

Supplementary materials

Subtyping and staging of Alzheimer's disease from routine structural MRI with PHASE-AD
Baumeister et al.

Supplementary methods

Inclusion criteria

The following descriptions provide an overview of the main inclusion criteria for each cohort study. They are not intended to be exhaustive. Readers are referred to the respective online resources and clinical trial registry entries for complete and detailed information.

A4/LEARN

The A4 study (NCT02008357, see <https://clinicaltrials.gov>) was conducted at 68 locations in the US, Canada, Australia, and Japan. It included clinically normal older adults with evidence of brain amyloid pathology. Inclusion criteria required a MMSE score between 25 and 30, a global CDR score of 0, and a Logical Memory II score between 6 and 18 at screening. Participants also had to show evidence of brain amyloid pathology on ¹⁸F-florbetapir PET and have a study partner with at least weekly contact who could provide collateral information (in person, by phone, or electronically). Key exclusion criteria included treatment with acetylcholinesterase inhibitors or memantine at screening or baseline, inadequate venous access, unstable or serious medical conditions, recent serious infectious disease affecting the brain, history of malignancy (except certain treated *in situ* cancers), history of human immunodeficiency virus (HIV), severe drug allergies or hypersensitivity reactions, major psychiatric illness (e.g., major depression or bipolar disorder in the past 2 years), chronic alcohol or drug abuse/dependence in the past 5 years, or serious suicide risk.

The A4 trial was a randomized, double-blind, placebo-controlled trial of with an open-label extension. During the double-blind period (240 weeks), participants were assigned to either intravenous (IV) solanezumab, a monoclonal antibody targeting monomeric amyloid, or placebo every 4 weeks. In the active treatment arm, solanezumab was administered in escalating doses of 400 mg, 800 mg, and then 1600 mg IV every 4 weeks. In the placebo arm, participants received matching placebo infusions on the same schedule. Following completion of the double-blind phase, all participants entered an open-label extension in which they received 1600 mg solanezumab IV every 4 weeks for an additional 204 weeks, resulting in a total treatment duration of approximately 444 weeks. After 240 weeks, the A4 trial did not show a significant slowing of cognitive decline on its primary endpoint in participants receiving solanezumab compared to those receiving placebo.¹

The LEARN study (NCT02488720, see <https://clinicaltrials.gov>) was conducted at 40 U.S. locations and recruited individuals who had consented to the A4 trial and met its demographic, cognitive, and clinical criteria but did not meet the amyloid PET threshold required for randomization into the treatment arms of A4. Additional inclusion criteria required stable use of permitted medications for at least 8 weeks prior to baseline, the availability of a reliable study partner with sufficient contact to provide meaningful functional information, and willingness and ability to comply with study procedures for up to 240 weeks. Participants also needed adequate English or Spanish literacy and sufficient vision and hearing to complete psychometric testing. Exclusion criteria included treatment with acetylcholinesterase inhibitors or memantine at baseline, unstable or serious medical illness, contraindications for MRI, MRI findings of more than four hemosiderin deposits, or amyloid-related imaging abnormalities (ARIA-E), and use of exclusionary medications with significant central nervous system anticholinergic effects. Individuals currently enrolled in other interventional clinical trials or incompatible medical research were also excluded. For participants opting into the lumbar puncture sub-study, current use of anticoagulants such as warfarin or dabigatran was an additional exclusion criterion.

ADNI

Data used in the preparation of this article were obtained from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database (adni.loni.usc.edu). The ADNI was launched in 2003 as a public-private partnership, led by Principal Investigator Michael W. Weiner, MD. The primary goal of ADNI has been to test whether serial magnetic resonance imaging (MRI), positron emission tomography (PET), other biological

markers, and clinical and neuropsychological assessment can be combined to measure the progression of mild cognitive impairment and early Alzheimer's disease (AD).

In addition to ADNI's and our own general inclusion criteria, we included only participants whose MRI scans had been successfully processed with FreeSurfer, as documented by the University of California, San Francisco. This ensured the exclusion of scans more likely to yield low-quality FastSurfer segmentations.

ADNI-1

To be eligible for enrollment in ADNI-1 (NCT00106899, see <https://clinicaltrials.gov>), participants were required to have a Hachinski score ≤ 4 , be between 55 and 90 years of age, have a Geriatric Depression Scale score < 6 , have an available study partner with at least 10 hours contact per week and who is able to accompany study visits, have visual and auditory acuity adequate for neuropsychological testing, be in good health with no diseases precluding enrollment, be willing to complete a three-year imaging study (two years for DAT participants), have six grades education or work history, be fluent in English or Spanish, express commitment to neuroimaging and have no contraindications to MRI, agree to blood collection for APOE genotyping and DNA banking, agree to blood and urine collection for biomarker testing, and not be enrolled in other trials or studies. In addition, Women had to be post-menopausal for at least two years or surgically sterile.

The group-specific inclusion criteria for CU participants included reporting no memory complaints beyond what is common for their age, normal memory performance based on education-adjusted cut-offs on the delayed paragraph recall scores from the Wechsler Memory Scale – Revised (WMS-R), an MMSE score ≥ 24 , a global CDR score of 0 (with a Memory Box score of 0), and no significant impairment in cognition or daily functioning. The MCI group included individuals who reported a memory complaint (or whose study partner reported one, with confirmation by the partner), abnormal memory performance based on education-adjusted cut-offs on the WMS-R delayed recall, an MMSE score ≥ 24 , a CDR score of 0.5 (with a Memory Box score of 0.5), and general cognitive and functional performance insufficient for a diagnosis of DAT by the site physician. The DAT group included individuals who reported a memory complaint (or whose study partner did, with confirmation by the partner), had abnormal memory performance on the WMS-R delayed recall, an MMSE score between 20 and 26, a CDR score of 0.5 or 1.0, and met the NINCDS-ADRDA criteria for probable AD.

ADNI-GO

To be eligible for enrollment in ADNI-GO (NCT01078636, see <https://clinicaltrials.gov>), participants were required to have a Hachinski score ≤ 4 , be between 55 and 90 years of age, have a Geriatric Depression Scale score < 6 , have an available study partner with at least 10 hours contact per week and who is able to accompany study visits, have visual and auditory acuity adequate for neuropsychological testing, be in good health with no diseases precluding enrollment, be willing to participate in a longitudinal imaging study, have six grades education or work history, be fluent in English or Spanish, express commitment to repeated 3T MRI and at least two PET scans, have no contraindications to MRI, agree to blood collection for GWAS, APOE genotyping and DNA banking, agree to blood collection for biomarker testing, agree to at least one lumbar puncture for CSF collection, and not be enrolled in other trials or studies. In addition, women were required to be either sterile or at least two years past childbearing potential. The administration of permitted medications was required to be stable for four weeks.

The aim of ADNI-GO was to newly enroll participants with early MCI, which included individuals who reported a memory complaint (or whose study partner reported one), abnormal memory performance based on education-adjusted cut-offs on the WMS-R delayed recall, an MMSE score ≥ 24 , a global CDR score of 0.5 (with a Memory Box score of 0.5), and general cognitive and functional performance insufficient for a diagnosis of DAT by the site physician.

ADNI-2

In ADNI-2 (NCT01231971, see <https://clinicaltrials.gov>), participants were required to be between 55 and 90 years of age, in good general health, and free of conditions expected to interfere with study participation. They had to have a Geriatric Depression Scale score < 6 , a Hachinski Ischemic Score ≤ 4 , at least six years of education or equivalent work history, and sufficient visual and auditory acuity for neuropsychological testing. Eligible participants needed to be fluent in English or Spanish, not pregnant or of childbearing potential, and willing to participate in a longitudinal imaging study with repeated 3T MRI and PET scans. A reliable study partner with frequent contact (≥ 10 hours per week) and availability for clinic visits was

required. Participants also agreed to provide blood samples for genetic and biomarker testing, as well as at least one lumbar puncture for CSF collection.

Participants in ADNI-2 were stratified into five diagnostic groups: cognitively unimpaired (CU), significant memory concern (SMC), early MCI, late MCI, and mild DAT. CU participants were required to be free of memory complaints, as verified by a study partner. They had to demonstrate normal memory function by scoring above education-adjusted cutoffs on the Logical Memory II subscale of the WMS-R, and achieve an MMSE score ≥ 24 . Global CDR scores had to be 0 with a Memory Box score of 0, and participants could not exhibit significant impairment in cognition or activities of daily living. The SMC group met the same criteria as the CU group, but also required a significant subjective memory concern reported by the participant, study partner, or clinician, confirmed by a Cognitive Change Index score ≥ 16 . Early MCI participants were required to report a subjective memory concern and demonstrate abnormal memory performance within a prespecified intermediate range on the Logical Memory II subscale. They also needed an MMSE score ≥ 24 and a global CDR of 0.5 with a Memory Box score of at least 0.5. General cognition and daily functioning had to be sufficiently preserved to preclude a DAT diagnosis by the site physician. Late MCI participants met the same general requirements as early MCI participants but demonstrated greater memory impairment based on Logical Memory II scores. DAT participants had to meet the NINCDS-ADRDA criteria for probable AD. They were required to have a memory complaint, impaired memory function on the Logical Memory II subscale (same as late MCI), an MMSE score between 20 and 26, and a global CDR of 0.5 or 1.0.

Participants were excluded if they had a significant neurologic disease or structural brain abnormality other than AD that could explain cognitive impairment. Excluded conditions included Parkinson's disease, multi-infarct dementia, Huntington's disease, normal pressure hydrocephalus, brain tumor, progressive supranuclear palsy, seizure disorders, subdural hematoma, multiple sclerosis, or significant head trauma with persistent deficits. For the CU and SMC groups, any such condition was exclusionary; for both MCI groups, suspected incipient Alzheimer's disease was permissible; and for the DAT group, neurologic diseases other than AD were exclusionary. In addition, participants were excluded if screening MRI revealed evidence of infection, infarction, or other focal lesions, including multiple lacunes or lacunes in critical memory structures, or if they had contraindications to MRI (e.g., pacemakers, aneurysm clips, metal implants). Major psychiatric illness was exclusionary, including major depression or bipolar disorder within the past year, schizophrenia, or recent psychotic features, agitation, or behavioral disturbances that could impair compliance. Current treatment for obsessive-compulsive disorder or attention deficit disorder, as well as a history of alcohol or substance abuse within the past two years, were also exclusionary. Additional exclusion criteria included unstable systemic illness, clinically significant abnormalities in vitamin B12 or thyroid function tests, residence in a skilled nursing facility, and current use of certain psychoactive medications, anticoagulants (warfarin or dabigatran, relevant to lumbar puncture), or other exclusionary drugs. Use of investigational agents within one month of enrollment or concurrent participation in other clinical studies involving repeated neuropsychological testing was not permitted. Finally, participants were excluded if prior or ongoing exposure to radioactive agents would exceed regulatory safety limits for PET imaging procedures.

ADNI-3

For inclusion in ADNI-3 (NCT02854033, see <https://clinicaltrials.gov>), participants had to be 55–90 years old, in good general health, and free of conditions likely to interfere with the study. Additional requirements included a Geriatric Depression Scale score < 6 , adequate vision and hearing for neuropsychological testing, and the availability of a study partner with frequent contact (≥ 10 hours per week) who could accompany the participant to all study visits. Women had to be post-menopausal for at least two years or surgically sterile. Participants had to be willing and able to take part in a longitudinal imaging study, including repeated 3T MRI and at least two PET scans, and to undergo at least one lumbar puncture. Finally, they were required to provide blood samples for genomic testing (including APOE genotyping and GWAS), biomarker analyses, and biospecimen banking, with consent to share resulting data and samples.

Participants in ADNI-3 were stratified into three diagnostic groups: cognitively unimpaired (CU), MCI, and mild DAT. CU participants could be participants with or without subjective memory complaints, provided memory performance was within the prespecified normal range on the Logical Memory II subscale. They were required to score ≥ 24 on the MMSE and have a global CDR score of 0 with a Memory Box score of 0. MCI participants were required to report a subjective memory concern, either self-reported or recalled by a study partner or clinician, and demonstrate abnormal memory performance below prespecified cutoffs on the Logical Memory II. They also needed an MMSE score between 24 and 30 and a global CDR of 0.5 with a Memory Box score ≥ 0.5 . General cognition and functional performance had to be sufficiently preserved

so that a diagnosis of dementia could not be made by a site physician. Stable treatment with cholinesterase inhibitors or memantine was permitted if ongoing for ≥ 12 weeks prior to screening. DAT participants were required to report a memory concern (either self-reported or recalled by a partner or clinician), demonstrate abnormal memory performance in the impaired range on the Logical Memory II subscale, and score between 20 and 26 on the MMSE. A global CDR score of 0.5 or 1.0 was required, and participants had to meet NINCDS-ADRDA criteria for probable AD.

Participants were excluded if baseline MRI showed focal lesions, multiple lacunes, or lacunes in critical memory structures, or if they had contraindications to MRI (e.g., pacemakers, metal implants, foreign objects in the body). Major psychiatric illness was exclusionary, including major depression or bipolar disorder within the past year, psychosis, agitation or behavioral problems within the past three months, current treatment for obsessive-compulsive disorder or attention-deficit/hyperactivity disorder, or a history of schizophrenia. Substance abuse or dependence within the past two years also led to exclusion. Additional criteria included unstable systemic illness, clinically significant abnormalities in vitamin B12 or thyroid function tests, or residence in a skilled nursing facility. Participants were excluded if they were taking psychoactive medications (e.g., certain antidepressants, neuroleptics, chronic anxiolytics, sedative hypnotics), anticoagulants (warfarin, dabigatran, rivaroxaban, apixaban), or other exclusionary drugs. Use of investigational agents within one month of entry, or concurrent participation in other studies involving repeated neuropsychological testing, was not permitted. For the CU group, the presence of any significant neurologic disease was exclusionary, including Parkinson's disease, multi-infarct dementia, Huntington's disease, normal pressure hydrocephalus, brain tumor, progressive supranuclear palsy, seizure disorder, subdural hematoma, multiple sclerosis, or a history of significant head trauma with persistent deficits or structural brain abnormalities. For MCI group, the same neurologic conditions were exclusionary, with the exception that suspected incipient AD was permissible. For the DAT group, all significant neurologic conditions other than AD itself were exclusionary.

ARWIBO

Data used in the preparation of this article were obtained from the Alzheimer's Disease Repository Without Borders (ARWIBO) (<https://www.arwibo.it>). The primary aim of ARWIBO is to publish all clinical, neuropsychological, EEG, neuroimaging, and biological data of patients with neurodegenerative diseases and healthy controls collected in over 10 years by a number of researchers of IRCCS Fatebenefratelli, Brescia, Italy.^{2,3} The overall goal of ARWIBO is to contribute, thorough synergy with neuGRID (<https://neugrid2.eu>), to global data sharing and analysis in order to develop effective therapies, prevention methods and a cure for Alzheimer' and other neurodegenerative diseases.

Based on the predefined threshold requiring at least 15 scans per scanner manufacturer within each sample, we excluded scans acquired on 1.5T Philips ($n = 12$) and Siemens ($n = 9$) systems.

DELCODE

The DELCODE study (DRKS00007966, see German Clinical Trial Registry [DRKS]) included two control groups and three patient groups. Clinical screening of the patient groups (subjective cognitive decline [SCD], MCI, and DAT) was performed at the respective memory clinics.

Participants in the SCD group met research criteria for SCD, reported concerns about a subjectively perceived cognitive decline to a physician, and were cognitively unimpaired, defined as scoring better than -1.5 *SD* below German age-, sex-, and education-adjusted norms on the Consortium to Establish a Registry for Alzheimer's Disease (CERAD) test battery. The MCI group met research criteria for amnesic MCI, defined by performance below -1.5 *SD* on the delayed recall trial of the CERAD word-list episodic memory test. The DAT group met research criteria for DAT (ref.⁴) and had Mini-Mental State Examination (MMSE) scores ≥ 18 . One control group included first-degree relatives of AD patients, and the other comprised unrelated controls. Control participants performed better than -1.5 *SD* below German age-, sex-, and education-adjusted CERAD norms and reported no subjective concerns about cognitive decline. For the present study, these two control groups and the SCD group were combined into a single CU group.

Inclusion criteria for all diagnostic groups were age of 60 years or older, fluency in German, the ability to provide informed consent, and the availability of a study partner. Exclusion criteria included conditions that would prevent participation in the study protocol (e.g., significant sensorimotor impairments), current or past psychiatric disorders (such as major depressive disorder or disorders due to psychoactive substance use), neurodegenerative disorders other than AD, vascular dementia, and a history of stroke with persistent clinical symptoms. The use of sedative, anticholinergic, or other anti-dementia medication, as well as

investigational agents for the treatment of cognitive impairment or dementia, up to one month prior to screening and during the study period, led to exclusion in all groups except for the DAT group.

NACC

The NACC Uniform Data Set has captured the enrollment of the Alzheimer's Disease Research Center (ADRC) program since 2005 and includes participants across the full cognitive spectrum found in AD. Enrollment procedures differ by ADRC and may involve clinician referral, self-referral by participants or family members, or active community recruitment. Many ADRCs also enroll CU volunteers. In some ADRCs, agreement to brain autopsy is required for participation, which may introduce additional selection biases. Written informed consent is obtained from all participants and co-participants prior to enrollment.

Three NACC-3T participants were excluded due to impossible (e.g., negative) intracranial volume estimates generated by FastSurfer. Based on the predefined threshold requiring at least 15 scans per scanner manufacturer within each sample, we excluded scans acquired on 1.5T Philips ($n = 8$) and Siemens ($n = 12$) systems.

Biomarkers of A β burden in each cohort

In A4/LEARN, A β burden was assessed using ^{18}F -Florbetapir PET. Global neocortical standardized uptake value ratios (SUVRs) were calculated with a cerebellar reference. SUVRs ≥ 1.10 indicated A β positivity. In ADNI, A β status was determined using the biomarker measure closest to the MRI scan. CSF-based classification relied on the p-tau₁₈₁/A β ₄₂ ratio (cut-off at ≥ 0.025).⁵ PET data were obtained using the ^{18}F -Florbetapir or ^{18}F -Florbetaben radiotracers, applying established cohort-specific cut-offs for global cortical SUVRs with a cerebellar reference (≥ 1.11 and ≥ 1.08 , respectively). In DELCODE-3T, A β status was primarily derived from CSF A β ₄₂/A β ₄₀ ratios (≤ 0.08).⁶ For participants lacking CSF data, a previously described probabilistic model of CSF-based A β positivity that relies on demographic, genetic, and plasma biomarker information was applied.⁷ In NACC, A β status was determined from A β PET, using four different radiotracers and cohort-specific cut-offs for global cortical SUVRs with a cerebellar reference (≥ 1.12 for ^{18}F -Florbetaben, ≥ 1.17 for ^{18}F -Florbetapir, ≥ 1.14 for ^{18}F -NAV4694, ≥ 1.14 for ^{11}C -Pittsburgh Compound B).

Neuropsychological data availability and processing

Only neuropsychological measures with at least 75% baseline availability within a given sample were considered, leading to the exclusion of TMT B–A scores from ARWIBO-1.5T (available in 16.6% of participants). In addition, A4/LEARN-3T lacked TMT B–A and FAQ data, and ARWIBO-1.5T lacked Logical Memory Delayed Recall and FAQ data. In A4/LEARN-3T, 18 Logical Memory Delayed Recall scores closest to MRI acquisition (1.46%) were obtained using a version other than “A.” These were excluded from cross-sectional analyses to ensure comparability, while longitudinal analyses controlled for version effects. The availability of cross-sectional neuropsychological test scores is summarized in Supplementary Figure 1.

Visual inspection of the neuropsychological test score distributions revealed pronounced deviations from normality for MMSE, FAQ, and TMT B–A scores across samples. Consequently, these scores were pre-normalized within each sample using latent process modeling implemented in the *lcmm* R package (ref.⁸), following published recommendations.⁹ Supplementary Figure 2 shows the distributions of raw and pre-normalized scores. MMSE, Logical Memory Delayed Recall, and TMT B–A scores were z-standardized within each sample using the mean and standard deviations (*SDs*) from baseline CU group distributions. Expectedly, FAQ scores showed insufficient variability within CU groups to permit meaningful scaling and were therefore z-standardized to the whole samples.

Markers standardization

MTL volumes were corrected for total intracranial volume following the regression-based approach as described by Voevodskaya *et al.*¹⁰ To compute *w*-scores, we first evaluated four OLS regression specifications for each marker:

1. age + sex + vendor + field strength (fs)
2. natural spline of age ($df = 2$) + sex + vendor + fs
3. age + sex + vendor $\times$ fs
4. natural spline of age ($df = 2$) + sex + vendor $\times$ fs

For each marker, we fitted the models using all available CU participants and selected the lowest AIC model to derive a fixed formula structure that was applied in all modelling iterations.

Outlier removal

All raw MRI measures were screened for numerical outliers. Prior to standardization, observations with total intracranial volume outside $\pm 5 SD$ from the mean, stratified by sample, scanner manufacturer, and participant sex, were excluded, resulting in the following thresholds:

Sample	Manufacturer	Sex	Mean	SD	Lower cut-off	Upper cut-off
A4/LEARN-3T	GE	female	1486357.75	111929.91	926708.20	2046007.30
		male	1330770.88	124571.12	707915.28	1953626.48
	Philips	female	1609235.98	138052.11	918975.43	2299496.54
		male	1418524.11	125447.58	791286.22	2045761.99
	Siemens	female	1554149.94	131489.63	896701.80	2211598.08
		male	1371582.49	128987.94	726642.77	2016522.20
ADNI-1.5T	GE	female	1449425.05	113637.06	881239.73	2017610.37
		male	1653646.89	140077.62	953258.78	2354035.00
	Philips	female	1471159.39	100506.11	968628.85	1973689.92
		male	1629031.74	137395.51	942054.18	2316009.30
	Siemens	female	1421330.09	113044.38	856108.18	1986552.00
		male	1650845.04	161012.43	845782.88	2455907.19
ADNI-3T	GE	female	1361090.23	167716.63	522507.07	2199673.39
		male	1480231.80	134187.87	809292.45	2151171.14
	Philips	female	1406654.51	130884.42	752232.41	2061076.60
		male	1629318.76	129194.25	983347.50	2275290.02
	Siemens	female	1386173.75	130765.05	732348.49	2039999.00
		male	1547612.64	140756.52	843830.06	2251395.23
ARWIBO-1.5T	GE	female	1303548.35	111819.44	744451.17	1862645.54
		male	1448996.50	165751.44	620239.29	2277753.71
DELCODE-3T	Siemens	female	1512815.57	113543.84	945096.37	2080534.77
		male	1735791.64	141958.26	1026000.32	2445582.96
NACC-1.5T	GE	female	1391967.43	128848.69	747723.97	2036210.88
		male	1577128.73	160958.77	772334.89	2381922.57
NACC-3T	GE	female	1304766.89	247761.04	65961.69	2543572.09
		male	1474749.02	189224.97	528624.16	2420873.89
	Philips	female	1383175.17	127510.65	745621.93	2020728.42
		male	1596260.62	157548.90	808516.13	2384005.10
	Siemens	female	1384425.76	132880.84	720021.56	2048829.96
		male	1574795.63	150677.88	821406.22	2328185.03

This led to the exclusion of $n = 1$ in ADNI-3T, $n = 1$ in ARWIBO-1.5T, $n = 1$ in DELCODE-3T, and $n = 6$ in NACC-3T.

