	0.5
	L superior temporal	t(46)=1.2	0.4
Letter fluency	**L middle temporal**	**t(73)=3.7**	**0.003**
	L superior temporal	**t(73)=3.2**	**0.007**
Forward digit span	**L middle temporal**	**t(66)=4.3**	**0.0007**
	L superior temporal	**t(66)=5.1**	**0.0002**
Rey copy	**R angular**	**t(40)=3.5**	**0.005**
	R middle temporal	**t(40)=3.5**	**0.005**
	R precuneus	**t(40)=3.6**	**0.005**
	R superior parietal lobule	t(40)=2.3	0.06
	R supramarginal	**t(40)=3.4**	**0.006**
Judgment of line orientation	R angular	t(37)=1.6	0.2
	R middle temporal	t(37)=2.1	0.07
	R precuneus	**t(37)=2.6**	**0.03**
	R superior parietal lobule	t(37)=2.1	0.07
	R supramarginal	t(37)=2.1	0.08
Social behavior	L anterior insula	t(44)=1.2	0.4
	L middle frontal	t(44)=-0.4	0.8
	R middle temporal	t(44)=0.4	0.8
Oral Trails	L anterior insula	t(18)=-0.3	0.8
	L middle frontal	t(18)=1.0	0.5
	R middle temporal	t(18)=1.0	0.4
Reverse digit span	**L anterior insula**	**t(65)=2.5**	**0.04**
	L middle frontal	**t(65)=2.9**	**0.02**
	R middle temporal	**t(65)=3.0**	**0.02**

Supplementary Table 13. Fixed effects for neuropsychological change models reported in Supplementary Figure 5a.

Task	Effect	Value	Std.Error	DF	t-value	p-value
MMSETotal	(Intercept)	8.53	5.34	122	1.60	0.11
	Group2PCA	-1.31	1.60	86	-0.81	0.42
	Group2aAD	-2.52	1.67	86	-1.51	0.13
	Group2fvAD	-4.38	1.92	86	-2.28	0.03
	Group2Control	4.64	1.60	86	2.91	0.00
	Time	-2.51	0.35	122	-7.12	0.00
	AgeatFirstMRI	0.08	0.08	86	1.03	0.31
	SexMale	1.25	1.10	86	1.14	0.26
	Education	0.63	0.20	86	3.11	0.00
	Group2PCA:Time	0.94	0.57	122	1.65	0.10
	Group2aAD:Time	0.66	0.56	122	1.19	0.24
	Group2fvAD:Time	0.47	0.89	122	0.53	0.60
	Group2Control:Time	2.51	0.53	122	4.73	0.00
Recognition	(Intercept)	1.16	0.26	93	4.52	0.00
	Group2PCA	-0.12	0.06	65	-1.87	0.07
	Group2aAD	-0.32	0.08	65	-3.89	0.00
	Group2fvAD	-0.15	0.08	65	-2.00	0.05
	Group2Control	0.14	0.09	65	1.58	0.12
	Time	-0.03	0.02	93	-1.94	0.06
	AgeatFirstMRI	-0.01	0.00	65	-2.27	0.03
	SexMale	0.03	0.05	65	0.64	0.52
	Education	0.01	0.01	65	1.22	0.23
	Group2PCA:Time	0.02	0.02	93	0.95	0.35
	Group2aAD:Time	0.05	0.03	93	1.74	0.09
	Group2fvAD:Time	-0.07	0.04	93	-1.59	0.11
	Group2Control:Time	0.04	0.04	93	1.00	0.32
Speech	(Intercept)	3.78	1.11	57	3.40	0.00
	Group2PCA	0.76	0.25	49	3.01	0.00
	Group2aAD	0.05	0.32	49	0.15	0.88
	Group2fvAD	0.58	0.28	49	2.09	0.04
	Group2Control	1.48	0.45	49	3.24	0.00
	Time	0.00	0.06	57	0.04	0.97
	AgeatFirstMRI	-0.01	0.02	49	-0.64	0.52
	SexMale	-0.02	0.19	49	-0.09	0.93
	Education	-0.04	0.03	49	-1.13	0.26
	Group2PCA:Time	-0.13	0.09	57	-1.33	0.19
	Group2aAD:Time	0.13	0.11	57	1.22	0.23
	Group2fvAD:Time	-0.05	0.14	57	-0.37	0.71
	Group2Control:Time	-0.34	0.20	57	-1.74	0.09
FLetterFluency	(Intercept)	-10.28	6.87	57	-1.50	0.14
	Group2PCA	3.60	1.56	49	2.30	0.03
	Group2aAD	1.13	1.96	49	0.58	0.57
	Group2fvAD	-1.24	1.72	49	-0.72	0.48
	Group2Control	13.42	2.81	49	4.78	0.00
	Time	-0.91	0.36	57	-2.56	0.01
	AgeatFirstMRI	0.14	0.09	49	1.53	0.13
	SexMale	2.42	1.16	49	2.08	0.04
	Education	0.54	0.22	49	2.51	0.02
	Group2PCA:Time	-0.04	0.56	57	-0.08	0.94
	Group2aAD:Time	-0.04	0.70	57	-0.05	0.96
	Group2fvAD:Time	-1.13	0.87	57	-1.31	0.20
	Group2Control:Time	1.37	1.24	57	1.10	0.27
ForwardSpan	(Intercept)	2.48	1.73	101	1.43	0.16
	Group2PCA	1.07	0.44	69	2.45	0.02
	Group2aAD	-0.06	0.59	69	-0.10	0.92
	Group2fvAD	0.48	0.53	69	0.92	0.36
	Group2Control	2.23	0.52	69	4.27	0.00
	Time	-0.26	0.11	101	-2.30	0.02
	AgeatFirstMRI	0.01	0.03	69	0.51	0.61
	SexMale	0.31	0.32	69	0.98	0.33
	Education	0.08	0.06	69	1.39	0.17
	Group2PCA:Time	-0.08	0.19	101	-0.45	0.65
	Group2aAD:Time	-0.00	0.22	101	-0.00	1.00
	Group2fvAD:Time	-0.06	0.29	101	-0.22	0.83
	Group2Control:Time	0.58	0.22	101	2.62	0.01