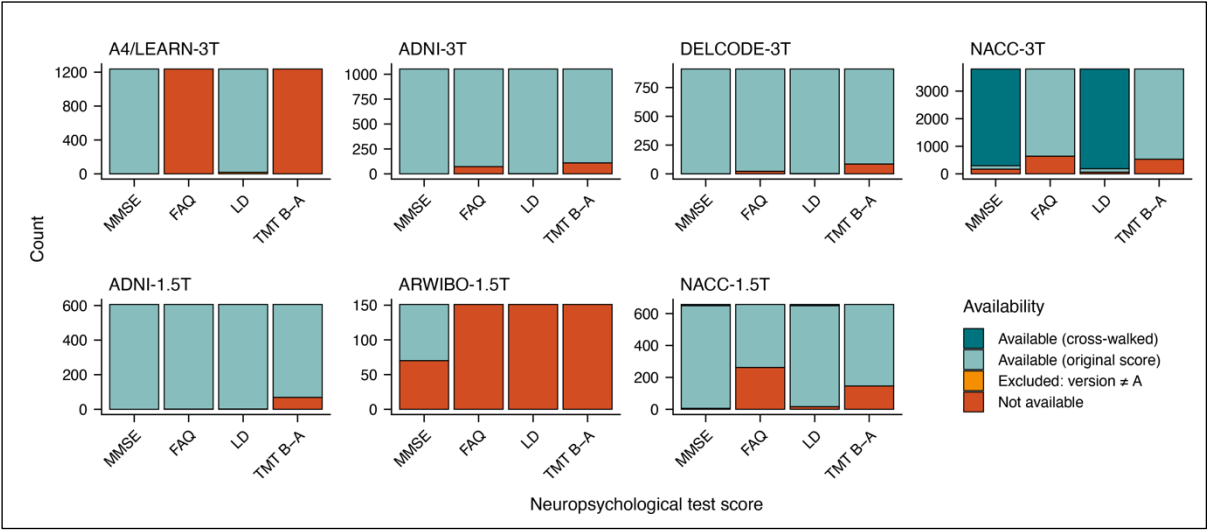
After standardization, observations were further excluded if any w -scored atrophy marker lay outside $-4 < w < 4$ for CU participants or $-7 < w < 7$ for MCI and DAT participants. This resulted in the exclusion of participants as follows: ADNI-1.5T ($n = 1$), ARWIBO-1.5T ($n = 1$), A4/LEARN-3T ($n = 3$), ADNI-3T ($n = 3$), NACC-1.5T ($n = 3$), and NACC-3T ($n = 19$).

References

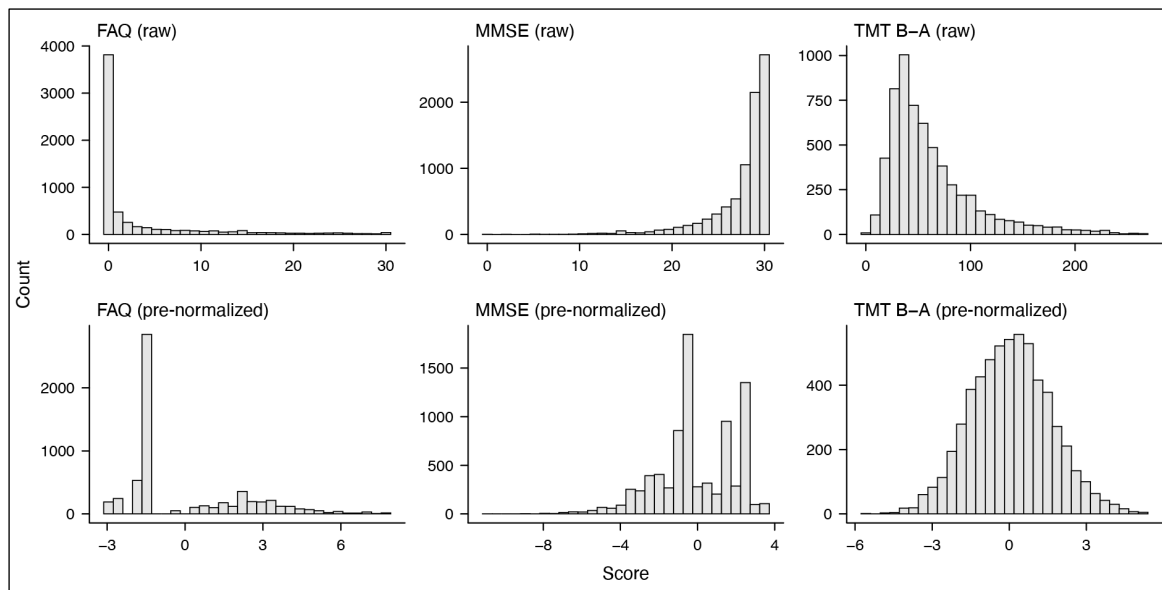
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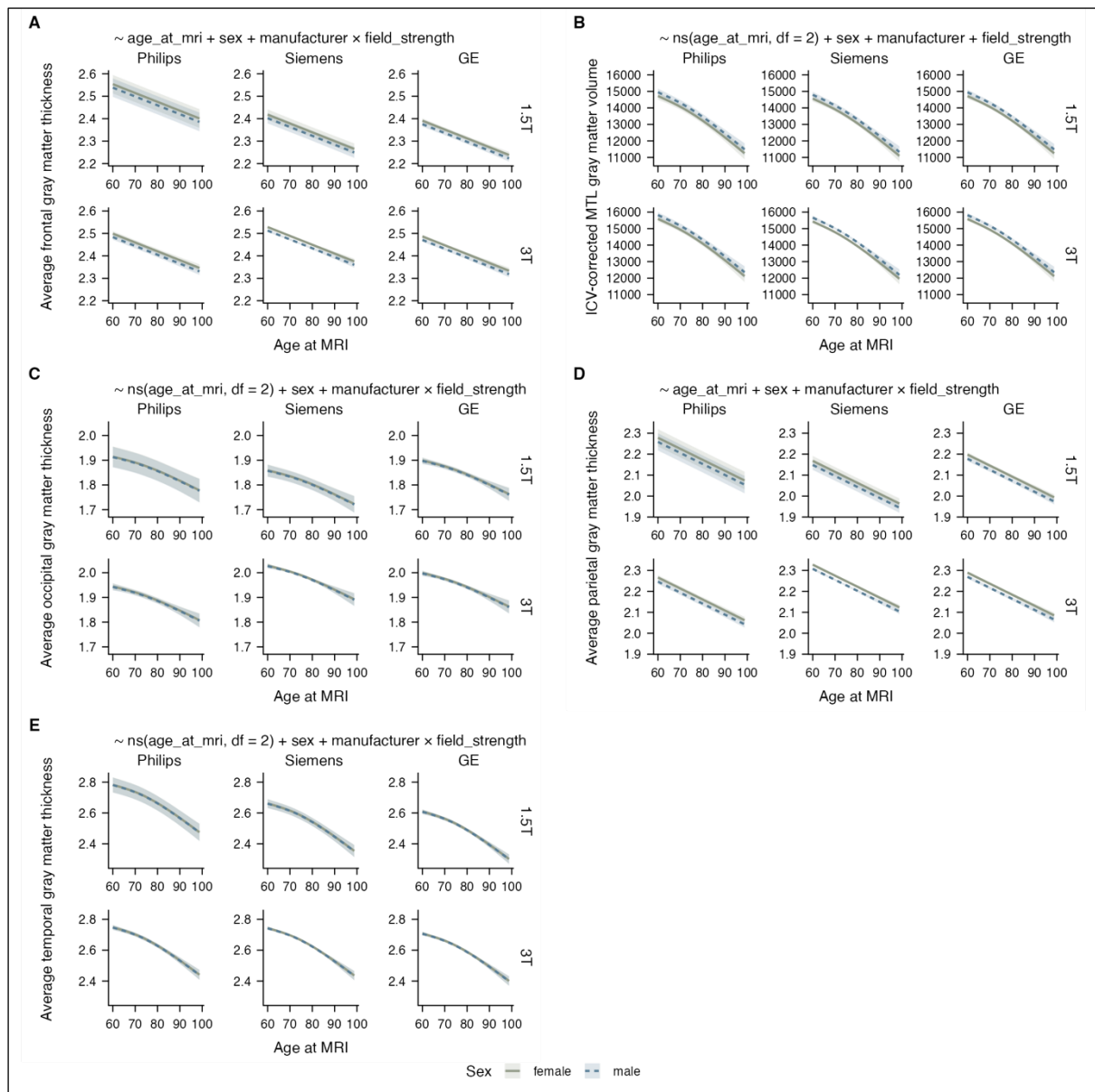
Supplementary figures



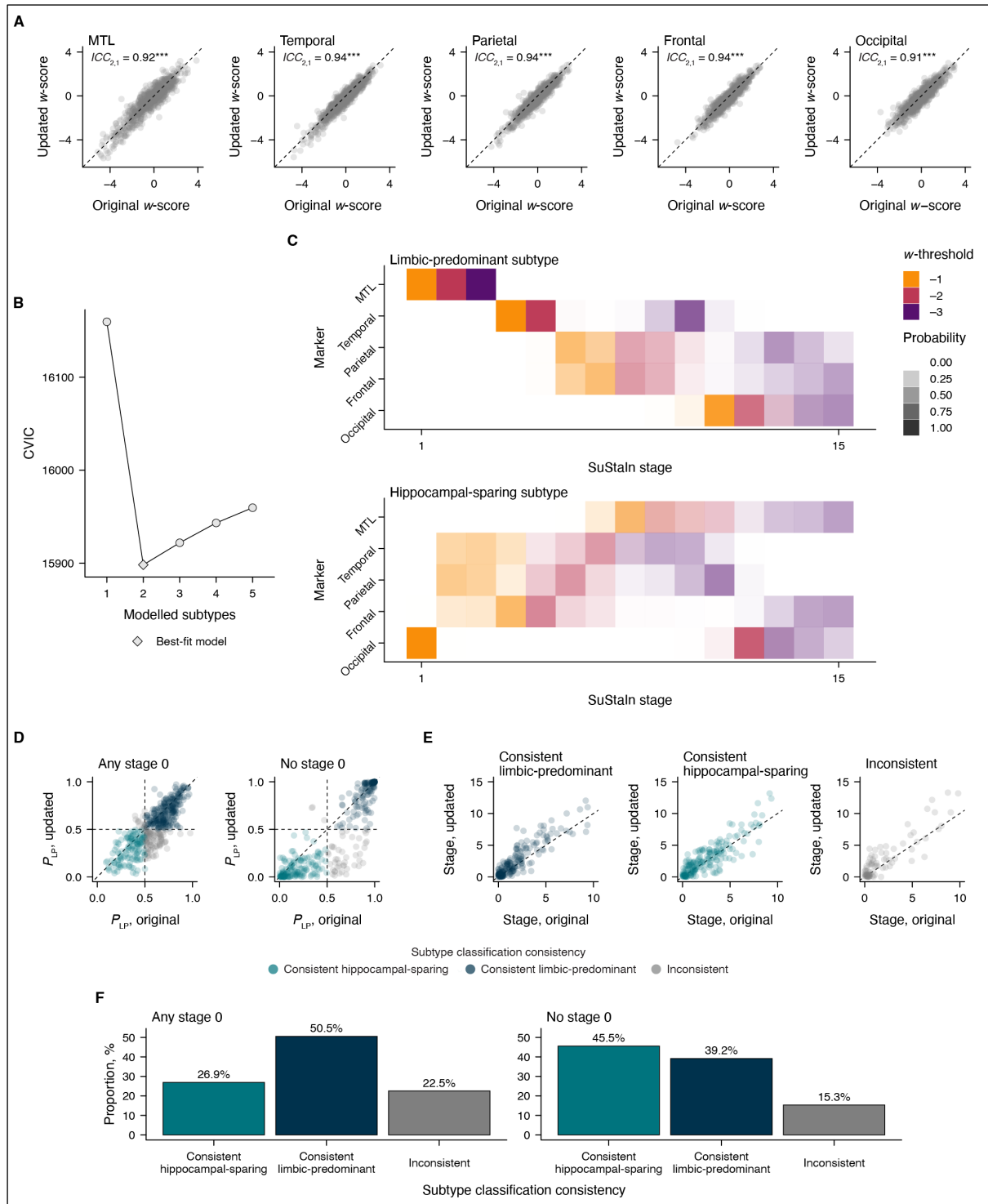
Supplementary Figure 1 Data availability in the study sample.



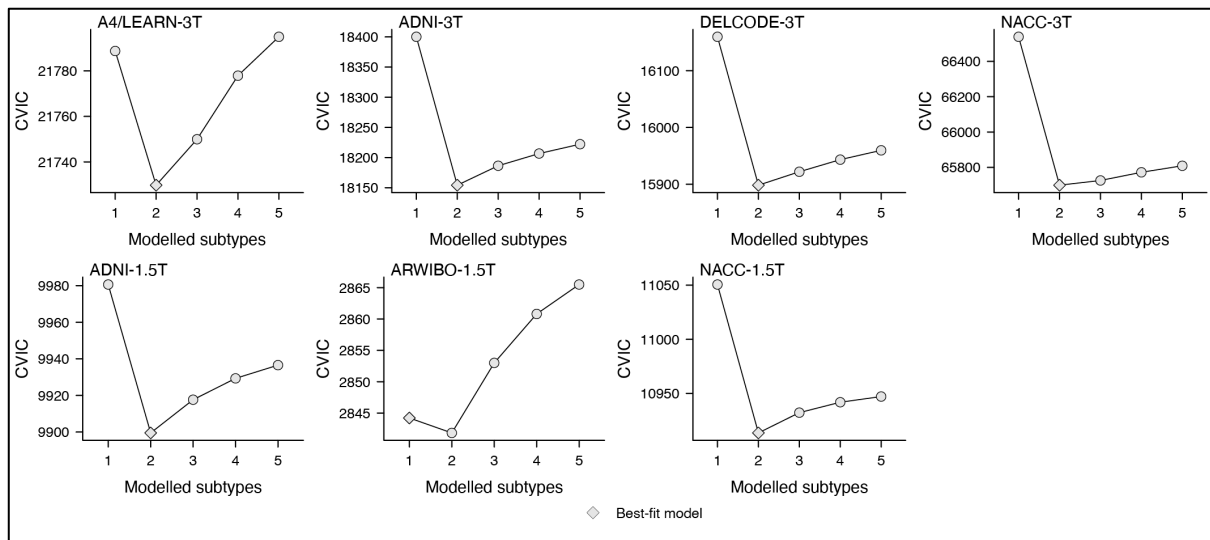
Supplementary Figure 2 Distributions of FAQ, MMSE, and TMT B-A scores before (top row) and after (bottom row) pre-normalization.



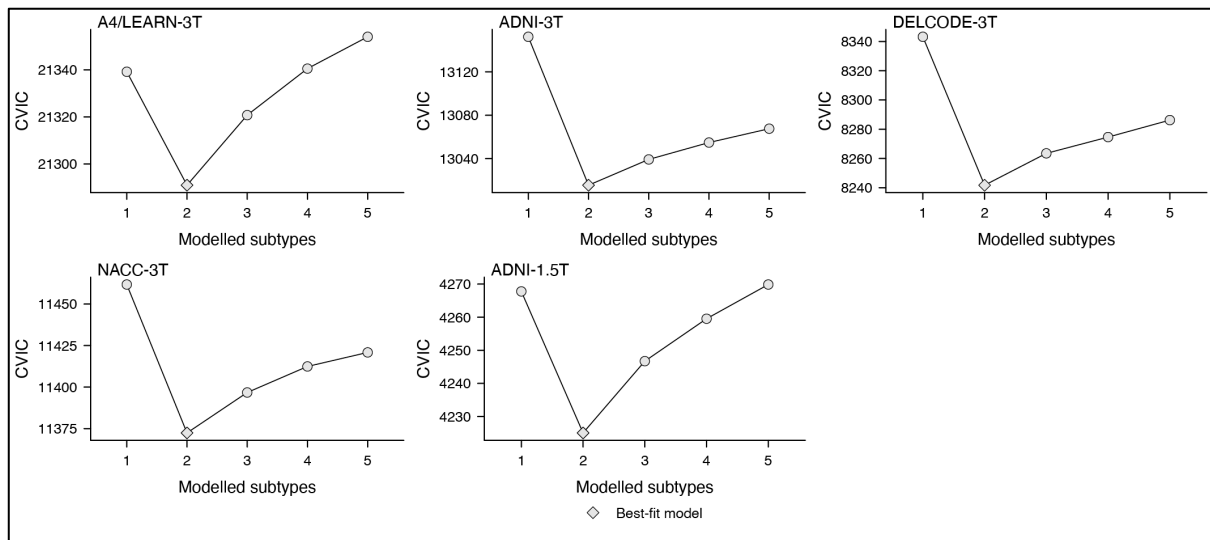
Supplementary Figure 3 Modeled relationships between age and MRI markers in CU participants, stratified by scanner manufacturer, magnetic field strength, and participant sex. The optimal model used for visualization and marker standardization is indicated above each respective plot. Ribbons depict 95% C.I.s. Abbreviations: ICV, intracranial volume.



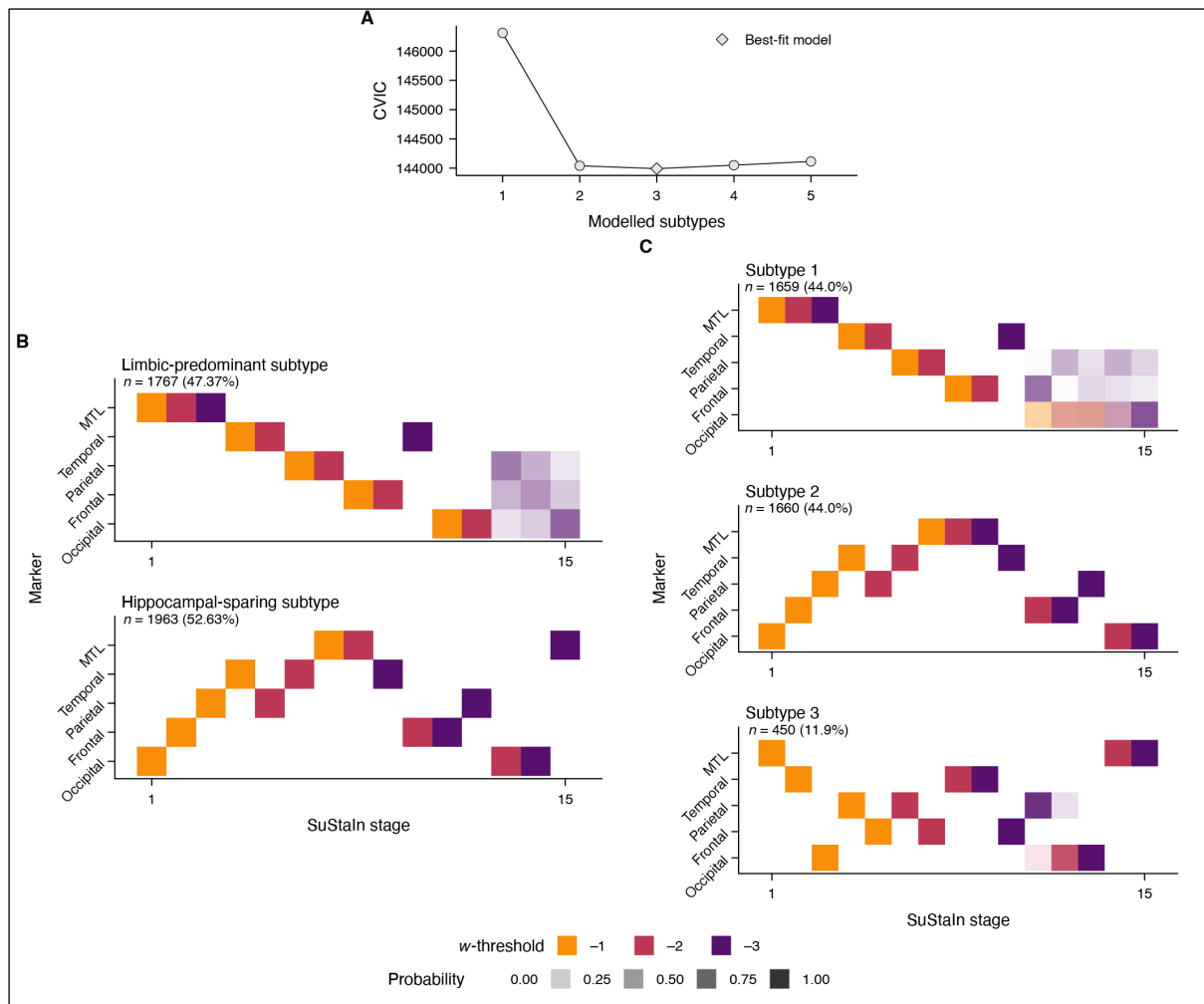
Supplementary Figure 4. Replication of the original subtyping and staging results in DELCODE-3T using updated methods for faster and more accessible atrophy subtyping and staging. (A) Scatter plots comparing the original and updated w-scored atrophy markers used for SuStain modeling. The original model based on these markers was published in Baumeister *et al.*¹¹ (B) Cross-validation information criterion (CVIC) from ten-fold cross-validation used to identify the most likely number of atrophy subtypes within the DELCODE-3T sample. (C) Positional variance diagram visualizing the optimal two-subtype model. (D, E) Scatter plots showing individual probabilities of limbic-predominant atrophy (P_{LP}) and atrophy stage as estimated by the original and updated models. The “Any stage 0” panel includes observations classified as stage 0 by at least one of the two models, whereas the “No stage 0” panel includes only those not classified as stage 0 by either model. (F) Proportions of consistent and inconsistent subtype classifications between the two models. All axes representing atrophy stage were jittered by up to ± 0.5 stages to improve visual clarity.



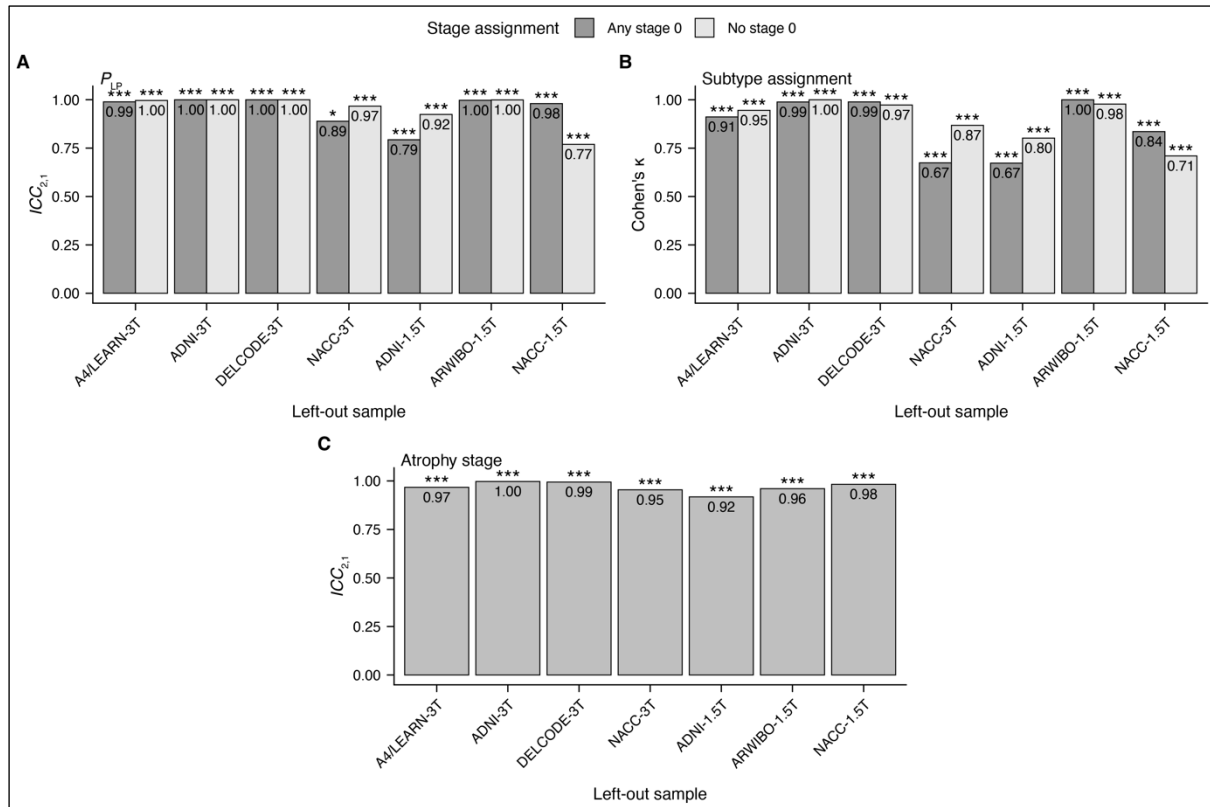
Supplementary Figure 5 Model selection criteria derived from within-sample SuStaIn modeling, including all available data.



Supplementary Figure 7 Model selection criteria derived from within-sample SuStaln modeling, including only the A β -positive subsets.



Supplementary Figure 9 Results from atrophy subtyping and staging as part of PHASE-AD. (A) Cross-validation information criterion (CVIC) from ten-fold cross-validation used to identify the most likely number of atrophy subtypes. (B) Positional variance diagram visualizing the two-subtype model. (C) Positional variance diagram visualizing the three-subtype model. The proportions shown above each plot in (B, C) refer to participants with an assigned atrophy stage > 0.

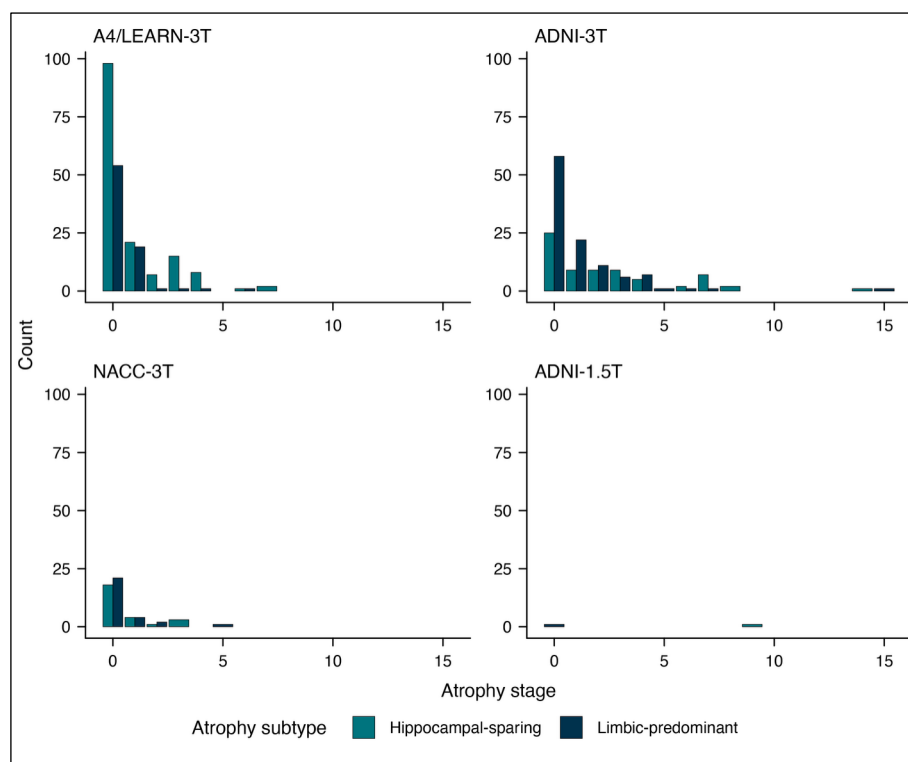


Supplementary Figure 10 Robustness of PHASE-AD classifications to sample removal. Leave-one-sample-out (LOSO) cross-validation results are shown for (A) probabilistic likelihood of progression (P_{LP} , $ICC_{2,1}$), (B) subtype assignment (Cohen's κ), and (C) atrophy stage ($ICC_{2,1}$). In (A,B), dark gray bars indicate agreement between observed and predicted classifications for participants assigned to stage 0 by either model, while light gray bars indicate agreement for all other participants. Significance levels: * $p < .05$, ** $p < .01$, *** $p < .001$

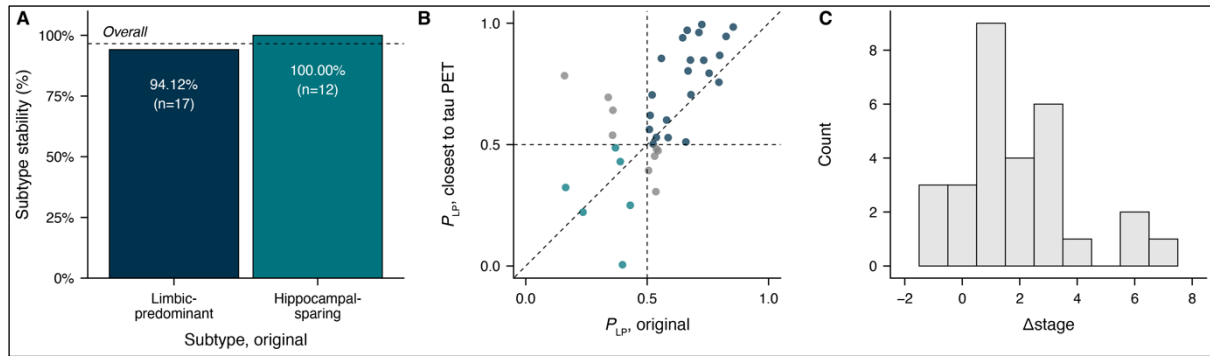


Supplementary Figure 11 Robustness of PHASE-AD classifications across scanner manufacturers and field strengths.

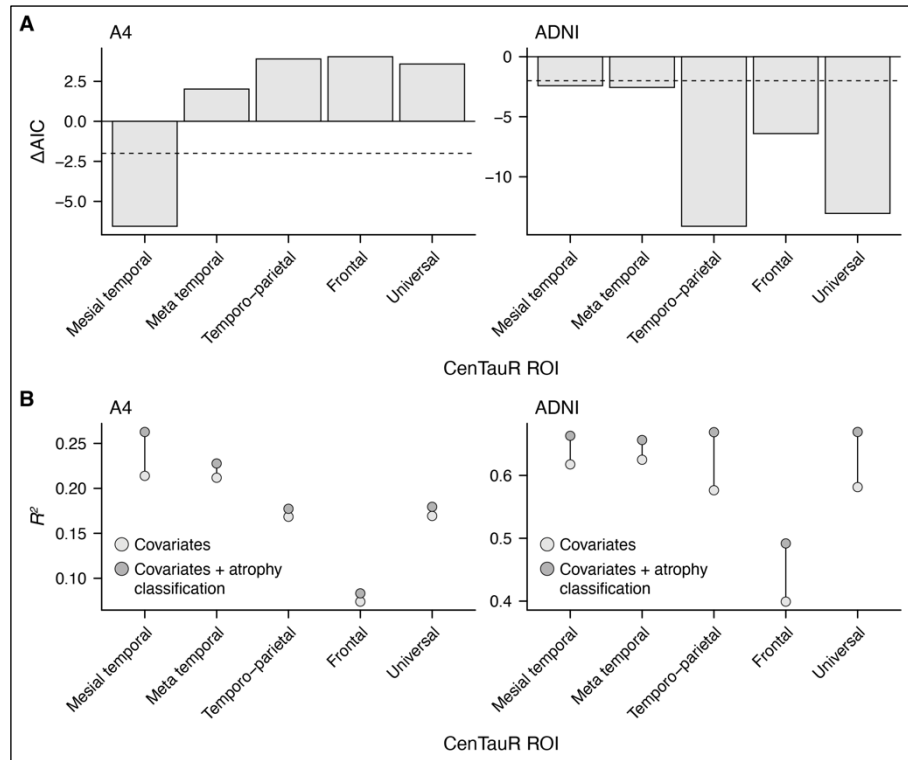
Heatmap of robustness indices for PHASE-AD classifications stratified by scanner manufacturer and MRI field strength, shown separately for the applied 10-fold stratified and LOSO cross-validation schemes. Rows correspond to stratification groups, columns correspond to robustness metrics. Abbreviations: HS, hippocampal-sparing. LP, limbic-predominant.



Supplementary Figure 12 Distribution of atrophy subtypes and stages across samples in the tau PET sample. Bar plots show the number of participants at each atrophy stage, stratified by subtype and sample. Only A β -positive individuals with available tau PET data are included.



Supplementary Figure 13 Stability of atrophy subtype and stage classifications across longitudinal MRI acquisitions in the tau PET analysis sample. (A) Proportion of individuals with stable subtype classification between the original MRI and the MRI closest to tau PET, stratified by baseline subtype. The dashed line indicates overall stability across subtypes. (B) Agreement of limbic-predominant subtype probabilities (P_{LP}) between timepoints for individuals initially classified as stage 0. Points are colored by consistency of subtype assignment. (C) Distribution of change in atrophy stage (Δ stage) between timepoints among individuals with baseline stage > 0. Negative values indicate violations of stage monotonicity. Participants classified as stage 0 at baseline were excluded, as stage decreases (violations of monotonicity) cannot occur from this baseline level.



Supplementary Figure 14 Associations between atrophy stage, subtype, and regional tau burden using plasma p-tau as covariate in A β -positive participants. (A) Model comparison across CenTauR ROIs, showing ΔAIC for full models relative to covariates-only models. The dashed line indicates $\Delta AIC = -2$, prespecified as evidence of improved model fit. (B) Total variance explained (R^2) for covariates-only and full models across CenTauR ROIs. Results are shown separately for A4 and ADNI samples.

Supplementary tables

Supplementary Table 1 FastSurfer cortical labels grouped into meta-regions used for subsequent analyses.

Meta-region	Included labels
MTL	entorhinal (from <lh/rh>.BA_exvivo.stats), hippocampus, amygdala (both from aseg+DKT.stats)
Temporal	inferiortemporal, fusiform, bankssts, middletemporal, temporalpole, superiortemporal, transversetemporal
Parietal	isthmuscingulate, inferiorparietal, precuneus, superiorparietal, supramarginal, posteriorcingulate, postcentral
Occipital	lateraloccipital, lingual, pericalcarine, cuneus
Frontal	caudalanteriorcingulate, caudalmiddlefrontal, lateralorbitofrontal, medialorbitofrontal, parsopercularis, parsorbitalis, paracentral, parstriangularis, precentral, rostralanteriorcingulate, rostralmiddlefrontal, superiorfrontal, insula, frontalpoles

Supplementary Table 2 Summary statistics of cross-sectional subtype effects derived from linear regression models predicting numeric outcome variables.

Sample	Sample	Subtype 1 (n)	Subtype 2 (n)	b	SE (b)	Cohen's d	SE (d)	95% C.I. (d)	p _{Tukey}	τ ²	I ²	Pooled p _{raw}	Pooled p _{DFR}
Outcome: age (years)													
Pooled	Whole sample	HS (1963)	A- (4685)			0.02	0.07	[-0.12; 0.16]		0.03	81.44	.763	.842
Pooled	Whole sample	LP (1767)	A- (4685)			0.10	0.07	[-0.04; 0.25]		0.03	75.44	.168	.231
Pooled	Whole sample	HS (1963)	HS (1963)			0.07	0.12	[-0.17; 0.32]		0.09	90.60	.553	.676
Pooled	Aβ-positive	HS (525)	A- (893)			-0.10	0.10	[-0.29; 0.09]		0.03	58.68	.293	.410
Pooled	Aβ-positive	LP (518)	A- (893)			0.11	0.11	[-0.10; 0.32]		0.03	57.34	.302	.410
Pooled	Aβ-positive	HS (518)	HS (525)			0.21	0.13	[-0.05; 0.47]		0.06	72.95	.107	.161
A4/LEARN-3T	Whole sample	LP (81)	HS (347)	1.67	0.57	0.36	0.12	[0.12; 0.61]	.009**				
A4/LEARN-3T	Whole sample	LP (81)	A- (809)	1.82	0.53	0.40	0.12	[0.17; 0.63]	.002**				
A4/LEARN-3T	Whole sample	HS (347)	A- (809)	0.16	0.29	0.03	0.06	[-0.09; 0.16]	.851				
A4/LEARN-3T	Aβ-positive	LP (56)	HS (191)	1.81	0.72	0.38	0.15	[0.08; 0.68]	.033*				
A4/LEARN-3T	Aβ-positive	LP (56)	A- (458)	2.16	0.67	0.46	0.14	[0.18; 0.74]	.004**				
A4/LEARN-3T	Aβ-positive	HS (191)	A- (458)	0.35	0.41	0.08	0.09	[-0.09; 0.24]	.658				
ADNI-3T	Whole sample	LP (225)	HS (289)	0.65	0.64	0.10	0.09	[-0.09; 0.28]	.565				
ADNI-3T	Whole sample	LP (225)	A- (538)	1.22	0.62	0.18	0.09	[0.00; 0.36]	.117				
ADNI-3T	Whole sample	HS (289)	A- (538)	0.57	0.51	0.08	0.07	[-0.06; 0.23]	.494				
ADNI-3T	Aβ-positive	LP (145)	HS (143)	0.88	0.81	0.13	0.12	[-0.11; 0.37]	.526				
ADNI-3T	Aβ-positive	LP (145)	A- (162)	0.54	0.87	0.08	0.13	[-0.17; 0.33]	.807				
ADNI-3T	Aβ-positive	HS (143)	A- (162)	-0.34	0.80	-0.05	0.12	[-0.29; 0.18]	.906				
DELCODE-3T	Whole sample	LP (265)	HS (254)	2.55	0.55	0.44	0.09	[0.25; 0.62]	< .001***				
DELCODE-3T	Whole sample	LP (265)	A- (392)	1.61	0.53	0.28	0.09	[0.10; 0.46]	.008**				
DELCODE-3T	Whole sample	HS (254)	A- (392)	-0.95	0.48	-0.16	0.08	[-0.32; 0.00]	.115				
DELCODE-3T	Aβ-positive	LP (132)	HS (71)	2.58	0.88	0.45	0.15	[0.15; 0.75]	.010*				
DELCODE-3T	Aβ-positive	LP (132)	A- (77)	-0.06	0.95	-0.01	0.17	[-0.34; 0.32]	.998				
DELCODE-3T	Aβ-positive	HS (71)	A- (77)	-2.64	0.97	-0.46	0.17	[-0.80; -0.13]	.019*				
NACC-3T	Whole sample	LP (784)	HS (698)	1.62	0.38	0.23	0.05	[0.13; 0.34]	< .001***				
NACC-3T	Whole sample	LP (784)	A- (2319)	0.17	0.33	0.02	0.05	[-0.07; 0.12]	.863				
NACC-3T	Whole sample	HS (698)	A- (2319)	-1.45	0.31	-0.21	0.04	[-0.29; -0.12]	< .001***				
NACC-3T	Aβ-positive	LP (98)	HS (64)	2.54	1.14	0.37	0.17	[0.04; 0.71]	.069				
NACC-3T	Aβ-positive	LP (98)	A- (152)	1.00	1.05	0.15	0.16	[-0.16; 0.45]	.607				
NACC-3T	Aβ-positive	HS (64)	A- (152)	-1.53	1.04	-0.23	0.15	[-0.53; 0.08]	.303				
ADNI-1.5T	Whole sample	LP (200)	HS (170)	-1.61	0.64	-0.27	0.11	[-0.47; -0.06]	.033*				
ADNI-1.5T	Whole sample	LP (200)	A- (236)	-0.39	0.67	-0.06	0.11	[-0.28; 0.15]	.834				
ADNI-1.5T	Whole sample	HS (170)	A- (236)	1.23	0.65	0.20	0.11	[-0.01; 0.41]	.145				
ADNI-1.5T	Aβ-positive	LP (87)	HS (56)	-1.76	1.02	-0.30	0.17	[-0.64; 0.04]	.197				
ADNI-1.5T	Aβ-positive	LP (87)	A- (44)	-1.33	1.18	-0.23	0.20	[-0.63; 0.17]	.498				
ADNI-1.5T	Aβ-positive	HS (56)	A- (44)	0.43	1.23	0.07	0.21	[-0.34; 0.49]	.935				
ARWIBO-1.5T	Whole sample	LP (54)	HS (38)	0.37	1.44	0.06	0.24	[-0.41; 0.53]	.964				
ARWIBO-1.5T	Whole sample	LP (54)	A- (59)	0.36	1.28	0.06	0.21	[-0.36; 0.48]	.958				
ARWIBO-1.5T	Whole sample	HS (38)	A- (59)	-0.02	1.27	0.00	0.21	[-0.42; 0.41]	.999				
NACC-1.5T	Whole sample	LP (158)	HS (167)	-3.15	0.85	-0.43	0.12	[-0.67; -0.20]	< .001***				
NACC-1.5T	Whole sample	LP (158)	A- (332)	-1.22	0.82	-0.17	0.11	[-0.39; 0.05]	.299				
NACC-1.5T	Whole sample	HS (167)	A- (332)	1.93	0.71	0.27	0.10	[0.07; 0.46]	.018*				
Outcome: education (years)													
Pooled	Whole sample	HS (1820)	A- (4224)			-0.05	0.04	[-0.12; 0.03]		0.00	34.13	.215	.284
Pooled	Whole sample	LP (1646)	A- (4224)			0.00	0.03	[-0.07; 0.06]		0.00	0.00	.932	.932
Pooled	Whole sample	HS (1820)	HS (1820)			0.04	0.04	[-0.03; 0.12]		0.00	2.57	.251	.319
Pooled	Aβ-positive	HS (518)	A- (869)			0.01	0.06	[-0.10; 0.13]		0.00	0.00	.839	.933
Pooled	Aβ-positive	LP (507)	A- (869)			0.01	0.08	[-0.14; 0.16]		0.01	18.17	.907	.972
Pooled	Aβ-positive	LP (507)	HS (518)			-0.03	0.07	[-0.17; 0.10]		0.00	0.00	.628	.725
A4/LEARN-3T	Whole sample	LP (81)	HS (347)	0.21	0.34	0.08	0.12	[-0.17; 0.32]	.811				
A4/LEARN-3T	Whole sample	LP (81)	A- (809)	0.05	0.32	0.02	0.12	[-0.21; 0.25]	.984				
A4/LEARN-3T	Whole sample	HS (347)	A- (809)	-0.15	0.18	-0.06	0.06	[-0.18; 0.07]	.655				
A4/LEARN-3T	Aβ-positive	LP (56)	HS (191)	-0.16	0.43	-0.06	0.15	[-0.36; 0.24]	.924				
A4/LEARN-3T	Aβ-positive	LP (56)	A- (458)	-0.23	0.40	-0.08	0.14	[-0.36; 0.20]	.838				
A4/LEARN-3T	Aβ-positive	HS (191)	A- (458)	-0.06	0.24	-0.02	0.09	[-0.19; 0.15]	.963				
ADNI-3T	Whole sample	LP (220)	HS (281)	-0.09	0.24	-0.04	0.09	[-0.22; 0.15]	.924				