Supplementary Table 14. Fixed effects for neuropsychological change models reported in Supplementary Figure 5b.

Task	Effect	Value	Std.Error	DF	t-value	p-value
ReyCopy	(Intercept)	11.83	6.12	53	1.93	0.06
	Group2PCA	-6.45	1.43	47	-4.50	0.00
	Group2aAD	-3.62	1.71	47	-2.12	0.04
	Group2fvAD	-3.98	1.51	47	-2.63	0.01
	Group2Control	1.32	2.44	47	0.54	0.59
	Time	0.02	0.23	53	0.08	0.94
	AgeatFirstMRI	-0.05	0.08	47	-0.57	0.57
	SexMale	2.91	1.07	47	2.72	0.01
	Education	0.05	0.20	47	0.27	0.79
	Group2PCA:Time	-0.98	0.41	53	-2.42	0.02
	Group2aAD:Time	-1.01	0.47	53	-2.18	0.03
	Group2fvAD:Time	-0.81	0.57	53	-1.43	0.16
	Group2Control:Time	-0.11	0.81	53	-0.14	0.89
JOLO	(Intercept)	7.32	3.39	48	2.16	0.04
	Group2PCA	-2.44	0.73	46	-3.35	0.00
	Group2aAD	-2.05	0.90	46	-2.29	0.03
	Group2fvAD	-1.62	0.79	46	-2.05	0.05
	Group2Control	1.41	1.23	46	1.14	0.26
	Time	-0.26	0.14	48	-1.85	0.07
	AgeatFirstMRI	-0.04	0.05	46	-0.78	0.44
	SexMale	1.29	0.53	46	2.42	0.02
	Education	-0.05	0.10	46	-0.55	0.59
	Group2PCA:Time	0.22	0.28	48	0.78	0.44
	Group2aAD:Time	0.17	0.33	48	0.51	0.61
	Group2fvAD:Time	0.26	0.36	48	0.70	0.48
	Group2Control:Time	0.21	0.50	48	0.41	0.68
BehavioralScale	(Intercept)	12.01	4.72	55	2.54	0.01
	Group2PCA	-0.53	1.13	49	-0.47	0.64
	Group2aAD	0.71	1.46	49	0.48	0.63
	Group2fvAD	-3.78	1.26	49	-2.99	0.00
	Group2Control	0.17	2.10	49	0.08	0.93
	Time	0.13	0.36	55	0.35	0.73
	AgeatFirstMRI	0.02	0.06	49	0.34	0.73
	SexMale	0.42	0.78	49	0.54	0.59
	Education	0.20	0.15	49	1.38	0.17
	Group2PCA:Time	0.19	0.61	55	0.30	0.76
	Group2aAD:Time	-0.39	0.76	55	-0.52	0.61
	Group2fvAD:Time	-1.54	0.91	55	-1.69	0.10
	Group2Control:Time	-0.13	1.25	55	-0.10	0.92
OralTrails	(Intercept)	-1.13	2.53	33	-0.44	0.66
	Group2PCA	-0.37	0.71	33	-0.52	0.60
	Group2aAD	-0.47	0.90	33	-0.52	0.60
	Group2fvAD	-0.25	0.81	33	-0.31	0.76
	Group2Control	3.76	1.03	33	3.63	0.00
	Time	-0.07	0.29	18	-0.25	0.80
	AgeatFirstMRI	-0.00	0.04	33	-0.03	0.97
	SexMale	0.87	0.47	33	1.83	0.08
	Education	0.17	0.09	33	2.02	0.05
	Group2PCA:Time	-0.42	0.52	18	-0.80	0.43
	Group2aAD:Time	-0.21	0.69	18	-0.31	0.76
	Group2fvAD:Time	-0.48	0.62	18	-0.77	0.45
	Group2Control:Time	-0.32	0.66	18	-0.49	0.63
ReverseSpan	(Intercept)	1.33	1.23	102	1.08	0.28
	Group2PCA	-0.42	0.32	70	-1.32	0.19
	Group2aAD	-0.62	0.41	70	-1.50	0.14
	Group2fvAD	-0.53	0.38	70	-1.40	0.17
	Group2Control	2.21	0.37	70	5.90	0.00
	Time	-0.26	0.09	102	-2.98	0.00
	AgeatFirstMRI	0.01	0.02	70	0.74	0.46
	SexMale	0.40	0.22	70	1.81	0.08
	Education	0.06	0.04	70	1.50	0.14
	Group2PCA:Time	-0.03	0.15	102	-0.22	0.83
	Group2aAD:Time	0.06	0.18	102	0.36	0.72
	Group2fvAD:Time	-0.26	0.23	102	-1.14	0.26
	Group2Control:Time	0.31	0.17	102	1.79	0.08