Sample	Sample	Subtype 1 (n)	Subtype 2 (n)	<i>b</i>	<i>SE (b)</i>	Cohen's <i>d</i>	<i>SE (d)</i>	95% C.I. (<i>d</i>)	<i>p</i> _{Tukey}	τ^2	<i>I</i> ²	Pooled <i>p</i> _{raw}	Pooled <i>p</i> _{FDR}
ADNI-3T	Whole sample	LP (220)	A- (501)	-0.20	0.24	-0.08	0.09	[-0.26; 0.10]	.659				
ADNI-3T	Whole sample	HS (281)	A- (501)	-0.11	0.19	-0.04	0.08	[-0.19; 0.10]	.829				
ADNI-3T	Aβ-positive	LP (143)	HS (140)	-0.20	0.32	-0.08	0.12	[-0.32; 0.16]	.809				
ADNI-3T	Aβ-positive	LP (143)	A- (154)	-0.46	0.34	-0.18	0.13	[-0.44; 0.08]	.365				
ADNI-3T	Aβ-positive	HS (140)	A- (154)	-0.27	0.32	-0.10	0.12	[-0.34; 0.14]	.679				
DELCODE-3T	Whole sample	LP (265)	HS (254)	-0.02	0.28	-0.01	0.09	[-0.19; 0.18]	.996				
DELCODE-3T	Whole sample	LP (265)	A- (392)	0.21	0.27	0.07	0.09	[-0.11; 0.25]	.716				
DELCODE-3T	Whole sample	HS (254)	A- (392)	0.23	0.24	0.08	0.08	[-0.08; 0.24]	.597				
DELCODE-3T	Aβ-positive	LP (132)	HS (71)	-0.27	0.47	-0.09	0.15	[-0.39; 0.21]	.834				
DELCODE-3T	Aβ-positive	LP (132)	A- (77)	0.57	0.50	0.19	0.17	[-0.14; 0.52]	.497				
DELCODE-3T	Aβ-positive	HS (71)	A- (77)	0.84	0.51	0.28	0.17	[-0.06; 0.61]	.235				
NACC-3T	Whole sample	LP (714)	HS (613)	0.25	0.15	0.10	0.06	[-0.01; 0.21]	.194				
NACC-3T	Whole sample	LP (714)	A- (2009)	0.01	0.13	0.00	0.05	[-0.09; 0.10]	.996				
NACC-3T	Whole sample	HS (613)	A- (2009)	-0.24	0.12	-0.09	0.05	[-0.19; 0.00]	.115				
NACC-3T	Aβ-positive	LP (90)	HS (60)	0.16	0.43	0.06	0.18	[-0.28; 0.41]	.931				
NACC-3T	Aβ-positive	LP (90)	A- (136)	0.20	0.41	0.08	0.17	[-0.24; 0.41]	.873				
NACC-3T	Aβ-positive	HS (60)	A- (136)	0.05	0.39	0.02	0.16	[-0.30; 0.33]	.992				
ADNI-1.5T	Whole sample	LP (199)	HS (168)	-0.30	0.32	-0.10	0.11	[-0.31; 0.11]	.612				
ADNI-1.5T	Whole sample	LP (199)	A- (234)	0.07	0.34	0.02	0.11	[-0.20; 0.24]	.979				
ADNI-1.5T	Whole sample	HS (168)	A- (234)	0.37	0.33	0.12	0.11	[-0.09; 0.33]	.493				
ADNI-1.5T	Aβ-positive	LP (86)	HS (56)	0.20	0.54	0.06	0.17	[-0.28; 0.41]	.930				
ADNI-1.5T	Aβ-positive	LP (86)	A- (44)	0.62	0.63	0.20	0.20	[-0.20; 0.60]	.586				
ADNI-1.5T	Aβ-positive	HS (56)	A- (44)	0.42	0.65	0.14	0.21	[-0.28; 0.55]	.792				
ARWIBO-1.5T	Whole sample	LP (26)	HS (20)	1.25	1.64	0.27	0.35	[-0.43; 0.97]	.728				
ARWIBO-1.5T	Whole sample	LP (26)	A- (35)	0.36	1.51	0.08	0.32	[-0.57; 0.72]	.969				
ARWIBO-1.5T	Whole sample	HS (20)	A- (35)	-0.88	1.33	-0.19	0.28	[-0.76; 0.38]	.784				
NACC-1.5T	Whole sample	LP (141)	HS (137)	0.44	0.37	0.15	0.13	[-0.10; 0.40]	.467				
NACC-1.5T	Whole sample	LP (141)	A- (244)	-0.33	0.36	-0.11	0.12	[-0.35; 0.13]	.644				
NACC-1.5T	Whole sample	HS (137)	A- (244)	-0.77	0.33	-0.26	0.11	[-0.47; -0.04]	.051				
Outcome: FAQ (inv.)													
Pooled	Whole sample	HS (1265)	A- (2970)			-0.13	0.04	[-0.20; -0.05]		0.00	11.23	< .001***	.002**
Pooled	Whole sample	LP (1292)	A- (2970)			-0.41	0.04	[-0.50; -0.32]		0.00	14.73	< .001***	< .001***
Pooled	Whole sample	LP (1292)	HS (1265)			-0.28	0.04	[-0.36; -0.20]		0.00	0.00	< .001***	< .001***
Pooled	Aβ-positive	HS (317)	A- (394)			-0.29	0.08	[-0.45; -0.13]		0.00	0.00	< .001***	< .001***
Pooled	Aβ-positive	LP (431)	A- (394)			-0.43	0.08	[-0.59; -0.27]		0.00	0.00	< .001***	< .001***
Pooled	Aβ-positive	LP (431)	HS (317)			-0.14	0.08	[-0.29; 0.01]		0.00	0.00	.070	.111
ADNI-3T	Whole sample	HS (266)	A- (463)	-0.27	0.11	-0.19	0.08	[-0.34; -0.03]	.046*				
ADNI-3T	Whole sample	LP (203)	A- (463)	-0.81	0.14	-0.56	0.10	[-0.75; -0.37]	< .001***				
ADNI-3T	Whole sample	LP (203)	HS (266)	-0.54	0.14	-0.37	0.10	[-0.56; -0.18]	< .001***				
ADNI-3T	Aβ-positive	HS (140)	A- (153)	-0.46	0.19	-0.30	0.12	[-0.54; -0.06]	.041*				
ADNI-3T	Aβ-positive	LP (142)	A- (153)	-0.83	0.21	-0.54	0.13	[-0.80; -0.27]	< .001***				
ADNI-3T	Aβ-positive	LP (142)	HS (140)	-0.37	0.19	-0.24	0.12	[-0.48; 0.01]	.132				
DELCODE-3T	Whole sample	HS (248)	A- (381)	-0.12	0.11	-0.09	0.08	[-0.25; 0.07]	.527				
DELCODE-3T	Whole sample	LP (260)	A- (381)	-0.45	0.12	-0.34	0.09	[-0.52; -0.16]	< .001***				
DELCODE-3T	Whole sample	LP (260)	HS (248)	-0.33	0.13	-0.25	0.10	[-0.44; -0.06]	.025*				
DELCODE-3T	Aβ-positive	HS (68)	A- (76)	-0.49	0.26	-0.33	0.18	[-0.68; 0.01]	.140				
DELCODE-3T	Aβ-positive	LP (130)	A- (76)	-0.52	0.24	-0.36	0.17	[-0.69; -0.03]	.084				
DELCODE-3T	Aβ-positive	LP (130)	HS (68)	-0.04	0.23	-0.02	0.16	[-0.34; 0.29]	.987				
NACC-3T	Whole sample	HS (514)	A- (1733)	-0.10	0.08	-0.07	0.05	[-0.17; 0.03]	.391				
NACC-3T	Whole sample	LP (560)	A- (1733)	-0.52	0.08	-0.36	0.06	[-0.47; -0.25]	< .001***				
NACC-3T	Whole sample	LP (560)	HS (514)	-0.43	0.09	-0.29	0.06	[-0.42; -0.17]	< .001***				
NACC-3T	Aβ-positive	HS (53)	A- (121)	-0.38	0.29	-0.22	0.17	[-0.56; 0.12]	.406				
NACC-3T	Aβ-positive	LP (73)	A- (121)	-0.58	0.31	-0.34	0.18	[-0.70; 0.02]	.152				
NACC-3T	Aβ-positive	LP (73)	HS (53)	-0.20	0.33	-0.12	0.19	[-0.50; 0.26]	.816				
ADNI-1.5T	Whole sample	HS (168)	A- (234)	-0.38	0.18	-0.23	0.11	[-0.44; -0.01]	.091				
ADNI-1.5T	Whole sample	LP (198)	A- (234)	-0.77	0.19	-0.46	0.11	[-0.68; -0.24]	< .001***				
ADNI-1.5T	Whole sample	LP (198)	HS (168)	-0.39	0.18	-0.23	0.11	[-0.45; -0.02]	.076				
ADNI-1.5T	Aβ-positive	HS (56)	A- (44)	-0.50	0.37	-0.29	0.21	[-0.71; 0.13]	.360				

Sample	Sample	Subtype 1 (n)	Subtype 2 (n)	<i>b</i>	<i>SE (b)</i>	Cohen's <i>d</i>	<i>SE (d)</i>	95% C.I. (<i>d</i>)	<i>p</i> _{Tukey}	τ^2	<i>I</i> ²	Pooled <i>p</i> _{raw}	Pooled <i>p</i> _{FDR}
ADNI-1.5T	Aβ-positive	LP (86)	A- (44)	-0.69	0.35	-0.40	0.21	[-0.80; 0.01]	.128				
ADNI-1.5T	Aβ-positive	LP (86)	HS (56)	-0.19	0.30	-0.11	0.18	[-0.46; 0.24]	.810				
NACC-1.5T	Whole sample	HS (69)	A- (159)	-0.49	0.27	-0.28	0.15	[-0.58; 0.03]	.174				
NACC-1.5T	Whole sample	LP (71)	A- (159)	-0.79	0.30	-0.45	0.17	[-0.79; -0.11]	.025*				
NACC-1.5T	Whole sample	LP (71)	HS (69)	-0.30	0.32	-0.17	0.18	[-0.53; 0.18]	.605				
Outcome: MMSE													
Pooled	Whole sample	HS (1790)	A- (4130)			-0.27	0.09	[-0.45; -0.09]		0.05	87.08	.003**	.006**
Pooled	Whole sample	LP (1605)	A- (4130)			-0.34	0.06	[-0.46; -0.22]		0.01	57.67	< .001***	< .001***
Pooled	Whole sample	LP (1605)	HS (1790)			-0.06	0.04	[-0.14; 0.01]		0.00	0.00	.090	.129
Pooled	Aβ-positive	HS (514)	A- (863)			-0.34	0.14	[-0.61; -0.07]		0.07	78.45	.013*	.024*
Pooled	Aβ-positive	LP (499)	A- (863)			-0.43	0.09	[-0.60; -0.25]		0.01	34.73	< .001***	< .001***
Pooled	Aβ-positive	LP (499)	HS (514)			-0.08	0.08	[-0.24; 0.08]		0.01	23.89	.328	.410
A4/LEARN-3T	Whole sample	LP (81)	HS (346)	-0.24	0.15	-0.19	0.13	[-0.44; 0.05]	.270				
A4/LEARN-3T	Whole sample	LP (81)	A- (809)	-0.18	0.14	-0.14	0.12	[-0.37; 0.09]	.441				
A4/LEARN-3T	Whole sample	HS (346)	A- (809)	0.06	0.08	0.05	0.06	[-0.08; 0.18]	.723				
A4/LEARN-3T	Aβ-positive	LP (56)	HS (191)	-0.33	0.19	-0.28	0.15	[-0.58; 0.03]	.178				
A4/LEARN-3T	Aβ-positive	LP (56)	A- (458)	-0.20	0.17	-0.16	0.14	[-0.44; 0.12]	.499				
A4/LEARN-3T	Aβ-positive	HS (191)	A- (458)	0.14	0.11	0.11	0.09	[-0.06; 0.28]	.391				
ADNI-3T	Whole sample	LP (220)	HS (281)	-0.16	0.11	-0.13	0.10	[-0.32; 0.05]	.347				
ADNI-3T	Whole sample	LP (220)	A- (501)	-0.48	0.11	-0.40	0.09	[-0.58; -0.22]	< .001***				
ADNI-3T	Whole sample	HS (281)	A- (501)	-0.32	0.09	-0.27	0.08	[-0.42; -0.12]	.001**				
ADNI-3T	Aβ-positive	LP (143)	HS (140)	-0.21	0.14	-0.18	0.12	[-0.43; 0.06]	.297				
ADNI-3T	Aβ-positive	LP (143)	A- (154)	-0.70	0.15	-0.60	0.13	[-0.86; -0.34]	< .001***				
ADNI-3T	Aβ-positive	HS (140)	A- (154)	-0.49	0.14	-0.42	0.12	[-0.66; -0.18]	.002**				
DELCODE-3T	Whole sample	LP (264)	HS (254)	-0.06	0.11	-0.05	0.10	[-0.24; 0.13]	.839				
DELCODE-3T	Whole sample	LP (264)	A- (392)	-0.28	0.11	-0.24	0.09	[-0.42; -0.06]	.026*				
DELCODE-3T	Whole sample	HS (254)	A- (392)	-0.22	0.10	-0.18	0.08	[-0.35; -0.02]	.062				
DELCODE-3T	Aβ-positive	LP (131)	HS (71)	0.18	0.18	0.16	0.16	[-0.14; 0.47]	.548				
DELCODE-3T	Aβ-positive	LP (131)	A- (77)	-0.41	0.19	-0.37	0.17	[-0.70; -0.04]	.072				
DELCODE-3T	Aβ-positive	HS (71)	A- (77)	-0.60	0.19	-0.53	0.17	[-0.88; -0.19]	.006**				
NACC-3T	Whole sample	LP (680)	HS (593)	-0.05	0.09	-0.03	0.06	[-0.14; 0.08]	.862				
NACC-3T	Whole sample	LP (680)	A- (1923)	-0.45	0.08	-0.30	0.05	[-0.40; -0.20]	< .001***				
NACC-3T	Whole sample	HS (593)	A- (1923)	-0.40	0.07	-0.27	0.05	[-0.37; -0.18]	< .001***				
NACC-3T	Aβ-positive	LP (83)	HS (56)	-0.07	0.28	-0.04	0.19	[-0.41; 0.32]	.970				
NACC-3T	Aβ-positive	LP (83)	A- (130)	-0.81	0.26	-0.54	0.18	[-0.89; -0.19]	.006**				
NACC-3T	Aβ-positive	HS (56)	A- (130)	-0.74	0.25	-0.50	0.17	[-0.83; -0.17]	.008**				
ADNI-1.5T	Whole sample	LP (199)	HS (168)	-0.10	0.13	-0.08	0.11	[-0.30; 0.13]	.722				
ADNI-1.5T	Whole sample	LP (199)	A- (234)	-0.47	0.13	-0.40	0.11	[-0.62; -0.18]	.001**				
ADNI-1.5T	Whole sample	HS (168)	A- (234)	-0.38	0.13	-0.31	0.11	[-0.53; -0.10]	.011*				
ADNI-1.5T	Aβ-positive	LP (86)	HS (56)	0.02	0.22	0.02	0.18	[-0.33; 0.37]	.994				
ADNI-1.5T	Aβ-positive	LP (86)	A- (44)	-0.61	0.26	-0.49	0.21	[-0.89; -0.08]	.048*				
ADNI-1.5T	Aβ-positive	HS (56)	A- (44)	-0.64	0.27	-0.50	0.21	[-0.92; -0.08]	.048*				
ARWIBO-1.5T	Whole sample	LP (21)	HS (12)	0.25	0.76	0.14	0.43	[-0.72; 1.00]	.944				
ARWIBO-1.5T	Whole sample	LP (21)	A- (29)	-0.10	0.67	-0.05	0.38	[-0.81; 0.70]	.988				
ARWIBO-1.5T	Whole sample	HS (12)	A- (29)	-0.34	0.62	-0.19	0.35	[-0.89; 0.51]	.845				
NACC-1.5T	Whole sample	LP (140)	HS (136)	0.06	0.20	0.04	0.13	[-0.21; 0.29]	.953				
NACC-1.5T	Whole sample	LP (140)	A- (242)	-1.07	0.20	-0.67	0.13	[-0.92; -0.43]	< .001***				
NACC-1.5T	Whole sample	HS (136)	A- (242)	-1.13	0.18	-0.71	0.11	[-0.93; -0.49]	< .001***				
Outcome: Logical Memory Delayed Recall													
Pooled	Whole sample	HS (1778)	A- (4154)			-0.16	0.04	[-0.25; -0.08]		0.00	46.59	< .001***	< .001***
Pooled	Whole sample	LP (1585)	A- (4154)			-0.52	0.03	[-0.59; -0.45]		0.00	0.00	< .001***	< .001***
Pooled	Whole sample	LP (1585)	HS (1778)			-0.37	0.04	[-0.44; -0.29]		0.00	0.00	< .001***	< .001***
Pooled	Aβ-positive	HS (512)	A- (859)			-0.34	0.08	[-0.49; -0.18]		0.01	34.98	< .001***	< .001***
Pooled	Aβ-positive	LP (503)	A- (859)			-0.81	0.14	[-1.09; -0.54]		0.07	71.92	< .001***	< .001***
Pooled	Aβ-positive	LP (503)	HS (512)			-0.44	0.07	[-0.57; -0.30]		0.00	0.00	< .001***	< .001***
A4/LEARN-3T	Whole sample	LP (80)	HS (341)	-1.17	0.43	-0.34	0.13	[-0.59; -0.09]	.018*				
A4/LEARN-3T	Whole sample	LP (80)	A- (798)	-1.59	0.41	-0.46	0.12	[-0.70; -0.23]	< .001***				
A4/LEARN-3T	Whole sample	HS (341)	A- (798)	-0.42	0.22	-0.12	0.07	[-0.25; 0.01]	.148				

Sample	Sample	Subtype 1 (n)	Subtype 2 (n)	<i>b</i>	<i>SE</i> (<i>b</i>)	Cohen's <i>d</i>	<i>SE</i> (<i>d</i>)	95% C.I. (<i>d</i>)	<i>p</i> _{Tukey}	τ^2	<i>I</i> ²	Pooled <i>p</i> _{raw}	Pooled <i>p</i> _{FDR}
A4/LEARN-3T	Aβ-positive	LP (56)	HS (188)	-1.37	0.55	-0.39	0.16	[-0.69; -0.08]	.035*				
A4/LEARN-3T	Aβ-positive	LP (56)	A- (448)	-2.03	0.51	-0.57	0.15	[-0.86; -0.29]	< .001***				
A4/LEARN-3T	Aβ-positive	HS (188)	A- (448)	-0.66	0.31	-0.19	0.09	[-0.36; -0.01]	.083				
ADNI-3T	Whole sample	LP (219)	HS (281)	-1.34	0.28	-0.45	0.10	[-0.63; -0.26]	< .001***				
ADNI-3T	Whole sample	LP (219)	A- (500)	-1.74	0.28	-0.58	0.09	[-0.77; -0.40]	< .001***				
ADNI-3T	Whole sample	HS (281)	A- (500)	-0.41	0.23	-0.14	0.08	[-0.29; 0.01]	.173				
ADNI-3T	Aβ-positive	LP (143)	HS (140)	-1.22	0.36	-0.42	0.12	[-0.66; -0.18]	.002**				
ADNI-3T	Aβ-positive	LP (143)	A- (154)	-2.37	0.38	-0.82	0.14	[-1.08; -0.55]	< .001***				
ADNI-3T	Aβ-positive	HS (140)	A- (154)	-1.16	0.35	-0.40	0.12	[-0.64; -0.16]	.003**				
DELCODE-3T	Whole sample	LP (264)	HS (253)	-1.57	0.36	-0.41	0.10	[-0.60; -0.22]	< .001***				
DELCODE-3T	Whole sample	LP (264)	A- (392)	-1.72	0.35	-0.45	0.09	[-0.63; -0.27]	< .001***				
DELCODE-3T	Whole sample	HS (253)	A- (392)	-0.15	0.31	-0.04	0.08	[-0.20; 0.12]	.888				
DELCODE-3T	Aβ-positive	LP (132)	HS (70)	-1.01	0.61	-0.26	0.16	[-0.57; 0.05]	.227				
DELCODE-3T	Aβ-positive	LP (132)	A- (77)	-1.81	0.65	-0.47	0.17	[-0.80; -0.13]	.015*				
DELCODE-3T	Aβ-positive	HS (70)	A- (77)	-0.80	0.67	-0.21	0.17	[-0.55; 0.14]	.463				
NACC-3T	Whole sample	LP (690)	HS (602)	-1.41	0.23	-0.35	0.06	[-0.47; -0.24]	< .001***				
NACC-3T	Whole sample	LP (690)	A- (1987)	-1.95	0.20	-0.49	0.05	[-0.59; -0.39]	< .001***				
NACC-3T	Whole sample	HS (602)	A- (1987)	-0.53	0.19	-0.13	0.05	[-0.23; -0.04]	.015*				
NACC-3T	Aβ-positive	LP (86)	HS (59)	-2.61	0.70	-0.68	0.18	[-1.04; -0.31]	< .001***				
NACC-3T	Aβ-positive	LP (86)	A- (136)	-4.69	0.65	-1.22	0.18	[-1.56; -0.87]	< .001***				
NACC-3T	Aβ-positive	HS (59)	A- (136)	-2.09	0.63	-0.54	0.16	[-0.86; -0.22]	.003**				
ADNI-1.5T	Whole sample	LP (198)	HS (167)	-1.23	0.31	-0.43	0.11	[-0.64; -0.22]	< .001***				
ADNI-1.5T	Whole sample	LP (198)	A- (234)	-2.08	0.32	-0.72	0.11	[-0.95; -0.50]	< .001***				
ADNI-1.5T	Whole sample	HS (167)	A- (234)	-0.84	0.31	-0.29	0.11	[-0.51; -0.08]	.020*				
ADNI-1.5T	Aβ-positive	LP (86)	HS (55)	-1.19	0.39	-0.54	0.18	[-0.89; -0.19]	.007**				
ADNI-1.5T	Aβ-positive	LP (86)	A- (44)	-2.35	0.45	-1.06	0.21	[-1.49; -0.64]	< .001***				
ADNI-1.5T	Aβ-positive	HS (55)	A- (44)	-1.16	0.47	-0.53	0.21	[-0.95; -0.10]	.038*				
NACC-1.5T	Whole sample	LP (134)	HS (134)	-0.49	0.49	-0.13	0.13	[-0.38; 0.13]	.577				
NACC-1.5T	Whole sample	LP (134)	A- (243)	-2.09	0.47	-0.56	0.13	[-0.80; -0.31]	< .001***				
NACC-1.5T	Whole sample	HS (134)	A- (243)	-1.60	0.42	-0.43	0.11	[-0.65; -0.20]	< .001***				
Outcome: TMT B-A (inv.)													
Pooled	Whole sample	HS (1144)	A- (3098)			-0.21	0.04	[-0.28; -0.14]		0.00	0.00	< .001***	< .001***
Pooled	Whole sample	LP (1105)	A- (3098)			-0.01	0.04	[-0.08; 0.07]		0.00	0.00	.871	.899
Pooled	Whole sample	LP (1105)	HS (1144)			0.20	0.04	[0.12; 0.29]		0.00	0.00	< .001***	< .001***
Pooled	Aβ-positive	HS (252)	A- (390)			-0.28	0.09	[-0.45; -0.11]		0.00	2.70	.001**	.002**
Pooled	Aβ-positive	LP (339)	A- (390)			0.00	0.09	[-0.17; 0.17]		0.00	0.00	.977	.990
Pooled	Aβ-positive	LP (339)	HS (252)			0.30	0.09	[0.12; 0.48]		0.00	2.21	.001**	.002**
ADNI-3T	Whole sample	HS (249)	A- (462)	-0.34	0.12	-0.24	0.08	[-0.39; -0.08]	.009**				
ADNI-3T	Whole sample	LP (180)	A- (462)	0.00	0.14	0.00	0.10	[-0.20; 0.19]	.999				
ADNI-3T	Whole sample	LP (180)	HS (249)	0.34	0.15	0.23	0.10	[0.03; 0.44]	.063				
ADNI-3T	Aβ-positive	HS (123)	A- (151)	-0.57	0.19	-0.37	0.13	[-0.62; -0.12]	.009**				
ADNI-3T	Aβ-positive	LP (122)	A- (151)	0.04	0.21	0.03	0.14	[-0.24; 0.30]	.978				
ADNI-3T	Aβ-positive	LP (122)	HS (123)	0.61	0.20	0.40	0.13	[0.14; 0.66]	.007**				
DELCODE-3T	Whole sample	HS (234)	A- (383)	-0.19	0.11	-0.15	0.08	[-0.32; 0.01]	.170				
DELCODE-3T	Whole sample	LP (207)	A- (383)	-0.03	0.12	-0.03	0.10	[-0.22; 0.16]	.959				
DELCODE-3T	Whole sample	LP (207)	HS (234)	0.16	0.13	0.12	0.10	[-0.08; 0.33]	.445				
DELCODE-3T	Aβ-positive	HS (57)	A- (72)	-0.17	0.24	-0.13	0.18	[-0.49; 0.23]	.747				
DELCODE-3T	Aβ-positive	LP (89)	A- (72)	0.00	0.24	0.00	0.18	[-0.35; 0.35]	.999				
DELCODE-3T	Aβ-positive	LP (89)	HS (57)	0.17	0.24	0.13	0.18	[-0.22; 0.49]	.745				
NACC-3T	Whole sample	HS (455)	A- (1826)	-0.29	0.08	-0.20	0.05	[-0.31; -0.10]	< .001***				
NACC-3T	Whole sample	LP (473)	A- (1826)	0.05	0.08	0.03	0.06	[-0.08; 0.14]	.839				
NACC-3T	Whole sample	LP (473)	HS (455)	0.34	0.10	0.23	0.07	[0.10; 0.37]	.002**				
NACC-3T	Aβ-positive	HS (33)	A- (123)	-0.10	0.28	-0.07	0.20	[-0.47; 0.33]	.935				
NACC-3T	Aβ-positive	LP (51)	A- (123)	-0.06	0.29	-0.04	0.21	[-0.45; 0.37]	.980				
NACC-3T	Aβ-positive	LP (51)	HS (33)	0.04	0.36	0.03	0.26	[-0.48; 0.54]	.992				
ADNI-1.5T	Whole sample	HS (123)	A- (233)	-0.37	0.15	-0.28	0.12	[-0.51; -0.05]	.042*				
ADNI-1.5T	Whole sample	LP (171)	A- (233)	-0.13	0.15	-0.09	0.12	[-0.32; 0.13]	.694				
ADNI-1.5T	Whole sample	LP (171)	HS (123)	0.24	0.16	0.19	0.12	[-0.06; 0.43]	.296				

Sample	Sample	Subtype 1 (<i>n</i>)	Subtype 2 (<i>n</i>)	<i>b</i>	<i>SE (b)</i>	Cohen's <i>d</i>	<i>SE (d)</i>	95% C.I. (<i>d</i>)	<i>p</i> _{Tukey}	τ^2	I^2	Pooled <i>p</i> _{raw}	Pooled <i>p</i> _{FDR}
ADNI-1.5T	Aβ-positive	HS (39)	A- (44)	-0.69	0.32	-0.50	0.23	[-0.95; -0.04]	.080				
ADNI-1.5T	Aβ-positive	LP (77)	A- (44)	-0.05	0.29	-0.04	0.21	[-0.45; 0.38]	.983				
ADNI-1.5T	Aβ-positive	LP (77)	HS (39)	0.64	0.30	0.46	0.21	[0.04; 0.88]	.081				
NACC-1.5T	Whole sample	HS (83)	A- (194)	-0.43	0.20	-0.29	0.14	[-0.56; -0.02]	.083				
NACC-1.5T	Whole sample	LP (74)	A- (194)	-0.15	0.24	-0.10	0.16	[-0.41; 0.21]	.806				
NACC-1.5T	Whole sample	LP (74)	HS (83)	0.29	0.26	0.19	0.17	[-0.15; 0.53]	.509				

p* < .05. *p* < .01. ****p* < .001. Abbreviations: A-, atrophy negative. HS, hippocampal-sparing. inv., inverted. LP, limbic-predominant.

Supplementary Table 3 Summary statistics of cross-sectional stage effects derived from partial correlation predicting numeric outcome variables.

Sample	Sample	Subtype (n)	PCC	Fisher's z-transformed PCC	SE	95% C.I.	p	τ^2	I ²	Pooled p_{raw}	Pooled p_{FDR}
Outcome: age (years)											
Pooled	Whole sample	HS (1963)		0.09	0.05	[-0.01; 0.19]		0.01	76.33	< .001***	.100
Pooled	Whole sample	LP (1767)		-0.05	0.05	[-0.15; 0.05]		0.01	73.41	< .001***	.457
Pooled	A β -positive	HS (525)		0.08	0.08	[-0.08; 0.23]		0.02	65.11	< .001***	.426
Pooled	A β -positive	LP (518)		0.02	0.10	[-0.16; 0.21]		0.04	77.46	< .001***	.946
A4/LEARN-3T	Whole sample	HS (347)	0.18	0.18	0.05	[0.08; 0.28]	< .001***				
A4/LEARN-3T	Whole sample	LP (81)	0.29	0.29	0.11	[0.07; 0.48]	.010**				
A4/LEARN-3T	A β -positive	HS (191)	0.26	0.27	0.07	[0.12; 0.39]	< .001***				
A4/LEARN-3T	A β -positive	LP (56)	0.28	0.29	0.14	[0.02; 0.51]	.039*				
ADNI-3T	Whole sample	HS (289)	0.07	0.07	0.06	[-0.05; 0.18]	.249				
ADNI-3T	Whole sample	LP (225)	-0.07	-0.07	0.07	[-0.20; 0.07]	.329				
ADNI-3T	A β -positive	HS (143)	0.07	0.07	0.09	[-0.09; 0.23]	.395				
ADNI-3T	A β -positive	LP (145)	-0.01	-0.01	0.08	[-0.18; 0.15]	.867				
DELCODE-3T	Whole sample	HS (254)	0.13	0.13	0.06	[0.00; 0.24]	.047*				
DELCODE-3T	Whole sample	LP (265)	0.00	0.00	0.06	[-0.12; 0.12]	.972				
DELCODE-3T	A β -positive	HS (71)	0.19	0.19	0.12	[-0.05; 0.41]	.124				
DELCODE-3T	A β -positive	LP (132)	0.01	0.01	0.09	[-0.16; 0.18]	.902				
NACC-3T	Whole sample	HS (698)	-0.07	-0.07	0.04	[-0.14; 0.00]	.062				
NACC-3T	Whole sample	LP (784)	-0.18	-0.18	0.04	[-0.25; -0.11]	< .001***				
NACC-3T	A β -positive	HS (64)	-0.15	-0.15	0.13	[-0.38; 0.10]	.247				
NACC-3T	A β -positive	LP (98)	-0.29	-0.30	0.10	[-0.47; -0.10]	.004**				
ADNI-1.5T	Whole sample	HS (170)	-0.03	-0.03	0.08	[-0.18; 0.12]	.672				
ADNI-1.5T	Whole sample	LP (200)	-0.04	-0.04	0.07	[-0.18; 0.10]	.573				
ADNI-1.5T	A β -positive	HS (56)	-0.10	-0.10	0.14	[-0.36; 0.17]	.469				
ADNI-1.5T	A β -positive	LP (87)	0.19	0.19	0.11	[-0.02; 0.39]	.083				
ARWIBO-1.5T	Whole sample	HS (38)	0.09	0.09	0.17	[-0.25; 0.40]	.611				
ARWIBO-1.5T	Whole sample	LP (54)	-0.25	-0.25	0.14	[-0.49; 0.03]	.079				
NACC-1.5T	Whole sample	HS (167)	0.28	0.29	0.08	[0.14; 0.42]	< .001***				
NACC-1.5T	Whole sample	LP (158)	-0.07	-0.07	0.08	[-0.22; 0.09]	.406				
Outcome: education (years)											
Pooled	Whole sample	HS (1820)		-0.06	0.02	[-0.11; -0.02]		0.00	0.00	< .001***	.015*
Pooled	Whole sample	LP (1646)		-0.01	0.03	[-0.07; 0.05]		0.00	19.17	< .001***	.867
Pooled	A β -positive	HS (518)		0.01	0.04	[-0.08; 0.09]		0.00	0.00	< .001***	.910
Pooled	A β -positive	LP (507)		0.00	0.06	[-0.13; 0.12]		0.01	47.36	< .001***	.986
A4/LEARN-3T	Whole sample	HS (347)	0.01	0.01	0.05	[-0.10; 0.11]	.863				
A4/LEARN-3T	Whole sample	LP (81)	0.20	0.21	0.11	[-0.02; 0.40]	.071				
A4/LEARN-3T	A β -positive	HS (191)	0.02	0.02	0.07	[-0.12; 0.16]	.788				
A4/LEARN-3T	A β -positive	LP (56)	0.28	0.29	0.14	[0.02; 0.51]	.035*				
ADNI-3T	Whole sample	HS (281)	-0.09	-0.09	0.06	[-0.20; 0.03]	.143				
ADNI-3T	Whole sample	LP (220)	-0.12	-0.12	0.07	[-0.24; 0.02]	.088				
ADNI-3T	A β -positive	HS (140)	-0.02	-0.02	0.09	[-0.19; 0.14]	.792				
ADNI-3T	A β -positive	LP (143)	-0.14	-0.14	0.09	[-0.29; 0.03]	.109				
DELCODE-3T	Whole sample	HS (254)	-0.07	-0.07	0.06	[-0.19; 0.05]	.271				
DELCODE-3T	Whole sample	LP (265)	-0.07	-0.07	0.06	[-0.19; 0.05]	.275				
DELCODE-3T	A β -positive	HS (71)	-0.01	-0.01	0.12	[-0.25; 0.23]	.930				
DELCODE-3T	A β -positive	LP (132)	-0.03	-0.03	0.09	[-0.21; 0.14]	.700				
NACC-3T	Whole sample	HS (613)	-0.08	-0.09	0.04	[-0.16; -0.01]	.036*				
NACC-3T	Whole sample	LP (714)	-0.02	-0.02	0.04	[-0.09; 0.06]	.661				
NACC-3T	A β -positive	HS (60)	0.05	0.05	0.13	[-0.21; 0.30]	.710				
NACC-3T	A β -positive	LP (90)	-0.07	-0.07	0.11	[-0.28; 0.14]	.497				
ADNI-1.5T	Whole sample	HS (168)	0.01	0.01	0.08	[-0.14; 0.16]	.910				
ADNI-1.5T	Whole sample	LP (199)	0.06	0.06	0.07	[-0.08; 0.19]	.428				
ADNI-1.5T	A β -positive	HS (56)	0.00	0.00	0.14	[-0.27; 0.27]	.984				
ADNI-1.5T	A β -positive	LP (86)	0.07	0.07	0.11	[-0.15; 0.28]	.544				
ARWIBO-1.5T	Whole sample	HS (20)	0.22	0.22	0.25	[-0.26; 0.61]	.374				
ARWIBO-1.5T	Whole sample	LP (26)	0.01	0.01	0.22	[-0.39; 0.41]	.951				
NACC-1.5T	Whole sample	HS (137)	-0.20	-0.20	0.09	[-0.35; -0.03]	.023*				

Sample	Sample	Subtype (n)	PCC	Fisher's z-transformed PCC	SE	95% C.I.	p	τ^2	I ²	Pooled p_{raw}	Pooled p_{FDR}
NACC-1.5T	Whole sample	LP (141)	0.06	0.06	0.09	[-0.11; 0.22]	.489				
Outcome: FAQ (inv.)											
Pooled	Whole sample	HS (1265)		-0.09	0.05	[-0.18; 0.00]		0.01	53.16	< .001***	.059
Pooled	Whole sample	LP (1292)		-0.19	0.03	[-0.25; -0.14]		0.00	0.00	< .001***	< .001***
Pooled	A β -positive	HS (317)		-0.23	0.06	[-0.35; -0.11]		0.00	0.00	< .001***	< .001***
Pooled	A β -positive	LP (431)		-0.10	0.06	[-0.22; 0.03]		0.01	36.47	< .001***	.247
ADNI-3T	Whole sample	HS (266)	-0.23	-0.23	0.06	[-0.34; -0.11]	< .001***				
ADNI-3T	Whole sample	LP (203)	-0.22	-0.23	0.07	[-0.35; -0.09]	.002**				
ADNI-3T	A β -positive	HS (140)	-0.21	-0.21	0.09	[-0.36; -0.04]	.017*				
ADNI-3T	A β -positive	LP (142)	-0.20	-0.20	0.09	[-0.36; -0.03]	.020*				
DELCODE-3T	Whole sample	HS (248)	-0.10	-0.10	0.06	[-0.22; 0.03]	.125				
DELCODE-3T	Whole sample	LP (260)	-0.18	-0.18	0.06	[-0.29; -0.05]	.005**				
DELCODE-3T	A β -positive	HS (68)	-0.18	-0.19	0.13	[-0.41; 0.07]	.153				
DELCODE-3T	A β -positive	LP (130)	-0.12	-0.12	0.09	[-0.29; 0.06]	.200				
NACC-3T	Whole sample	HS (514)	-0.08	-0.08	0.04	[-0.16; 0.01]	.075				
NACC-3T	Whole sample	LP (560)	-0.21	-0.21	0.04	[-0.28; -0.12]	< .001***				
NACC-3T	A β -positive	HS (53)	-0.29	-0.30	0.15	[-0.53; 0.00]	.048*				
NACC-3T	A β -positive	LP (73)	0.13	0.13	0.12	[-0.11; 0.36]	.283				
ADNI-1.5T	Whole sample	HS (168)	-0.05	-0.05	0.08	[-0.20; 0.11]	.553				
ADNI-1.5T	Whole sample	LP (198)	-0.11	-0.11	0.07	[-0.25; 0.03]	.114				
ADNI-1.5T	A β -positive	HS (56)	-0.27	-0.27	0.15	[-0.51; 0.01]	.062				
ADNI-1.5T	A β -positive	LP (86)	-0.13	-0.13	0.11	[-0.34; 0.09]	.241				
NACC-1.5T	Whole sample	HS (69)	0.15	0.15	0.13	[-0.10; 0.38]	.250				
NACC-1.5T	Whole sample	LP (71)	-0.22	-0.22	0.13	[-0.44; 0.03]	.080				
Outcome: MMSE											
Pooled	Whole sample	HS (1790)		-0.10	0.04	[-0.18; -0.01]		0.01	61.20	< .001***	.034*
Pooled	Whole sample	LP (1605)		-0.20	0.05	[-0.30; -0.10]		0.01	67.26	< .001***	< .001***
Pooled	A β -positive	HS (514)		-0.10	0.08	[-0.26; 0.05]		0.02	61.10	< .001***	.271
Pooled	A β -positive	LP (499)		-0.19	0.05	[-0.28; -0.10]		0.00	0.00	< .001***	< .001***
A4/LEARN-3T	Whole sample	HS (346)	0.03	0.03	0.05	[-0.08; 0.13]	.642				
A4/LEARN-3T	Whole sample	LP (81)	-0.02	-0.02	0.12	[-0.24; 0.21]	.879				
A4/LEARN-3T	A β -positive	HS (191)	0.06	0.06	0.07	[-0.08; 0.21]	.389				
A4/LEARN-3T	A β -positive	LP (56)	-0.07	-0.07	0.14	[-0.34; 0.21]	.614				
ADNI-3T	Whole sample	HS (281)	-0.24	-0.24	0.06	[-0.35; -0.12]	< .001***				
ADNI-3T	Whole sample	LP (220)	-0.14	-0.14	0.07	[-0.27; -0.01]	.036*				
ADNI-3T	A β -positive	HS (140)	-0.32	-0.33	0.09	[-0.46; -0.16]	< .001***				
ADNI-3T	A β -positive	LP (143)	-0.21	-0.22	0.09	[-0.37; -0.05]	.012*				
DELCODE-3T	Whole sample	HS (254)	-0.05	-0.05	0.06	[-0.17; 0.08]	.439				
DELCODE-3T	Whole sample	LP (264)	-0.15	-0.15	0.06	[-0.27; -0.03]	.014*				
DELCODE-3T	A β -positive	HS (71)	-0.06	-0.06	0.13	[-0.30; 0.18]	.608				
DELCODE-3T	A β -positive	LP (131)	-0.13	-0.13	0.09	[-0.30; 0.04]	.136				
NACC-3T	Whole sample	HS (593)	-0.15	-0.15	0.04	[-0.23; -0.07]	< .001***				
NACC-3T	Whole sample	LP (680)	-0.29	-0.30	0.04	[-0.36; -0.22]	< .001***				
NACC-3T	A β -positive	HS (56)	-0.10	-0.10	0.15	[-0.37; 0.18]	.474				
NACC-3T	A β -positive	LP (83)	-0.22	-0.22	0.12	[-0.42; 0.01]	.056				
ADNI-1.5T	Whole sample	HS (168)	-0.01	-0.01	0.08	[-0.16; 0.15]	.930				
ADNI-1.5T	Whole sample	LP (199)	-0.08	-0.08	0.07	[-0.22; 0.06]	.253				
ADNI-1.5T	A β -positive	HS (56)	-0.08	-0.08	0.15	[-0.35; 0.20]	.573				
ADNI-1.5T	A β -positive	LP (86)	-0.25	-0.26	0.11	[-0.45; -0.03]	.024*				
ARWIBO-1.5T	Whole sample	HS (12)	-0.19	-0.19	0.45	[-0.79; 0.60]	.658				
ARWIBO-1.5T	Whole sample	LP (21)	-0.54	-0.61	0.28	[-0.82; -0.06]	.030*				
NACC-1.5T	Whole sample	HS (136)	-0.15	-0.15	0.09	[-0.32; 0.02]	.083				
NACC-1.5T	Whole sample	LP (140)	-0.36	-0.38	0.09	[-0.50; -0.21]	< .001***				
Outcome: Logical Memory Delayed Recall											
Pooled	Whole sample	HS (1778)		-0.13	0.02	[-0.18; -0.09]		0.00	0.90	< .001***	< .001***
Pooled	Whole sample	LP (1585)		-0.10	0.03	[-0.15; -0.05]		0.00	0.00	< .001***	< .001***
Pooled	A β -positive	HS (512)		-0.18	0.05	[-0.27; -0.08]		0.00	0.02	< .001***	< .001***
Pooled	A β -positive	LP (503)		-0.04	0.05	[-0.13; 0.06]		0.00	3.33	< .001***	.767

Sample	Sample	Subtype (n)	PCC	Fisher's z-transformed PCC	SE	95% C.I.	p	τ^2	I ²	Pooled p_{raw}	Pooled p_{FDR}
A4/LEARN-3T	Whole sample	HS (341)	-0.06	-0.06	0.05	[-0.16; 0.05]	.306				
A4/LEARN-3T	Whole sample	LP (80)	-0.09	-0.09	0.12	[-0.31; 0.14]	.464				
A4/LEARN-3T	A β -positive	HS (188)	-0.12	-0.12	0.07	[-0.26; 0.02]	.094				
A4/LEARN-3T	A β -positive	LP (56)	-0.06	-0.06	0.14	[-0.33; 0.22]	.675				
ADNI-3T	Whole sample	HS (281)	-0.10	-0.10	0.06	[-0.22; 0.02]	.098				
ADNI-3T	Whole sample	LP (219)	-0.13	-0.13	0.07	[-0.26; 0.00]	.051				
ADNI-3T	A β -positive	HS (140)	-0.21	-0.22	0.09	[-0.37; -0.05]	.013*				
ADNI-3T	A β -positive	LP (143)	-0.13	-0.13	0.09	[-0.29; 0.03]	.120				
DELCODE-3T	Whole sample	HS (253)	-0.19	-0.19	0.06	[-0.31; -0.07]	.002**				
DELCODE-3T	Whole sample	LP (264)	-0.08	-0.08	0.06	[-0.20; 0.04]	.199				
DELCODE-3T	A β -positive	HS (70)	-0.27	-0.27	0.13	[-0.48; -0.02]	.033*				
DELCODE-3T	A β -positive	LP (132)	0.04	0.04	0.09	[-0.14; 0.21]	.672				
NACC-3T	Whole sample	HS (602)	-0.17	-0.17	0.04	[-0.24; -0.09]	< .001***				
NACC-3T	Whole sample	LP (690)	-0.13	-0.13	0.04	[-0.20; -0.06]	< .001***				
NACC-3T	A β -positive	HS (59)	0.01	0.01	0.14	[-0.26; 0.28]	.957				
NACC-3T	A β -positive	LP (86)	-0.09	-0.09	0.11	[-0.31; 0.13]	.417				
ADNI-1.5T	Whole sample	HS (167)	-0.14	-0.14	0.08	[-0.29; 0.02]	.084				
ADNI-1.5T	Whole sample	LP (198)	-0.03	-0.03	0.07	[-0.17; 0.11]	.678				
ADNI-1.5T	A β -positive	HS (55)	-0.31	-0.32	0.15	[-0.54; -0.03]	.031*				
ADNI-1.5T	A β -positive	LP (86)	0.09	0.09	0.11	[-0.13; 0.31]	.420				
NACC-1.5T	Whole sample	HS (134)	-0.14	-0.14	0.09	[-0.30; 0.04]	.127				
NACC-1.5T	Whole sample	LP (134)	-0.06	-0.06	0.09	[-0.23; 0.11]	.503				
Outcome: TMT B-A (inv)											
Pooled	Whole sample	HS (1144)		-0.04	0.05	[-0.15; 0.07]		0.01	64.48	< .001***	.510
Pooled	Whole sample	LP (1105)		-0.09	0.03	[-0.15; -0.03]		0.00	0.02	< .001***	.008**
Pooled	A β -positive	HS (252)		-0.12	0.09	[-0.30; 0.06]		0.01	35.40	< .001***	.271
Pooled	A β -positive	LP (339)		-0.11	0.07	[-0.25; 0.03]		0.01	30.09	< .001***	.247
ADNI-3T	Whole sample	HS (249)	-0.20	-0.20	0.06	[-0.32; -0.07]	.002**				
ADNI-3T	Whole sample	LP (180)	-0.20	-0.20	0.08	[-0.34; -0.05]	.008**				
ADNI-3T	A β -positive	HS (123)	-0.22	-0.22	0.09	[-0.39; -0.04]	.018*				
ADNI-3T	A β -positive	LP (122)	-0.22	-0.22	0.09	[-0.39; -0.04]	.018*				
DELCODE-3T	Whole sample	HS (234)	-0.07	-0.07	0.07	[-0.20; 0.06]	.315				
DELCODE-3T	Whole sample	LP (207)	-0.02	-0.02	0.07	[-0.15; 0.12]	.814				
DELCODE-3T	A β -positive	HS (57)	0.12	0.12	0.14	[-0.17; 0.38]	.419				
DELCODE-3T	A β -positive	LP (89)	0.06	0.06	0.11	[-0.16; 0.27]	.619				
NACC-3T	Whole sample	HS (455)	0.00	0.00	0.05	[-0.10; 0.09]	.932				
NACC-3T	Whole sample	LP (473)	-0.09	-0.09	0.05	[-0.18; 0.00]	.061				
NACC-3T	A β -positive	HS (33)	-0.27	-0.28	0.20	[-0.59; 0.12]	.172				
NACC-3T	A β -positive	LP (51)	-0.20	-0.20	0.15	[-0.46; 0.10]	.195				
ADNI-1.5T	Whole sample	HS (123)	-0.02	-0.02	0.09	[-0.21; 0.16]	.791				
ADNI-1.5T	Whole sample	LP (171)	-0.12	-0.12	0.08	[-0.27; 0.04]	.131				
ADNI-1.5T	A β -positive	HS (39)	-0.10	-0.10	0.18	[-0.43; 0.25]	.585				
ADNI-1.5T	A β -positive	LP (77)	-0.08	-0.08	0.12	[-0.31; 0.15]	.496				
NACC-1.5T	Whole sample	HS (83)	0.19	0.19	0.12	[-0.04; 0.40]	.101				
NACC-1.5T	Whole sample	LP (74)	0.07	0.07	0.12	[-0.17; 0.30]	.586				

* $p < .05$. ** $p < .01$. *** $p < .001$. Abbreviations: HS, hippocampal-sparing, inv., inverted. LP, limbic-predominant.

Supplementary Table 4 Summary statistics of cross-sectional subtype effects derived from logistic regression models predicting binary outcome variables.