Supplementary Table 15. Post-hoc comparisons of longitudinal global cognition, as assessed by the MMSE. Group mean: cross-sectional differences in average group performance, independent of time. Group x time: differences in rate of longitudinal cognitive change. P-values are FDR-corrected, with a significance threshold of $p<0.05$.

Effect	Comparison	Z	P
Group mean	PCA<lvPPA	0.8	0.55
	aAD<lvPPA	1.5	0.22
	fvAD<lvPPA	2.3	0.056
	Controls>lvPPA	**2.9**	**0.012**
	aAD<PCA	0.7	0.62
	fvAD<PCA	1.5	0.22
	Controls>PCA	**3.4**	**0.0028**
	fvAD<aAD	0.9	0.52
	Controls>aAD	**4.1**	**0.00031**
	Controls>fvAD	**4.5**	**5.7e-05**
Group x time	PCA>lvPPA	1.7	0.2
	aAD>lvPPA	1.2	0.36
	fvAD>lvPPA	0.5	0.68
	Controls>lvPPA	**4.7**	**4.5e-05**
	aAD<PCA	0.5	0.69
	fvAD<PCA	0.5	0.68
	Controls>PCA	**2.6**	**0.025**
	fvAD<aAD	0.2	0.84
	Controls>aAD	**3.2**	**0.0063**
	Controls>fvAD	2.2	0.056

Supplementary Table 16. Post-hoc comparisons of longitudinal recognition discrimination. Group mean: cross-sectional differences in average group performance, independent of time. Group x time: differences in rate of longitudinal cognitive change. P-values are FDR-corrected, with a significance threshold of $p<0.05$.

Effect	Comparison	Z	P
Group mean	PCA<lvPPA	1.9	0.12
	aAD<lvPPA	**3.9**	**0.001**
	fvAD<lvPPA	2.0	0.1
	Controls>lvPPA	1.6	0.16
	aAD<PCA	2.4	0.06
	fvAD<PCA	0.4	0.72
	Controls>PCA	**2.8**	**0.028**
	fvAD>aAD	1.7	0.15
	Controls>aAD	**4.3**	**0.00042**
	Controls>fvAD	**2.9**	**0.023**
Group x time	PCA>lvPPA	0.9	0.43
	aAD>lvPPA	1.7	0.15
	fvAD<lvPPA	1.6	0.16
	Controls>lvPPA	1.0	0.42
	aAD>PCA	0.9	0.43
	fvAD<PCA	2.1	0.1
	Controls>PCA	0.4	0.72
	fvAD<aAD	**2.5**	**0.043**
	Controls<aAD	0.4	0.72
	Controls>fvAD	2.0	0.1

Supplementary Table 17. Post-hoc comparisons of longitudinal language performance. Group mean: cross-sectional differences in average group performance, independent of time. Group x time: differences in rate of longitudinal cognitive change. P-values are FDR-corrected, with a significance threshold of $p<0.05$.