Sample	Sample	Subtype 1 (n)	Subtype 2 (n)	Used Firth's penalization	log(OR)	SE	OR	SE	95% C.I.	p	τ^2	I ²	Pooled p_{raw}	Pooled p_{FDR}
Outcome: female versus male sex														
Pooled	Whole sample	HS (1963)	A- (4685)	no	0.03	0.11	1.03	1.11	[0.84; 1.28]		0.05	65.50	.766	.842
Pooled	Whole sample	LP (1767)	A- (4685)	no	0.05	0.15	1.05	1.16	[0.79; 1.40]		0.10	72.36	.715	.842
Pooled	Whole sample	LP (1767)	HS (1963)	no	0.05	0.19	1.05	1.21	[0.72; 1.53]		0.20	82.95	.814	.866
Pooled	A β -positive	HS (525)	A- (893)	no	0.27	0.12	1.31	1.12	[1.04; 1.65]		0.00	0.00	.020*	.033*
Pooled	A β -positive	LP (518)	A- (893)	no	0.00	0.24	1.00	1.28	[0.62; 1.62]		0.18	62.79	.990	.990
Pooled	A β -positive	LP (518)	HS (525)	no	-0.23	0.29	0.80	1.33	[0.45; 1.40]		0.31	75.32	.431	.517
A4/LEARN-3T	Whole sample	HS (347)	A- (809)	no	0.40	0.13	1.49	1.14	[1.10; 2.02]	.006**				
A4/LEARN-3T	Whole sample	LP (81)	A- (809)	no	-0.57	0.27	0.56	1.31	[0.30; 1.06]	.082				
A4/LEARN-3T	Whole sample	LP (81)	HS (347)	no	-0.97	0.28	0.38	1.32	[0.20; 0.73]	.001**				
A4/LEARN-3T	A β -positive	HS (191)	A- (458)	no	0.38	0.17	1.46	1.19	[0.97; 2.20]	.073				
A4/LEARN-3T	A β -positive	LP (56)	A- (458)	no	-0.77	0.34	0.46	1.40	[0.21; 1.02]	.056				
A4/LEARN-3T	A β -positive	LP (56)	HS (191)	no	-1.16	0.35	0.31	1.42	[0.14; 0.72]	.003**				
ADNI-3T	Whole sample	HS (289)	A- (538)	no	-0.13	0.15	0.88	1.16	[0.62; 1.25]	.670				
ADNI-3T	Whole sample	LP (225)	A- (538)	no	0.31	0.18	1.36	1.20	[0.89; 2.09]	.209				
ADNI-3T	Whole sample	LP (225)	HS (289)	no	0.44	0.19	1.55	1.21	[0.99; 2.42]	.054				
ADNI-3T	A β -positive	HS (143)	A- (162)	no	0.09	0.24	1.09	1.28	[0.62; 1.94]	.929				
ADNI-3T	A β -positive	LP (145)	A- (162)	no	0.55	0.26	1.74	1.30	[0.94; 3.23]	.090				
ADNI-3T	A β -positive	LP (145)	HS (143)	no	0.47	0.25	1.59	1.28	[0.89; 2.83]	.141				
DELCODE-3T	Whole sample	HS (254)	A- (392)	no	-0.17	0.16	0.84	1.18	[0.57; 1.23]	.533				
DELCODE-3T	Whole sample	LP (265)	A- (392)	no	-0.16	0.18	0.85	1.20	[0.55; 1.31]	.663				
DELCODE-3T	Whole sample	LP (265)	HS (254)	no	0.02	0.19	1.02	1.21	[0.65; 1.58]	.996				
DELCODE-3T	A β -positive	HS (71)	A- (77)	no	-0.02	0.35	0.98	1.42	[0.43; 2.22]	.998				
DELCODE-3T	A β -positive	LP (132)	A- (77)	no	0.07	0.34	1.08	1.41	[0.48; 2.39]	.975				
DELCODE-3T	A β -positive	LP (132)	HS (71)	no	0.09	0.31	1.10	1.37	[0.53; 2.28]	.953				
NACC-3T	Whole sample	HS (698)	A- (2319)	no	0.20	0.09	1.23	1.10	[0.99; 1.53]	.074				
NACC-3T	Whole sample	LP (784)	A- (2319)	no	0.03	0.10	1.03	1.10	[0.82; 1.29]	.963				
NACC-3T	Whole sample	LP (784)	HS (698)	no	-0.18	0.11	0.84	1.12	[0.64; 1.09]	.244				
NACC-3T	A β -positive	HS (64)	A- (152)	no	0.37	0.32	1.45	1.37	[0.69; 3.04]	.470				
NACC-3T	A β -positive	LP (98)	A- (152)	no	-0.23	0.31	0.79	1.37	[0.38; 1.65]	.738				
NACC-3T	A β -positive	LP (98)	HS (64)	no	-0.60	0.34	0.55	1.41	[0.24; 1.22]	.185				
ADNI-1.5T	Whole sample	HS (170)	A- (236)	no	0.00	0.23	1.00	1.26	[0.59; 1.71]	.999				
ADNI-1.5T	Whole sample	LP (200)	A- (236)	no	0.62	0.23	1.86	1.26	[1.08; 3.20]	.020*				
ADNI-1.5T	Whole sample	LP (200)	HS (170)	no	0.62	0.22	1.86	1.25	[1.11; 3.11]	.014*				
ADNI-1.5T	A β -positive	HS (56)	A- (44)	no	0.46	0.46	1.59	1.58	[0.54; 4.63]	.568				
ADNI-1.5T	A β -positive	LP (87)	A- (44)	no	0.40	0.44	1.49	1.56	[0.53; 4.21]	.639				
ADNI-1.5T	A β -positive	LP (87)	HS (56)	no	-0.06	0.36	0.94	1.43	[0.41; 2.17]	.983				
ARWIBO-1.5T	Whole sample	HS (38)	A- (59)	no	0.23	0.42	1.25	1.53	[0.47; 3.38]	.853				
ARWIBO-1.5T	Whole sample	LP (54)	A- (59)	no	0.52	0.43	1.68	1.54	[0.61; 4.61]	.451				
ARWIBO-1.5T	Whole sample	LP (54)	HS (38)	no	0.29	0.48	1.34	1.62	[0.43; 4.16]	.819				
NACC-1.5T	Whole sample	HS (167)	A- (332)	no	-0.34	0.20	0.71	1.22	[0.45; 1.14]	.205				
NACC-1.5T	Whole sample	LP (158)	A- (332)	no	-0.22	0.23	0.81	1.26	[0.47; 1.38]	.615				
NACC-1.5T	Whole sample	LP (158)	HS (167)	no	0.12	0.24	1.13	1.27	[0.65; 1.96]	.860				
Outcome: APOE ϵ4 carrier versus non-carrier														
Pooled	Whole sample	HS (1767)	A- (4127)	no	0.11	0.06	1.11	1.06	[0.99; 1.26]		0.00	0.00	.082	.129
Pooled	Whole sample	LP (1519)	A- (4127)	no	0.54	0.08	1.72	1.08	[1.47; 2.01]		0.01	11.46	< .001***	< .001***
Pooled	Whole sample	LP (1519)	HS (1767)	no	0.43	0.08	1.53	1.08	[1.32; 1.78]		0.00	0.00	< .001***	< .001***
Pooled	A β -positive	HS (509)	A- (873)	no	0.12	0.12	1.13	1.13	[0.89; 1.43]		0.00	0.00	.317	.410
Pooled	A β -positive	LP (495)	A- (873)	no	0.61	0.15	1.84	1.16	[1.37; 2.48]		0.00	0.00	< .001***	< .001***
Pooled	A β -positive	LP (495)	HS (509)	no	0.51	0.15	1.66	1.16	[1.23; 2.23]		0.00	0.00	< .001***	.002**
A4/LEARN-3T	Whole sample	HS (347)	A- (809)	no	0.07	0.13	1.07	1.14	[0.79; 1.46]	.861				
A4/LEARN-3T	Whole sample	LP (81)	A- (809)	no	0.37	0.24	1.45	1.27	[0.83; 2.55]	.263				
A4/LEARN-3T	Whole sample	LP (81)	HS (347)	no	0.30	0.25	1.36	1.29	[0.75; 2.46]	.453				
A4/LEARN-3T	A β -positive	HS (191)	A- (458)	no	0.04	0.17	1.04	1.19	[0.69; 1.57]	.968				
A4/LEARN-3T	A β -positive	LP (56)	A- (458)	no	0.37	0.30	1.44	1.35	[0.72; 2.89]	.435				
A4/LEARN-3T	A β -positive	LP (56)	HS (191)	no	0.32	0.32	1.38	1.37	[0.66; 2.91]	.566				
ADNI-3T	Whole sample	HS (273)	A- (501)	no	0.26	0.16	1.30	1.17	[0.89; 1.89]	.234				

Sample	Sample	Subtype 1 (n)	Subtype 2 (n)	Used Firth's penalization	log(OR)	SE	OR	SE	95% C.I.	p	τ^2	I ²	Pooled p_{raw}	Pooled p_{FDR}
ADNI-3T	Whole sample	LP (207)	A- (501)	no	0.74	0.19	2.10	1.21	[1.33; 3.32]	< .001***				
ADNI-3T	Whole sample	LP (207)	HS (273)	no	0.48	0.20	1.62	1.22	[1.01; 2.60]	.044*				
ADNI-3T	A β -positive	HS (141)	A- (162)	no	0.30	0.25	1.35	1.29	[0.75; 2.45]	.454				
ADNI-3T	A β -positive	LP (144)	A- (162)	no	0.77	0.29	2.17	1.34	[1.09; 4.31]	.022*				
ADNI-3T	A β -positive	LP (144)	HS (141)	no	0.47	0.28	1.60	1.33	[0.82; 3.12]	.219				
DELCODE-3T	Whole sample	HS (254)	A- (392)	no	0.03	0.18	1.04	1.20	[0.68; 1.58]	.980				
DELCODE-3T	Whole sample	LP (265)	A- (392)	no	0.51	0.19	1.67	1.21	[1.07; 2.62]	.021*				
DELCODE-3T	Whole sample	LP (265)	HS (254)	no	0.48	0.20	1.61	1.22	[1.02; 2.56]	.039*				
DELCODE-3T	A β -positive	HS (71)	A- (77)	no	0.20	0.35	1.22	1.42	[0.54; 2.77]	.838				
DELCODE-3T	A β -positive	LP (132)	A- (77)	no	0.67	0.36	1.95	1.43	[0.85; 4.48]	.146				
DELCODE-3T	A β -positive	LP (132)	HS (71)	no	0.47	0.33	1.60	1.39	[0.74; 3.44]	.323				
NACC-3T	Whole sample	HS (555)	A- (1852)	no	0.03	0.10	1.03	1.11	[0.80; 1.31]	.963				
NACC-3T	Whole sample	LP (611)	A- (1852)	no	0.40	0.11	1.49	1.11	[1.16; 1.93]	< .001***				
NACC-3T	Whole sample	LP (611)	HS (555)	no	0.37	0.13	1.45	1.13	[1.08; 1.95]	.008**				
NACC-3T	A β -positive	HS (50)	A- (132)	no	0.33	0.35	1.39	1.43	[0.61; 3.19]	.623				
NACC-3T	A β -positive	LP (76)	A- (132)	no	0.51	0.36	1.67	1.44	[0.71; 3.91]	.340				
NACC-3T	A β -positive	LP (76)	HS (50)	no	0.18	0.41	1.20	1.51	[0.46; 3.14]	.898				
ADNI-1.5T	Whole sample	HS (170)	A- (236)	no	0.32	0.22	1.38	1.25	[0.82; 2.33]	.321				
ADNI-1.5T	Whole sample	LP (200)	A- (236)	no	0.81	0.23	2.26	1.26	[1.31; 3.89]	.001**				
ADNI-1.5T	Whole sample	LP (200)	HS (170)	no	0.49	0.22	1.64	1.25	[0.97; 2.77]	.072				
ADNI-1.5T	A β -positive	HS (56)	A- (44)	no	-0.39	0.44	0.68	1.55	[0.24; 1.90]	.650				
ADNI-1.5T	A β -positive	LP (87)	A- (44)	no	0.86	0.47	2.37	1.59	[0.79; 7.08]	.154				
ADNI-1.5T	A β -positive	LP (87)	HS (56)	no	1.25	0.41	3.50	1.50	[1.35; 9.09]	.006**				
ARWIBO-1.5T	Whole sample	HS (8)	A- (16)	no	0.73	1.29	2.07	3.65	[0.10; 42.99]	.841				
ARWIBO-1.5T	Whole sample	LP (4)	A- (16)	no	2.34	1.33	10.33	3.79	[0.45; 234.98]	.186				
ARWIBO-1.5T	Whole sample	LP (4)	HS (8)	no	1.61	1.38	5.00	3.97	[0.20; 126.47]	.473				
NACC-1.5T	Whole sample	HS (160)	A- (321)	no	0.15	0.21	1.17	1.23	[0.72; 1.89]	.735				
NACC-1.5T	Whole sample	LP (151)	A- (321)	no	0.62	0.24	1.86	1.27	[1.07; 3.25]	.024*				
NACC-1.5T	Whole sample	LP (151)	HS (160)	no	0.47	0.24	1.60	1.28	[0.90; 2.84]	.135				
Outcome: Aβ positive versus negative														
Pooled	Whole sample	HS (1037)	A- (2123)	no	0.30	0.17	1.35	1.19	[0.96; 1.90]		0.10	70.39	.090	.129
Pooled	Whole sample	LP (727)	A- (123)	no	0.64	0.14	1.89	1.15	[1.43; 2.48]		0.02	25.42	< .001***	< .001***
Pooled	Whole sample	LP (727)	HS (1037)	no	0.31	0.13	1.37	1.13	[1.07; 1.75]		0.00	0.00	.013*	.022*
A4/LEARN-3T	Whole sample	HS (347)	A- (809)	no	-0.12	0.16	0.89	1.17	[0.61; 1.29]	.737				
A4/LEARN-3T	Whole sample	LP (81)	A- (809)	no	0.30	0.30	1.34	1.35	[0.66; 2.72]	.589				
A4/LEARN-3T	Whole sample	LP (81)	HS (347)	no	0.41	0.32	1.51	1.37	[0.72; 3.19]	.396				
ADNI-3T	Whole sample	HS (268)	A- (490)	no	0.55	0.17	1.73	1.18	[1.17; 2.56]	.003**				
ADNI-3T	Whole sample	LP (200)	A- (490)	no	0.83	0.21	2.29	1.24	[1.40; 3.76]	< .001***				
ADNI-3T	Whole sample	LP (200)	HS (268)	no	0.28	0.22	1.32	1.25	[0.79; 2.22]	.418				
DELCODE-3T	Whole sample	HS (211)	A- (309)	no	0.21	0.22	1.23	1.24	[0.74; 2.05]	.593				
DELCODE-3T	Whole sample	LP (212)	A- (309)	no	0.68	0.23	1.97	1.26	[1.15; 3.37]	.009**				
DELCODE-3T	Whole sample	LP (212)	HS (211)	no	0.47	0.24	1.60	1.27	[0.92; 2.78]	.119				
NACC-3T	Whole sample	HS (139)	A- (403)	no	0.10	0.23	1.11	1.26	[0.65; 1.91]	.893				
NACC-3T	Whole sample	LP (129)	A- (403)	no	0.22	0.30	1.24	1.35	[0.61; 2.52]	.749				
NACC-3T	Whole sample	LP (129)	HS (139)	no	0.11	0.34	1.12	1.40	[0.51; 2.46]	.938				
ADNI-1.5T	Whole sample	HS (72)	A- (112)	no	1.05	0.37	2.87	1.45	[1.20; 6.90]	.013*				
ADNI-1.5T	Whole sample	LP (105)	A- (112)	no	1.14	0.36	3.12	1.44	[1.33; 7.32]	.005**				
ADNI-1.5T	Whole sample	LP (105)	HS (72)	no	0.08	0.41	1.09	1.50	[0.42; 2.83]	.977				
Outcome: MCI versus CU diagnosis														
Pooled	Whole sample	HS (1323)	A- (3724)	no	0.68	0.13	1.97	1.14	[1.51; 2.55]		0.05	54.89	< .001***	< .001***
Pooled	Whole sample	LP (1003)	A- (3724)	no	1.95	0.13	7.05	1.14	[5.49; 9.05]		0.03	34.93	< .001***	< .001***
Pooled	Whole sample	LP (1003)	HS (1323)	no	1.24	0.10	3.47	1.10	[2.86; 4.20]		0.00	0.00	< .001***	< .001***
Pooled	A β -positive	HS (242)	A- (409)	no	0.70	0.18	2.02	1.20	[1.41; 2.88]		0.00	0.00	< .001***	< .001***
Pooled	A β -positive	LP (243)	A- (409)	no	2.00	0.22	7.36	1.24	[4.81; 11.25]		0.00	0.00	< .001***	< .001***
Pooled	A β -positive	LP (243)	HS (242)	no	1.28	0.27	3.60	1.32	[2.10; 6.16]		0.08	26.30	< .001***	< .001***
ADNI-3T	Whole sample	HS (247)	A- (523)	no	0.43	0.16	1.54	1.17	[1.06; 2.23]	.020*				
ADNI-3T	Whole sample	LP (134)	A- (523)	no	1.97	0.25	7.17	1.28	[4.01; 12.83]	< .001***				
ADNI-3T	Whole sample	LP (134)	HS (247)	no	1.54	0.27	4.67	1.30	[2.50; 8.70]	< .001***				

Sample	Sample	Subtype 1 (n)	Subtype 2 (n)	Used Firth's penalization	log(OR)	SE	OR	SE	95% C.I.	p	τ^2	I ²	Pooled p_{raw}	Pooled p_{FDR}
ADNI-3T	A β -positive	HS (105)	A- (150)	no	0.84	0.28	2.32	1.32	[1.21; 4.44]	.007**				
ADNI-3T	A β -positive	LP (75)	A- (150)	no	2.28	0.41	9.75	1.50	[3.76; 25.29]	< .001***				
ADNI-3T	A β -positive	LP (75)	HS (105)	no	1.44	0.43	4.20	1.53	[1.55; 11.43]	.002**				
DELCODE-3T	Whole sample	HS (234)	A- (389)	no	0.88	0.25	2.42	1.29	[1.34; 4.36]	.001**				
DELCODE-3T	Whole sample	LP (185)	A- (389)	no	2.01	0.24	7.45	1.27	[4.28; 12.97]	< .001***				
DELCODE-3T	Whole sample	LP (185)	HS (234)	no	1.13	0.23	3.08	1.26	[1.79; 5.31]	< .001***				
DELCODE-3T	A β -positive	HS (56)	A- (77)	no	0.85	0.42	2.33	1.52	[0.87; 6.22]	.108				
DELCODE-3T	A β -positive	LP (72)	A- (77)	no	1.55	0.38	4.72	1.46	[1.93; 11.52]	< .001***				
DELCODE-3T	A β -positive	LP (72)	HS (56)	no	0.71	0.38	2.03	1.47	[0.83; 4.96]	.154				
NACC-3T	Whole sample	HS (573)	A- (2255)	no	0.61	0.12	1.84	1.12	[1.40; 2.43]	< .001***				
NACC-3T	Whole sample	LP (492)	A- (2255)	no	1.75	0.11	5.78	1.12	[4.47; 7.48]	< .001***				
NACC-3T	Whole sample	LP (492)	HS (573)	no	1.14	0.14	3.14	1.15	[2.28; 4.32]	< .001***				
NACC-3T	A β -positive	HS (46)	A- (142)	no	0.42	0.36	1.52	1.44	[0.65; 3.54]	.483				
NACC-3T	A β -positive	LP (47)	A- (142)	no	2.22	0.41	9.18	1.51	[3.51; 24.03]	< .001***				
NACC-3T	A β -positive	LP (47)	HS (46)	no	1.80	0.48	6.06	1.62	[1.95; 18.82]	< .001***				
ADNI-1.5T	Whole sample	HS (121)	A- (224)	no	1.17	0.25	3.24	1.28	[1.82; 5.75]	< .001***				
ADNI-1.5T	Whole sample	LP (115)	A- (224)	no	2.28	0.31	9.82	1.37	[4.72; 20.46]	< .001***				
ADNI-1.5T	Whole sample	LP (115)	HS (121)	no	1.11	0.34	3.04	1.41	[1.35; 6.80]	.004**				
ADNI-1.5T	A β -positive	HS (35)	A- (40)	no	0.58	0.51	1.78	1.67	[0.54; 5.92]	.494				
ADNI-1.5T	A β -positive	LP (49)	A- (40)	no	2.01	0.64	7.49	1.89	[1.68; 33.49]	.005**				
ADNI-1.5T	A β -positive	LP (49)	HS (35)	no	1.43	0.68	4.20	1.97	[0.85; 20.66]	.088				
ARWIBO-1.5T	Whole sample	HS (34)	A- (52)	no	-0.59	0.58	0.56	1.79	[0.14; 2.19]	.573				
ARWIBO-1.5T	Whole sample	LP (26)	A- (52)	no	1.08	0.55	2.94	1.73	[0.81; 10.67]	.123				
ARWIBO-1.5T	Whole sample	LP (26)	HS (34)	no	1.67	0.65	5.29	1.91	[1.16; 24.00]	.027*				
NACC-1.5T	Whole sample	HS (114)	A- (281)	no	0.81	0.26	2.25	1.30	[1.22; 4.16]	.005**				
NACC-1.5T	Whole sample	LP (51)	A- (281)	no	2.56	0.36	12.93	1.44	[5.53; 30.26]	< .001***				
NACC-1.5T	Whole sample	LP (51)	HS (114)	no	1.75	0.38	5.74	1.47	[2.33; 14.13]	< .001***				
Outcome: DAT versus CU/MCI diagnosis														
Pooled	Whole sample	HS (1616)	A- (3876)	no	1.55	0.32	4.70	1.38	[2.50; 8.83]		0.48	84.59	< .001***	< .001***
Pooled	Whole sample	LP (1686)	A- (3876)	no	2.77	0.18	15.98	1.20	[11.19; 22.83]		0.10	56.74	< .001***	< .001***
Pooled	Whole sample	LP (1686)	HS (1616)	no	1.19	0.17	3.28	1.19	[2.34; 4.59]		0.11	68.78	< .001***	< .001***
Pooled	A β -positive	HS (334)	A- (435)	no	1.62	0.24	5.03	1.27	[3.14; 8.07]		0.00	0.00	< .001***	< .001***
Pooled	A β -positive	LP (462)	A- (435)	no	2.47	0.23	11.85	1.25	[7.60; 18.48]		0.00	0.00	< .001***	< .001***
Pooled	A β -positive	LP (462)	HS (334)	no	0.81	0.16	2.24	1.17	[1.64; 3.06]		0.00	0.00	< .001***	< .001***
ADNI-3T	Whole sample	HS (289)	A- (538)	no	1.72	0.31	5.61	1.36	[2.73; 11.50]	< .001***				
ADNI-3T	Whole sample	LP (225)	A- (538)	no	3.08	0.29	21.68	1.34	[10.95; 42.92]	< .001***				
ADNI-3T	Whole sample	LP (225)	HS (289)	no	1.35	0.22	3.87	1.24	[2.33; 6.43]	< .001***				
ADNI-3T	A β -positive	HS (143)	A- (162)	no	1.50	0.35	4.46	1.42	[1.96; 10.14]	< .001***				
ADNI-3T	A β -positive	LP (145)	A- (162)	no	2.40	0.34	11.06	1.40	[5.00; 24.48]	< .001***				
ADNI-3T	A β -positive	LP (145)	HS (143)	no	0.91	0.26	2.48	1.29	[1.36; 4.51]	.001**				
DELCODE-3T	Whole sample	HS (254)	A- (392)	no	2.36	0.58	10.60	1.79	[2.71; 41.53]	< .001***				
DELCODE-3T	Whole sample	LP (265)	A- (392)	no	3.68	0.55	39.68	1.74	[10.88; 144.74]	< .001***				
DELCODE-3T	Whole sample	LP (265)	HS (254)	no	1.32	0.27	3.74	1.32	[1.97; 7.13]	< .001***				
DELCODE-3T	A β -positive	HS (71)	A- (77)	no	3.95	1.45	51.78	4.24	[1.75; 1531.30]	.017*				
DELCODE-3T	A β -positive	LP (132)	A- (77)	no	4.78	1.42	119.27	4.15	[4.25; 3349.95]	.002**				
DELCODE-3T	A β -positive	LP (132)	HS (71)	no	0.83	0.35	2.30	1.42	[1.01; 5.27]	.047*				
NACC-3T	Whole sample	HS (698)	A- (2319)	no	2.07	0.16	7.95	1.17	[5.45; 11.60]	< .001***				
NACC-3T	Whole sample	LP (784)	A- (2319)	no	3.00	0.15	20.16	1.16	[14.30; 28.43]	< .001***				
NACC-3T	Whole sample	LP (784)	HS (698)	no	0.93	0.12	2.53	1.13	[1.89; 3.40]	< .001***				
NACC-3T	A β -positive	HS (64)	A- (152)	no	1.62	0.42	5.06	1.53	[1.87; 13.67]	< .001***				
NACC-3T	A β -positive	LP (98)	A- (152)	no	2.68	0.38	14.60	1.46	[5.99; 35.58]	< .001***				
NACC-3T	A β -positive	LP (98)	HS (64)	no	1.06	0.35	2.89	1.42	[1.26; 6.62]	.008**				
ADNI-1.5T	Whole sample	HS (170)	A- (236)	no	2.04	0.34	7.66	1.41	[3.44; 17.07]	< .001***				
ADNI-1.5T	Whole sample	LP (200)	A- (236)	no	2.62	0.33	13.68	1.39	[6.32; 29.63]	< .001***				
ADNI-1.5T	Whole sample	LP (200)	HS (170)	no	0.58	0.23	1.79	1.25	[1.05; 3.04]	.028*				
ADNI-1.5T	A β -positive	HS (56)	A- (44)	no	1.57	0.57	4.78	1.77	[1.25; 18.31]	.017*				
ADNI-1.5T	A β -positive	LP (87)	A- (44)	no	1.87	0.55	6.52	1.73	[1.80; 23.56]	.002**				
ADNI-1.5T	A β -positive	LP (87)	HS (56)	no	0.31	0.36	1.36	1.43	[0.59; 3.17]	.665				

Sample	Sample	Subtype 1 (n)	Subtype 2 (n)	Used Firth's penalization	log(<i>OR</i>)	<i>SE</i>	<i>OR</i>	<i>SE</i>	95% C.I.	<i>p</i>	τ^2	I^2	Pooled <i>p</i> _{raw}	Pooled <i>p</i> _{FDR}
ARWIBO-1.5T	Whole sample	HS (38)	A- (59)	no	-0.07	0.64	0.93	1.89	[0.21; 4.17]	.994				
ARWIBO-1.5T	Whole sample	LP (54)	A- (59)	no	1.89	0.48	6.63	1.62	[2.14; 20.49]	< .001***				
ARWIBO-1.5T	Whole sample	LP (54)	HS (38)	no	1.96	0.58	7.10	1.78	[1.84; 27.46]	.002**				
NACC-1.5T	Whole sample	HS (167)	A- (332)	no	0.84	0.23	2.31	1.26	[1.35; 3.94]	< .001***				
NACC-1.5T	Whole sample	LP (158)	A- (332)	no	2.40	0.23	11.07	1.26	[6.46; 18.96]	< .001***				
NACC-1.5T	Whole sample	LP (158)	HS (167)	no	1.57	0.24	4.80	1.27	[2.72; 8.48]	< .001***				

p* < .05. *p* < .01. ****p* < .001. Abbreviations: A-, atrophy negative. HS, hippocampal-sparing. LP, limbic-predominant.

Supplementary Table 5 Summary statistics of cross-sectional stage effects derived from logistic regression models predicting binary outcome variables.

Sample	Sample	Subtype (n)	Used Firth's penalization	log(OR)	SE	OR	SE	95% C.I.	p	τ^2	I ²	Pooled p_{raw}	Pooled p_{FDR}
Outcome: female versus male sex													
Pooled	Whole sample	HS (3926)		-0.01	0.01	0.99	1.01	[0.96; 1.02]		0.00	0.00	.604	.604
Pooled	Whole sample	LP (3534)		-0.02	0.02	0.98	1.02	[0.95; 1.01]		0.00	0.00	.282	.442
Pooled	A β -positive	HS (1050)		0.02	0.03	1.02	1.03	[0.96; 1.09]		0.00	0.00	.439	.488
Pooled	A β -positive	LP (1036)		0.01	0.03	1.01	1.03	[0.95; 1.06]		0.00	0.00	.851	.946
A4/LEARN-3T	Whole sample	HS (347)	no	0.16	0.08	1.17	1.08	[1.00; 1.37]	.051				
A4/LEARN-3T	Whole sample	HS (347)	no	0.16	0.08	1.17	1.08	[1.00; 1.37]	.051				
A4/LEARN-3T	Whole sample	LP (81)	no	0.00	0.28	1.00	1.33	[0.57; 1.73]	.991				
A4/LEARN-3T	Whole sample	LP (81)	no	0.00	0.28	1.00	1.33	[0.57; 1.73]	.991				
A4/LEARN-3T	A β -positive	HS (191)	no	0.14	0.10	1.15	1.11	[0.94; 1.41]	.166				
A4/LEARN-3T	A β -positive	HS (191)	no	0.14	0.10	1.15	1.11	[0.94; 1.41]	.166				
A4/LEARN-3T	A β -positive	LP (56)	no	0.03	0.31	1.03	1.36	[0.56; 1.87]	.933				
A4/LEARN-3T	A β -positive	LP (56)	no	0.03	0.31	1.03	1.36	[0.56; 1.87]	.933				
ADNI-3T	Whole sample	HS (289)	no	-0.04	0.06	0.96	1.07	[0.85; 1.09]	.569				
ADNI-3T	Whole sample	HS (289)	no	-0.04	0.06	0.96	1.07	[0.85; 1.09]	.569				
ADNI-3T	Whole sample	LP (225)	no	0.03	0.05	1.03	1.06	[0.93; 1.15]	.550				
ADNI-3T	Whole sample	LP (225)	no	0.03	0.05	1.03	1.06	[0.93; 1.15]	.550				
ADNI-3T	A β -positive	HS (143)	no	-0.04	0.08	0.96	1.08	[0.83; 1.12]	.640				
ADNI-3T	A β -positive	HS (143)	no	-0.04	0.08	0.96	1.08	[0.83; 1.12]	.640				
ADNI-3T	A β -positive	LP (145)	no	0.02	0.06	1.02	1.06	[0.90; 1.15]	.735				
ADNI-3T	A β -positive	LP (145)	no	0.02	0.06	1.02	1.06	[0.90; 1.15]	.735				
DELCODE-3T	Whole sample	HS (254)	no	-0.05	0.07	0.95	1.08	[0.82; 1.10]	.531				
DELCODE-3T	Whole sample	HS (254)	no	-0.05	0.07	0.95	1.08	[0.82; 1.10]	.531				
DELCODE-3T	Whole sample	LP (265)	no	-0.05	0.06	0.95	1.06	[0.84; 1.08]	.440				
DELCODE-3T	Whole sample	LP (265)	no	-0.05	0.06	0.95	1.06	[0.84; 1.08]	.440				
DELCODE-3T	A β -positive	HS (71)	no	-0.07	0.12	0.93	1.13	[0.74; 1.18]	.569				
DELCODE-3T	A β -positive	HS (71)	no	-0.07	0.12	0.93	1.13	[0.74; 1.18]	.569				
DELCODE-3T	A β -positive	LP (132)	no	-0.03	0.08	0.97	1.09	[0.83; 1.15]	.763				
DELCODE-3T	A β -positive	LP (132)	no	-0.03	0.08	0.97	1.09	[0.83; 1.15]	.763				
NACC-3T	Whole sample	HS (698)	no	0.01	0.04	1.01	1.04	[0.93; 1.10]	.799				
NACC-3T	Whole sample	HS (698)	no	0.01	0.04	1.01	1.04	[0.93; 1.10]	.799				
NACC-3T	Whole sample	LP (784)	no	-0.02	0.03	0.98	1.03	[0.92; 1.04]	.501				
NACC-3T	Whole sample	LP (784)	no	-0.02	0.03	0.98	1.03	[0.92; 1.04]	.501				
NACC-3T	A β -positive	HS (64)	no	-0.07	0.12	0.94	1.13	[0.74; 1.19]	.598				
NACC-3T	A β -positive	HS (64)	no	-0.07	0.12	0.94	1.13	[0.74; 1.19]	.598				
NACC-3T	A β -positive	LP (98)	no	0.09	0.11	1.10	1.12	[0.88; 1.36]	.402				
NACC-3T	A β -positive	LP (98)	no	0.09	0.11	1.10	1.12	[0.88; 1.36]	.402				
ADNI-1.5T	Whole sample	HS (170)	no	0.02	0.06	1.02	1.06	[0.92; 1.14]	.702				
ADNI-1.5T	Whole sample	HS (170)	no	0.02	0.06	1.02	1.06	[0.92; 1.14]	.702				
ADNI-1.5T	Whole sample	LP (200)	no	-0.05	0.06	0.95	1.06	[0.84; 1.07]	.375				
ADNI-1.5T	Whole sample	LP (200)	no	-0.05	0.06	0.95	1.06	[0.84; 1.07]	.375				
ADNI-1.5T	A β -positive	HS (56)	no	0.12	0.09	1.13	1.10	[0.94; 1.35]	.192				
ADNI-1.5T	A β -positive	HS (56)	no	0.12	0.09	1.13	1.10	[0.94; 1.35]	.192				
ADNI-1.5T	A β -positive	LP (87)	yes	-0.06	0.09	0.94	1.10	[0.78; 1.13]	.541				
ADNI-1.5T	A β -positive	LP (87)	yes	-0.06	0.09	0.94	1.10	[0.78; 1.13]	.541				
ARWIBO-1.5T	Whole sample	HS (38)	no	-0.03	0.20	0.97	1.22	[0.65; 1.43]	.867				
ARWIBO-1.5T	Whole sample	HS (38)	no	-0.03	0.20	0.97	1.22	[0.65; 1.43]	.867				
ARWIBO-1.5T	Whole sample	LP (54)	no	-0.07	0.13	0.93	1.13	[0.73; 1.19]	.582				
ARWIBO-1.5T	Whole sample	LP (54)	no	-0.07	0.13	0.93	1.13	[0.73; 1.19]	.582				
NACC-1.5T	Whole sample	HS (167)	no	-0.04	0.03	0.96	1.03	[0.90; 1.02]	.210				
NACC-1.5T	Whole sample	HS (167)	no	-0.04	0.03	0.96	1.03	[0.90; 1.02]	.210				
NACC-1.5T	Whole sample	LP (158)	no	0.03	0.07	1.03	1.07	[0.90; 1.17]	.683				
NACC-1.5T	Whole sample	LP (158)	no	0.03	0.07	1.03	1.07	[0.90; 1.17]	.683				
Outcome: APOE ϵ4 carrier versus non-carrier													
Pooled	Whole sample	HS (3526)		0.06	0.02	1.06	1.02	[1.03; 1.09]		0.00	0.00	< .001***	< .001***
Pooled	Whole sample	LP (3030)		0.01	0.02	1.01	1.02	[0.97; 1.05]		0.00	14.75	.530	.648
Pooled	A β -positive	HS (1018)		0.05	0.03	1.05	1.03	[0.98; 1.12]		0.00	0.02	.134	.269

Sample	Sample	Subtype (n)	Used Firth's penalization	log(OR)	SE	OR	SE	95% C.I.	p	τ^2	I ²	Pooled p_{raw}	Pooled p_{FDR}
Pooled	A β -positive	LP (990)		0.01	0.04	1.01	1.04	[0.94; 1.08]		0.00	0.01	.747	.946
A4/LEARN-3T	Whole sample	HS (347)	no	0.06	0.08	1.06	1.08	[0.91; 1.24]	.463				
A4/LEARN-3T	Whole sample	HS (347)	no	0.06	0.08	1.06	1.08	[0.91; 1.24]	.463				
A4/LEARN-3T	Whole sample	LP (81)	no	0.42	0.30	1.52	1.35	[0.84; 2.75]	.168				
A4/LEARN-3T	Whole sample	LP (81)	no	0.42	0.30	1.52	1.35	[0.84; 2.75]	.168				
A4/LEARN-3T	A β -positive	HS (191)	no	0.00	0.10	1.00	1.10	[0.82; 1.22]	.986				
A4/LEARN-3T	A β -positive	HS (191)	no	0.00	0.10	1.00	1.10	[0.82; 1.22]	.986				
A4/LEARN-3T	A β -positive	LP (56)	no	0.66	0.49	1.94	1.63	[0.75; 5.03]	.175				
A4/LEARN-3T	A β -positive	LP (56)	no	0.66	0.49	1.94	1.63	[0.75; 5.03]	.175				
ADNI-3T	Whole sample	HS (273)	no	0.11	0.07	1.11	1.07	[0.98; 1.27]	.111				
ADNI-3T	Whole sample	HS (273)	no	0.11	0.07	1.11	1.07	[0.98; 1.27]	.111				
ADNI-3T	Whole sample	LP (207)	no	0.06	0.06	1.06	1.07	[0.94; 1.21]	.337				
ADNI-3T	Whole sample	LP (207)	no	0.06	0.06	1.06	1.07	[0.94; 1.21]	.337				
ADNI-3T	A β -positive	HS (141)	no	0.07	0.09	1.07	1.09	[0.90; 1.27]	.434				
ADNI-3T	A β -positive	HS (141)	no	0.07	0.09	1.07	1.09	[0.90; 1.27]	.434				
ADNI-3T	A β -positive	LP (144)	no	0.02	0.08	1.02	1.09	[0.87; 1.20]	.793				
ADNI-3T	A β -positive	LP (144)	no	0.02	0.08	1.02	1.09	[0.87; 1.20]	.793				
DELCODE-3T	Whole sample	HS (254)	no	0.19	0.08	1.21	1.08	[1.04; 1.41]	.013*				
DELCODE-3T	Whole sample	HS (254)	no	0.19	0.08	1.21	1.08	[1.04; 1.41]	.013*				
DELCODE-3T	Whole sample	LP (265)	no	-0.04	0.06	0.96	1.07	[0.85; 1.09]	.545				
DELCODE-3T	Whole sample	LP (265)	no	-0.04	0.06	0.96	1.07	[0.85; 1.09]	.545				
DELCODE-3T	A β -positive	HS (71)	no	0.24	0.13	1.27	1.14	[0.98; 1.64]	.071				
DELCODE-3T	A β -positive	HS (71)	no	0.24	0.13	1.27	1.14	[0.98; 1.64]	.071				
DELCODE-3T	A β -positive	LP (132)	no	0.00	0.09	1.00	1.09	[0.83; 1.19]	.973				
DELCODE-3T	A β -positive	LP (132)	no	0.00	0.09	1.00	1.09	[0.83; 1.19]	.973				
NACC-3T	Whole sample	HS (555)	no	0.00	0.05	1.00	1.05	[0.92; 1.10]	.918				
NACC-3T	Whole sample	HS (555)	no	0.00	0.05	1.00	1.05	[0.92; 1.10]	.918				
NACC-3T	Whole sample	LP (611)	no	0.04	0.04	1.04	1.04	[0.96; 1.12]	.328				
NACC-3T	Whole sample	LP (611)	no	0.04	0.04	1.04	1.04	[0.96; 1.12]	.328				
NACC-3T	A β -positive	HS (50)	no	-0.21	0.14	0.81	1.15	[0.61; 1.08]	.149				
NACC-3T	A β -positive	HS (50)	no	-0.21	0.14	0.81	1.15	[0.61; 1.08]	.149				
NACC-3T	A β -positive	LP (76)	no	0.07	0.13	1.07	1.14	[0.83; 1.38]	.602				
NACC-3T	A β -positive	LP (76)	no	0.07	0.13	1.07	1.14	[0.83; 1.38]	.602				
ADNI-1.5T	Whole sample	HS (170)	no	0.07	0.05	1.07	1.05	[0.96; 1.19]	.208				
ADNI-1.5T	Whole sample	HS (170)	no	0.07	0.05	1.07	1.05	[0.96; 1.19]	.208				
ADNI-1.5T	Whole sample	LP (200)	no	-0.11	0.07	0.89	1.07	[0.79; 1.02]	.088				
ADNI-1.5T	Whole sample	LP (200)	no	-0.11	0.07	0.89	1.07	[0.79; 1.02]	.088				
ADNI-1.5T	A β -positive	HS (56)	no	0.09	0.10	1.09	1.10	[0.91; 1.32]	.360				
ADNI-1.5T	A β -positive	HS (56)	no	0.09	0.10	1.09	1.10	[0.91; 1.32]	.360				
ADNI-1.5T	A β -positive	LP (87)	yes	-0.09	0.13	0.92	1.14	[0.71; 1.22]	.525				
ADNI-1.5T	A β -positive	LP (87)	yes	-0.09	0.13	0.92	1.14	[0.71; 1.22]	.525				
ARWIBO-1.5T	Whole sample	HS (8)	no	-0.41	0.83	0.66	2.30	[0.13; 3.38]	.619				
NACC-1.5T	Whole sample	HS (160)	no	0.04	0.04	1.04	1.04	[0.97; 1.12]	.260				
NACC-1.5T	Whole sample	HS (160)	no	0.04	0.04	1.04	1.04	[0.97; 1.12]	.260				
NACC-1.5T	Whole sample	LP (151)	no	0.08	0.08	1.08	1.08	[0.93; 1.25]	.321				
NACC-1.5T	Whole sample	LP (151)	no	0.08	0.08	1.08	1.08	[0.93; 1.25]	.321				
Outcome: Aβ positive versus negative													
Pooled	Whole sample	HS (2074)		0.18	0.03	1.20	1.03	[1.13; 1.28]		0.00	0.00	< .001***	< .001***
Pooled	Whole sample	LP (1454)		0.00	0.03	1.00	1.03	[0.94; 1.07]		0.00	0.00	.908	.908
A4/LEARN-3T	Whole sample	HS (347)	no	0.11	0.10	1.12	1.11	[0.91; 1.37]	.279				
A4/LEARN-3T	Whole sample	HS (347)	no	0.11	0.10	1.12	1.11	[0.91; 1.37]	.279				
A4/LEARN-3T	Whole sample	LP (81)	no	-0.24	0.37	0.79	1.45	[0.38; 1.63]	.525				
A4/LEARN-3T	Whole sample	LP (81)	no	-0.24	0.37	0.79	1.45	[0.38; 1.63]	.525				
ADNI-3T	Whole sample	HS (268)	no	0.27	0.09	1.31	1.09	[1.10; 1.55]	.002**				
ADNI-3T	Whole sample	HS (268)	no	0.27	0.09	1.31	1.09	[1.10; 1.55]	.002**				
ADNI-3T	Whole sample	LP (200)	no	0.09	0.08	1.09	1.08	[0.94; 1.26]	.244				
ADNI-3T	Whole sample	LP (200)	no	0.09	0.08	1.09	1.08	[0.94; 1.26]	.244				
DELCODE-3T	Whole sample	HS (211)	no	0.20	0.09	1.23	1.10	[1.02; 1.47]	.029*				

Sample	Sample	Subtype (n)	Used Firth's penalization	log(OR)	SE	OR	SE	95% C.I.	p	τ^2	I ²	Pooled p_{raw}	Pooled p_{FDR}
DELCODE-3T	Whole sample	HS (211)	no	0.20	0.09	1.23	1.10	[1.02; 1.47]	.029*				
DELCODE-3T	Whole sample	LP (212)	no	-0.01	0.08	0.99	1.08	[0.85; 1.16]	.920				
DELCODE-3T	Whole sample	LP (212)	no	-0.01	0.08	0.99	1.08	[0.85; 1.16]	.920				
NACC-3T	Whole sample	HS (139)	no	0.25	0.13	1.28	1.14	[1.00; 1.66]	.053				
NACC-3T	Whole sample	HS (139)	no	0.25	0.13	1.28	1.14	[1.00; 1.66]	.053				
NACC-3T	Whole sample	LP (129)	no	-0.11	0.14	0.90	1.15	[0.68; 1.19]	.451				
NACC-3T	Whole sample	LP (129)	no	-0.11	0.14	0.90	1.15	[0.68; 1.19]	.451				
ADNI-1.5T	Whole sample	HS (72)	no	0.05	0.11	1.05	1.11	[0.85; 1.30]	.658				
ADNI-1.5T	Whole sample	HS (72)	no	0.05	0.11	1.05	1.11	[0.85; 1.30]	.658				
ADNI-1.5T	Whole sample	LP (105)	no	-0.09	0.13	0.91	1.14	[0.71; 1.17]	.472				
ADNI-1.5T	Whole sample	LP (105)	no	-0.09	0.13	0.91	1.14	[0.71; 1.17]	.472				
Outcome: MCI versus CU diagnosis													
Pooled	Whole sample	HS (2646)		0.22	0.04	1.24	1.05	[1.14; 1.35]		0.01	72.60	< .001***	< .001***
Pooled	Whole sample	LP (2006)		0.38	0.06	1.46	1.06	[1.31; 1.64]		0.01	36.17	< .001***	< .001***
Pooled	A β -positive	HS (484)		0.26	0.06	1.29	1.06	[1.15; 1.45]		0.00	0.00	< .001***	< .001***
Pooled	A β -positive	LP (486)		0.24	0.07	1.27	1.08	[1.09; 1.47]		0.00	0.00	.002**	.005**
ADNI-3T	Whole sample	HS (247)	no	0.28	0.09	1.32	1.09	[1.11; 1.56]	.001**				
ADNI-3T	Whole sample	HS (247)	no	0.28	0.09	1.32	1.09	[1.11; 1.56]	.001**				
ADNI-3T	Whole sample	LP (134)	no	0.21	0.14	1.23	1.15	[0.93; 1.63]	.144				
ADNI-3T	Whole sample	LP (134)	no	0.21	0.14	1.23	1.15	[0.93; 1.63]	.144				
ADNI-3T	A β -positive	HS (105)	no	0.28	0.13	1.33	1.13	[1.04; 1.70]	.025*				
ADNI-3T	A β -positive	HS (105)	no	0.28	0.13	1.33	1.13	[1.04; 1.70]	.025*				
ADNI-3T	A β -positive	LP (75)	no	0.17	0.18	1.19	1.20	[0.83; 1.70]	.349				
ADNI-3T	A β -positive	LP (75)	no	0.17	0.18	1.19	1.20	[0.83; 1.70]	.349				
DELCODE-3T	Whole sample	HS (234)	no	0.29	0.10	1.33	1.10	[1.10; 1.61]	.003**				
DELCODE-3T	Whole sample	HS (234)	no	0.29	0.10	1.33	1.10	[1.10; 1.61]	.003**				
DELCODE-3T	Whole sample	LP (185)	no	0.55	0.12	1.73	1.13	[1.37; 2.19]	< .001***				
DELCODE-3T	Whole sample	LP (185)	no	0.55	0.12	1.73	1.13	[1.37; 2.19]	< .001***				
DELCODE-3T	A β -positive	HS (56)	no	0.09	0.15	1.09	1.17	[0.81; 1.48]	.553				
DELCODE-3T	A β -positive	HS (56)	no	0.09	0.15	1.09	1.17	[0.81; 1.48]	.553				
DELCODE-3T	A β -positive	LP (72)	no	0.23	0.14	1.25	1.15	[0.96; 1.64]	.097				
DELCODE-3T	A β -positive	LP (72)	no	0.23	0.14	1.25	1.15	[0.96; 1.64]	.097				
NACC-3T	Whole sample	HS (573)	no	0.25	0.06	1.28	1.06	[1.14; 1.45]	< .001***				
NACC-3T	Whole sample	HS (573)	no	0.25	0.06	1.28	1.06	[1.14; 1.45]	< .001***				
NACC-3T	Whole sample	LP (492)	no	0.40	0.08	1.49	1.09	[1.26; 1.75]	< .001***				
NACC-3T	Whole sample	LP (492)	no	0.40	0.08	1.49	1.09	[1.26; 1.75]	< .001***				
NACC-3T	A β -positive	HS (46)	no	0.39	0.20	1.47	1.22	[0.99; 2.18]	.055				
NACC-3T	A β -positive	HS (46)	no	0.39	0.20	1.47	1.22	[0.99; 2.18]	.055				
NACC-3T	A β -positive	LP (47)	no	1.47	0.87	4.34	2.39	[0.79; 23.89]	.091				
NACC-3T	A β -positive	LP (47)	no	1.47	0.87	4.34	2.39	[0.79; 23.89]	.091				
ADNI-1.5T	Whole sample	HS (121)	no	0.35	0.10	1.41	1.11	[1.15; 1.73]	< .001***				
ADNI-1.5T	Whole sample	HS (121)	no	0.35	0.10	1.41	1.11	[1.15; 1.73]	< .001***				
ADNI-1.5T	Whole sample	LP (115)	no	1.09	0.49	2.97	1.62	[1.15; 7.68]	.025*				
ADNI-1.5T	Whole sample	LP (115)	no	1.09	0.49	2.97	1.62	[1.15; 7.68]	.025*				
ADNI-1.5T	A β -positive	HS (35)	no	0.37	0.23	1.45	1.25	[0.93; 2.25]	.101				
ADNI-1.5T	A β -positive	HS (35)	no	0.37	0.23	1.45	1.25	[0.93; 2.25]	.101				
ADNI-1.5T	A β -positive	LP (49)	no	0.44	0.50	1.55	1.65	[0.59; 4.12]	.376				
ADNI-1.5T	A β -positive	LP (49)	no	0.44	0.50	1.55	1.65	[0.59; 4.12]	.376				
ARWIBO-1.5T	Whole sample	HS (34)	no	0.31	0.28	1.36	1.32	[0.79; 2.35]	.269				
ARWIBO-1.5T	Whole sample	HS (34)	no	0.31	0.28	1.36	1.32	[0.79; 2.35]	.269				
ARWIBO-1.5T	Whole sample	LP (26)	no	-0.01	0.21	0.99	1.24	[0.65; 1.49]	.945				
ARWIBO-1.5T	Whole sample	LP (26)	no	-0.01	0.21	0.99	1.24	[0.65; 1.49]	.945				
NACC-1.5T	Whole sample	HS (114)	no	-0.01	0.04	0.99	1.04	[0.91; 1.08]	.816				
NACC-1.5T	Whole sample	HS (114)	no	-0.01	0.04	0.99	1.04	[0.91; 1.08]	.816				
NACC-1.5T	Whole sample	LP (51)	no	0.73	0.39	2.07	1.47	[0.97; 4.42]	.061				
NACC-1.5T	Whole sample	LP (51)	no	0.73	0.39	2.07	1.47	[0.97; 4.42]	.061				
Outcome: DAT versus CU/MCI diagnosis													
Pooled	Whole sample	HS (3232)		0.46	0.08	1.58	1.09	[1.34; 1.86]		0.07	94.15	< .001***	< .001***