Task	Effect	Comparison	Z	P
Speech	Group mean	**PCA>lvPPA**	**3.0**	**0.026**
		aAD>lvPPA	0.2	0.88
		fvAD>lvPPA	2.1	0.1
		Controls>lvPPA	**3.2**	**0.024**
		PCA>aAD	2.3	0.098
		PCA>fvAD	0.6	0.64
		Controls>PCA	1.5	0.25
		fvAD>aAD	1.5	0.25
		Controls>aAD	**2.8**	**0.032**
		Controls>fvAD	1.9	0.16
	Group x time	lvPPA>PCA	1.3	0.31
		aAD>lvPPA	1.2	0.32
		lvPPA>fvAD	0.4	0.75
		lvPPA>Controls	1.7	0.18
		aAD>PCA	2.1	0.1
		fvAD>PCA	0.5	0.68
		PCA>Controls	1.1	0.36
		aAD>fvAD	1.2	0.32
		aAD>Controls	2.3	0.098
		fvAD>Controls	1.3	0.31
FLetterFluency	Group mean	PCA>lvPPA	2.3	0.071
		aAD>lvPPA	0.6	0.66
		lvPPA>fvAD	0.7	0.59
		Controls>lvPPA	**4.8**	**1.7e-05**
		PCA>aAD	1.3	0.39
		PCA>fvAD	**2.7**	**0.032**
		Controls>PCA	**3.4**	**0.0032**
		aAD>fvAD	1.1	0.39
		Controls>aAD	**3.9**	**0.00054**
		Controls>fvAD	**5.0**	**1.4e-05**
	Group x time	lvPPA>PCA	0.1	0.99
		lvPPA>aAD	0.1	0.99
		lvPPA>fvAD	1.3	0.39
		Controls>lvPPA	1.1	0.39
		aAD>PCA	0.0	0.99
		PCA>fvAD	1.2	0.39
		Controls>PCA	1.1	0.39
		aAD>fvAD	1.1	0.39
		Controls>aAD	1.1	0.39
		Controls>fvAD	1.8	0.23
ForwardSpan	Group mean	**PCA>lvPPA**	**2.4**	**0.048**
		lvPPA>aAD	0.1	1
		fvAD>lvPPA	0.9	0.59
		Controls>lvPPA	**4.3**	**0.00039**
		PCA>aAD	1.9	0.12
		PCA>fvAD	1.1	0.53
		Controls>PCA	2.1	0.089
		fvAD>aAD	0.8	0.68
		Controls>aAD	**3.4**	**0.0069**
		Controls>fvAD	**2.8**	**0.03**
	Group x time	lvPPA>PCA	0.4	0.93
		lvPPA>aAD	0.0	1
		lvPPA>fvAD	0.2	1
		Controls>lvPPA	**2.6**	**0.035**
		aAD>PCA	0.3	0.98
		fvAD>PCA	0.1	1
		Controls>PCA	**2.7**	**0.03**
		aAD>fvAD	0.2	1
		Controls>aAD	2.1	0.089
		Controls>fvAD	1.9	0.11

Supplementary Table 18. Post-hoc comparisons of longitudinal visuospatial performance. Group mean: cross-sectional differences in average group performance, independent of time. Group x time: differences in rate of longitudinal cognitive change. P-values are FDR-corrected, with a significance threshold of $p<0.05$.

Task	Effect	Comparison	Z	P
ReyCopy	Group mean	**lvPPA>PCA**	**4.5**	**0.00014**
		lvPPA>aAD	2.1	0.11
		lvPPA>fvAD	2.6	0.056
		Controls>lvPPA	0.5	0.79
		aAD>PCA	1.6	0.23
		fvAD>PCA	1.5	0.28
		Controls>PCA	**3.1**	**0.022**
		aAD>fvAD	0.2	0.94
		Controls>aAD	1.8	0.17
		Controls>fvAD	2.1	0.11
	Group x time	lvPPA>PCA	2.4	0.078
		lvPPA>aAD	2.2	0.11
		lvPPA>fvAD	1.4	0.28
		lvPPA>Controls	0.1	0.94
		PCA>aAD	0.1	0.95
		fvAD>PCA	0.3	0.93
		Controls>PCA	1.0	0.47
		fvAD>aAD	0.3	0.93
		Controls>aAD	1.0	0.47
		Controls>fvAD	0.7	0.65
JOLO	Group mean	**lvPPA>PCA**	**3.4**	**0.016**
		lvPPA>aAD	2.3	0.088
		lvPPA>fvAD	2.0	0.14
		Controls>lvPPA	1.1	0.72
		aAD>PCA	0.4	0.97
		fvAD>PCA	0.9	0.89
		Controls>PCA	**3.0**	**0.029**
		fvAD>aAD	0.4	0.97
		Controls>aAD	2.5	0.088
		Controls>fvAD	2.3	0.088
	Group x time	PCA>lvPPA	0.8	0.96
		aAD>lvPPA	0.5	0.97
		fvAD>lvPPA	0.7	0.96
		Controls>lvPPA	0.4	0.97
		PCA>aAD	0.1	0.99
		fvAD>PCA	0.1	0.99
		PCA>Controls	0.0	0.99
		fvAD>aAD	0.2	0.99
		Controls>aAD	0.1	0.99
		fvAD>Controls	0.1	0.99

Supplementary Table 19. Post-hoc comparisons of longitudinal behavioral and executive function. Group mean: cross-sectional differences in average group performance, independent of time. Group x time: differences in rate of longitudinal cognitive change. P-values are FDR-corrected, with a significance threshold of $p<0.05$.

Task	Effect	Comparison	Z	P
BehavioralScale	Group mean	lvPPA>PCA	0.5	0.93
		aAD>lvPPA	0.5	0.93
		lvPPA>fvAD	3.0	0.055
		Controls>lvPPA	0.1	0.93
		aAD>PCA	0.9	0.88
		PCA>fvAD	2.4	0.1
		Controls>PCA	0.3	0.93
		aAD>fvAD	2.7	0.065
		aAD>Controls	0.2	0.93
		Controls>fvAD	1.8	0.3
	Group x time	PCA>lvPPA	0.3	0.93
		lvPPA>aAD	0.5	0.93
		lvPPA>fvAD	1.7	0.3
		lvPPA>Controls	0.1	0.93
		PCA>aAD	0.7	0.93
		PCA>fvAD	1.8	0.3
		PCA>Controls	0.2	0.93
		aAD>fvAD	1.1	0.8
		Controls>aAD	0.2	0.93
		Controls>fvAD	1.0	0.84
OralTrails	Group mean	lvPPA>PCA	0.5	0.93
		lvPPA>aAD	0.5	0.93
		lvPPA>fvAD	0.3	0.93
		Controls>lvPPA	**3.6**	**0.002**
		PCA>aAD	0.1	0.93
		fvAD>PCA	0.1	0.93
		Controls>PCA	**3.9**	**0.0016**
		fvAD>aAD	0.2	0.93
		Controls>aAD	**3.5**	**0.002**
		Controls>fvAD	**3.6**	**0.002**
	Group x time	lvPPA>PCA	0.8	0.93
		lvPPA>aAD	0.3	0.93
		lvPPA>fvAD	0.8	0.93
		lvPPA>Controls	0.5	0.93
		aAD>PCA	0.3	0.93
		PCA>fvAD	0.1	0.93
		Controls>PCA	0.1	0.93
		aAD>fvAD	0.3	0.93
		aAD>Controls	0.1	0.93
		Controls>fvAD	0.2	0.93
ReverseSpan	Group mean	lvPPA>PCA	1.3	0.37
		lvPPA>aAD	1.5	0.33
		lvPPA>fvAD	1.4	0.36
		Controls>lvPPA	**5.9**	**1.8e-08**
		PCA>aAD	0.5	0.79
		PCA>fvAD	0.3	0.85
		Controls>PCA	**6.6**	**6.9e-10**
		fvAD>aAD	0.2	0.85
		Controls>aAD	**5.9**	**1.8e-08**
		Controls>fvAD	**6.1**	**8.3e-09**
	Group x time	lvPPA>PCA	0.2	0.85
		aAD>lvPPA	0.4	0.84
		lvPPA>fvAD	1.1	0.39
		Controls>lvPPA	1.8	0.21
		aAD>PCA	0.5	0.79
		PCA>fvAD	0.9	0.49
		Controls>PCA	1.8	0.21
		aAD>fvAD	1.3	0.38
		Controls>aAD	1.2	0.39
		Controls>fvAD	2.2	0.11