Sample	Sample	Subtype (n)	Used Firth's penalization	log(OR)	SE	OR	SE	95% C.I.	p	τ^2	I ²	Pooled p_{raw}	Pooled p_{FDR}
Pooled	Whole sample	LP (3372)		0.33	0.04	1.39	1.04	[1.29; 1.50]		0.01	71.35	< .001***	< .001***
Pooled	A β -positive	HS (668)		0.42	0.06	1.53	1.06	[1.36; 1.71]		0.01	40.77	< .001***	< .001***
Pooled	A β -positive	LP (924)		0.27	0.04	1.31	1.04	[1.21; 1.42]		0.00	34.12	< .001***	< .001***
ADNI-3T	Whole sample	HS (289)	no	0.60	0.09	1.82	1.09	[1.53; 2.16]	< .001***				
ADNI-3T	Whole sample	HS (289)	no	0.60	0.09	1.82	1.09	[1.53; 2.16]	< .001***				
ADNI-3T	Whole sample	LP (225)	no	0.20	0.06	1.22	1.06	[1.09; 1.37]	< .001***				
ADNI-3T	Whole sample	LP (225)	no	0.20	0.06	1.22	1.06	[1.09; 1.37]	< .001***				
ADNI-3T	A β -positive	HS (143)	no	0.49	0.10	1.63	1.10	[1.35; 1.96]	< .001***				
ADNI-3T	A β -positive	HS (143)	no	0.49	0.10	1.63	1.10	[1.35; 1.96]	< .001***				
ADNI-3T	A β -positive	LP (145)	no	0.16	0.07	1.17	1.07	[1.03; 1.34]	.017*				
ADNI-3T	A β -positive	LP (145)	no	0.16	0.07	1.17	1.07	[1.03; 1.34]	.017*				
DELCODE-3T	Whole sample	HS (254)	no	0.90	0.16	2.45	1.17	[1.80; 3.33]	< .001***				
DELCODE-3T	Whole sample	HS (254)	no	0.90	0.16	2.45	1.17	[1.80; 3.33]	< .001***				
DELCODE-3T	Whole sample	LP (265)	no	0.41	0.07	1.51	1.07	[1.31; 1.73]	< .001***				
DELCODE-3T	Whole sample	LP (265)	no	0.41	0.07	1.51	1.07	[1.31; 1.73]	< .001***				
DELCODE-3T	A β -positive	HS (71)	no	0.91	0.25	2.48	1.29	[1.51; 4.08]	< .001***				
DELCODE-3T	A β -positive	HS (71)	no	0.91	0.25	2.48	1.29	[1.51; 4.08]	< .001***				
DELCODE-3T	A β -positive	LP (132)	no	0.39	0.10	1.48	1.10	[1.22; 1.80]	< .001***				
DELCODE-3T	A β -positive	LP (132)	no	0.39	0.10	1.48	1.10	[1.22; 1.80]	< .001***				
NACC-3T	Whole sample	HS (698)	no	0.68	0.06	1.97	1.06	[1.76; 2.21]	< .001***				
NACC-3T	Whole sample	HS (698)	no	0.68	0.06	1.97	1.06	[1.76; 2.21]	< .001***				
NACC-3T	Whole sample	LP (784)	no	0.51	0.05	1.67	1.05	[1.52; 1.83]	< .001***				
NACC-3T	Whole sample	LP (784)	no	0.51	0.05	1.67	1.05	[1.52; 1.83]	< .001***				
NACC-3T	A β -positive	HS (64)	no	0.37	0.14	1.45	1.15	[1.10; 1.92]	.008**				
NACC-3T	A β -positive	HS (64)	no	0.37	0.14	1.45	1.15	[1.10; 1.92]	.008**				
NACC-3T	A β -positive	LP (98)	no	0.24	0.13	1.28	1.14	[0.99; 1.64]	.059				
NACC-3T	A β -positive	LP (98)	no	0.24	0.13	1.28	1.14	[0.99; 1.64]	.059				
ADNI-1.5T	Whole sample	HS (170)	no	0.25	0.06	1.29	1.06	[1.16; 1.44]	< .001***				
ADNI-1.5T	Whole sample	HS (170)	no	0.25	0.06	1.29	1.06	[1.16; 1.44]	< .001***				
ADNI-1.5T	Whole sample	LP (200)	no	0.33	0.07	1.40	1.07	[1.22; 1.60]	< .001***				
ADNI-1.5T	Whole sample	LP (200)	no	0.33	0.07	1.40	1.07	[1.22; 1.60]	< .001***				
ADNI-1.5T	A β -positive	HS (56)	no	0.26	0.10	1.30	1.10	[1.07; 1.57]	.007**				
ADNI-1.5T	A β -positive	HS (56)	no	0.26	0.10	1.30	1.10	[1.07; 1.57]	.007**				
ADNI-1.5T	A β -positive	LP (87)	no	0.35	0.11	1.42	1.12	[1.14; 1.78]	.002**				
ADNI-1.5T	A β -positive	LP (87)	no	0.35	0.11	1.42	1.12	[1.14; 1.78]	.002**				
ARWIBO-1.5T	Whole sample	HS (38)	no	0.23	0.23	1.26	1.25	[0.81; 1.96]	.312				
ARWIBO-1.5T	Whole sample	HS (38)	no	0.23	0.23	1.26	1.25	[0.81; 1.96]	.312				
ARWIBO-1.5T	Whole sample	LP (54)	no	0.24	0.14	1.27	1.15	[0.97; 1.66]	.085				
ARWIBO-1.5T	Whole sample	LP (54)	no	0.24	0.14	1.27	1.15	[0.97; 1.66]	.085				
NACC-1.5T	Whole sample	HS (167)	no	0.12	0.04	1.13	1.04	[1.05; 1.22]	.002**				
NACC-1.5T	Whole sample	HS (167)	no	0.12	0.04	1.13	1.04	[1.05; 1.22]	.002**				
NACC-1.5T	Whole sample	LP (158)	no	0.21	0.09	1.23	1.10	[1.03; 1.47]	.024*				
NACC-1.5T	Whole sample	LP (158)	no	0.21	0.09	1.23	1.10	[1.03; 1.47]	.024*				

* $p < .05$. ** $p < .01$. *** $p < .001$. Abbreviations: HS, hippocampal-sparing. LP, limbic-predominant.

Supplementary Table 6 Summary statistics of atrophy subtype and stage effects on regional CenTauR scores, extracted from linear regression models.

ROI	Predictor	Estimate	95% C.I.	SE	t	p
Frontal	Atrophy subtype (LP)	0.44	[-5.83; 6.71]	3.19	0.14	.891
	Atrophy stage (spline 1)	26.87	[9.28; 44.46]	8.95	3.00	.003**
	Atrophy stage (spline 2)	71.40	[44.82; 97.98]	13.53	5.28	< .001***
	Atrophy subtype (LP) × atrophy stage (spline 1)	90.73	[54.64; 126.83]	18.37	4.94	< .001***
	Atrophy subtype (LP) × atrophy stage (spline 2)	122.86	[49.93; 195.78]	37.10	3.31	.001**
Mesial temporal	Atrophy subtype (LP)	3.06	[-3.00; 9.12]	3.08	0.99	.321
	Atrophy stage (spline 1)	23.51	[6.52; 40.51]	8.65	2.72	.007**
	Atrophy stage (spline 2)	34.42	[8.73; 60.10]	13.07	2.63	.009**
	Atrophy subtype (LP) × atrophy stage (spline 1)	58.90	[24.03; 93.77]	17.74	3.32	< .001***
	Atrophy subtype (LP) × atrophy stage (spline 2)	-8.20	[-78.65; 62.25]	35.85	-0.23	.819
Meta temporal	Atrophy subtype (LP)	1.89	[-3.87; 7.66]	2.93	0.65	.519
	Atrophy stage (spline 1)	29.05	[12.89; 45.21]	8.22	3.53	< .001***
	Atrophy stage (spline 2)	47.86	[23.44; 72.29]	12.43	3.85	< .001***
	Atrophy subtype (LP) × atrophy stage (spline 1)	77.21	[44.05; 110.38]	16.88	4.58	< .001***
	Atrophy subtype (LP) × atrophy stage (spline 2)	85.75	[18.74; 152.76]	34.09	2.52	.012*
Temporo-parietal	Atrophy subtype (LP)	1.76	[-3.42; 6.94]	2.63	0.67	.505
	Atrophy stage (spline 1)	22.54	[8.02; 37.06]	7.39	3.05	.002**
	Atrophy stage (spline 2)	49.05	[27.11; 70.99]	11.16	4.39	< .001***
	Atrophy subtype (LP) × atrophy stage (spline 1)	94.39	[64.59; 124.18]	15.16	6.23	< .001***
	Atrophy subtype (LP) × atrophy stage (spline 2)	142.49	[82.30; 202.69]	30.63	4.65	< .001***
Universal	Atrophy subtype (LP)	1.36	[-3.87; 6.59]	2.66	0.51	.609
	Atrophy stage (spline 1)	21.79	[7.13; 36.45]	7.46	2.92	.004**
	Atrophy stage (spline 2)	46.93	[24.78; 69.08]	11.27	4.16	< .001***
	Atrophy subtype (LP) × atrophy stage (spline 1)	92.92	[62.84; 123.01]	15.31	6.07	< .001***
	Atrophy subtype (LP) × atrophy stage (spline 2)	133.61	[72.84; 194.38]	30.92	4.32	< .001***

Models additionally included age, sex, APOE ε4 status, diagnosis, treatment, and PET-MRI time interval as covariates (not shown). * $p < .05$. ** $p < .01$. *** $p < .001$. Abbreviations: LP, limbic-predominant.

Supplementary Table 7 Cohort-wise summary statistics of atrophy subtype and stage effects on regional CenTauR scores while controlling for plasma p-tau biomarkers, extracted from linear regression models.

Cohort	ROI	Predictor	Estimate	95% C.I.	SE	t	p
A4	Frontal	Atrophy subtype (LP)	-1.16	[-6.73; 4.41]	2.82	-0.41	.681
		Atrophy stage	-0.57	[-2.37; 1.22]	0.91	-0.63	.530
		Atrophy subtype (LP) × atrophy stage	2.92	[-1.37; 7.21]	2.17	1.34	.181
	Mesial temporal	Atrophy subtype (LP)	4.90	[-1.25; 11.05]	3.12	1.57	.118
		Atrophy stage	0.47	[-1.52; 2.45]	1.00	0.46	.643
		Atrophy subtype (LP) × atrophy stage	4.73	[0.00; 9.47]	2.40	1.97	.050
	Meta temporal	Atrophy subtype (LP)	1.51	[-2.71; 5.73]	2.14	0.70	.482
		Atrophy stage	0.05	[-1.31; 1.41]	0.69	0.08	.939
		Atrophy subtype (LP) × atrophy stage	2.09	[-1.16; 5.34]	1.65	1.27	.205
	Temporo-parietal	Atrophy subtype (LP)	0.41	[-3.45; 4.28]	1.96	0.21	.832
		Atrophy stage	-0.53	[-1.77; 0.72]	0.63	-0.83	.405
		Atrophy subtype (LP) × atrophy stage	1.57	[-1.40; 4.55]	1.51	1.04	.298
	Universal	Atrophy subtype (LP)	0.37	[-3.60; 4.35]	2.01	0.19	.853
		Atrophy stage	-0.59	[-1.87; 0.69]	0.65	-0.91	.365
		Atrophy subtype (LP) × atrophy stage	1.77	[-1.29; 4.84]	1.55	1.14	.254
ADNI	Frontal	Atrophy subtype (LP)	3.21	[-18.70; 25.11]	11.02	0.29	.772
		Atrophy stage (spline 1)	30.44	[-25.64; 86.53]	28.21	1.08	.283
		Atrophy stage (spline 2)	61.74	[5.83; 117.64]	28.12	2.20	.031*
		Atrophy subtype (LP) × atrophy stage (spline 1)	93.75	[5.46; 182.04]	44.41	2.11	.038*
		Atrophy subtype (LP) × atrophy stage (spline 2)	127.20	[-13.54; 267.94]	70.79	1.80	.076
	Mesial temporal	Atrophy subtype (LP)	4.05	[-13.36; 21.45]	8.75	0.46	.645
		Atrophy stage (spline 1)	20.85	[-23.72; 65.41]	22.41	0.93	.355
		Atrophy stage (spline 2)	35.46	[-8.96; 79.88]	22.34	1.59	.116
		Atrophy subtype (LP) × atrophy stage (spline 1)	32.55	[-37.61; 102.70]	35.28	0.92	.359
	Meta temporal	Atrophy subtype (LP) × atrophy stage (spline 2)	-64.15	[-175.98; 47.68]	56.25	-1.14	.257
		Atrophy stage (spline 1)	3.13	[-12.75; 19.00]	7.99	0.39	.696
		Atrophy stage (spline 2)	4.04	[0.03; 8.05]	2.02	2.00	.049*
		Atrophy subtype (LP) × atrophy stage (spline 1)	3.31	[-3.58; 10.20]	3.47	0.95	.343
	Temporo-parietal	Atrophy subtype (LP) × atrophy stage (spline 2)	-1.41	[-18.04; 15.21]	8.36	-0.17	.866
		Atrophy stage (spline 1)	13.02	[-29.56; 55.59]	21.41	0.61	.545
		Atrophy stage (spline 2)	53.39	[10.95; 95.82]	21.34	2.50	.014*
		Atrophy subtype (LP) × atrophy stage (spline 1)	105.49	[38.47; 172.51]	33.71	3.13	.002**
		Atrophy subtype (LP) × atrophy stage (spline 2)	137.47	[30.63; 244.30]	53.73	2.56	.012*
	Universal	Atrophy subtype (LP)	-0.44	[-17.08; 16.20]	8.37	-0.05	.958
		Atrophy stage (spline 1)	16.10	[-26.51; 58.70]	21.43	0.75	.455
		Atrophy stage (spline 2)	50.49	[8.02; 92.96]	21.36	2.36	.020*
		Atrophy subtype (LP) × atrophy stage (spline 1)	104.51	[37.44; 171.58]	33.73	3.10	.003**
		Atrophy subtype (LP) × atrophy stage (spline 2)	128.10	[21.18; 235.02]	53.77	2.38	.019*

Models additionally included age, sex, APOE ε4 status, diagnosis, treatment, PET-MRI time interval, and plasma p-tau as covariates (not shown). * $p < .05$. ** $p < .01$. *** $p < .001$. Abbreviations: LP, limbic-predominant.

Supplementary Table 8 Summary statistics of atrophy subtype and stage effects on tau burden group in two samples, extracted from the best-fit ordinal logistic regression model.

Sample	Predictor	Estimate	95% C.I.	SE	z	p
Whole sample $\Delta AIC = -12.02$ $\Delta R^2_{Nagelkerke} = 0.04$	Age at MRI	-0.01	[-0.04; 0.03]	0.02	-0.42	.676
	Sex (female)	0.20	[-0.27; 0.67]	0.24	0.85	.397
	APOE $\epsilon 4$ carriership (carrier)	0.19	[-0.31; 0.70]	0.26	0.73	.466
	PET-MRI interval	0.00	[-0.01; 0.00]	0.00	-0.45	.656
	Diagnosis (MCI)	2.08	[1.46; 2.72]	0.32	6.45	< .001***
	Diagnosis (DAT)	2.33	[1.45; 3.23]	0.45	5.16	< .001***
	Treatment (solanezumab)	-0.11	[-0.77; 0.51]	0.33	-0.35	.729
	Atrophy stage	0.21	[0.06; 0.36]	0.08	2.80	.005**
	Atrophy subtype (LP)	0.12	[-0.47; 0.72]	0.30	0.41	.683
	Atrophy subtype (LP) $\times$ atrophy stage	0.24	[-0.03; 0.51]	0.14	1.74	.082
ATT-eligible sample $\Delta AIC = -6.42$ $\Delta R^2_{Nagelkerke} = 0.17$	Age at MRI	-0.06	[-0.13; 0.00]	0.03	-1.86	.063
	Sex (female)	0.07	[-0.87; 1.01]	0.48	0.15	.883
	APOE $\epsilon 4$ carriership (carrier)	0.39	[-0.66; 1.46]	0.54	0.73	.464
	PET-MRI interval	0.00	[-0.01; 0.01]	0.01	-0.76	.450
	Diagnosis (DAT)	-0.38	[-1.47; 0.68]	0.54	-0.70	.482
	Atrophy stage	0.39	[0.11; 0.69]	0.15	2.68	.007**
	Atrophy subtype (LP)	0.32	[-1.10; 1.77]	0.73	0.44	.662
	Atrophy subtype (LP) $\times$ atrophy stage	0.07	[-0.36; 0.50]	0.22	0.32	.751

* $p < .05$. ** $p < .01$. *** $p < .001$. Abbreviations: LP, limbic-predominant.

Supplementary Table 9 Summary statistics of LMMs predicting longitudinal PACC-5 scores using baseline atrophy subtype and stage in the preclinical AD sample.

Predictor	Estimate	SE	df	t value	p
Intercept	-2.10	0.99	1556.14	-2.13	.033*
Years (spline 1)	16.45	3.48	849.35	4.73	< .001***
Years (spline 2)	7.56	2.26	886.37	3.35	< .001***
Age at MRI	0.03	0.01	1551.65	2.01	.045*
Sex (female)	-0.02	0.12	1501.30	-0.19	.853
APOE $\epsilon 4$ carriership (carrier)	0.01	0.12	1516.57	0.06	.949
Treatment (solanezumab)	0.09	0.12	1515.32	0.82	.414
Years of education	-0.01	0.02	1571.44	-0.67	.501
Version B: Martha Jackson	-0.26	0.04	5364.18	-6.73	< .001***
Version SC: Anna Thompson	-0.82	0.16	5839.51	-5.16	< .001***
Version SC: Robert Miller	-0.90	0.04	5399.67	-20.38	< .001***
Baseline atrophy subtype (LP)	0.12	0.14	1516.34	0.83	.409
Baseline atrophy stage	0.08	0.05	1592.84	1.65	.098
Years (spline 1) $\times$ age at MRI	-0.19	0.05	848.32	-4.26	< .001***
Years (spline 2) $\times$ age at MRI	-0.11	0.03	900.60	-3.64	< .001***
Years (spline 1) $\times$ sex (female)	0.65	0.43	825.07	1.50	.133
Years (spline 2) $\times$ sex (female)	0.57	0.27	822.37	2.08	.038*
Years (spline 1) $\times$ APOE $\epsilon 4$ carriership (carrier)	-0.94	0.42	831.23	-2.25	.024*
Years (spline 2) $\times$ APOE $\epsilon 4$ carriership (carrier)	-0.91	0.27	837.09	-3.41	< .001***
Years (spline 1) $\times$ treatment (solanezumab)	-0.32	0.41	828.91	-0.80	.426
Years (spline 2) $\times$ treatment (solanezumab)	-0.27	0.26	831.26	-1.06	.289
Years (spline 1) $\times$ years of education	-0.05	0.08	849.42	-0.61	.543
Years (spline 2) $\times$ years of education	0.02	0.05	884.62	0.41	.681
Years (spline 1) $\times$ baseline atrophy subtype (LP)	-0.32	0.49	826.25	-0.66	.510
Years (spline 2) $\times$ baseline atrophy subtype (LP)	-0.81	0.31	840.67	-2.61	.009**
Years (spline 1) $\times$ baseline atrophy stage	-0.93	0.17	852.96	-5.58	< .001***
Years (spline 2) $\times$ baseline atrophy stage	-0.77	0.11	944.64	-6.97	< .001***
Baseline atrophy subtype (LP) $\times$ baseline atrophy stage	0.14	0.14	1519.31	1.01	.312
Years (spline 1) $\times$ baseline atrophy subtype (LP) $\times$ baseline atrophy stage	-1.84	0.46	824.21	-3.98	< .001***
Years (spline 2) $\times$ baseline atrophy subtype (LP) $\times$ baseline atrophy stage	-1.13	0.30	906.25	-3.77	< .001***

Formula: $PACC-5 \sim ns(years, df = 2) \times age\ at\ MRI + ns(years, df = 2) \times sex + ns(years, df = 2) \times APOE\ \epsilon 4\ carriership + ns(years, df = 2) \times treatment + ns(years, df = 2) \times years\ of\ education + version + ns(years, df = 2) \times baseline\ atrophy\ subtype \times baseline\ atrophy\ stage + (years\ | participant)$. $R^2_{marginal}$ (REML/ML) = 0.27/0.16. * $p < .05$. ** $p < .01$. *** $p < .001$. Abbreviations: LP, limbic-predominant.

Supplementary Table 10 Summary statistics of LMMs predicting longitudinal CDR-SB scores using baseline atrophy subtype and stage in the mild symptomatic AD sample.

Predictor	Estimate	SE	df	t value	p
Intercept	3.59	2.00	1739.69	1.79	.074
Years (spline 1)	-5.33	3.79	1416.18	-1.41	.160
Years (spline 2)	1.45	2.10	1422.79	0.69	.489
Age at MRI	-0.03	0.02	1744.53	-1.17	.244
Sex (female)	-0.09	0.30	1749.84	-0.32	.751
Years of education	-0.03	0.05	1708.32	-0.67	.504
APOE ε4 carriership (carrier)	-0.41	0.34	1737.39	-1.22	.224
Diagnosis (DAT)	1.78	0.33	1772.42	5.34	< .001***
Baseline atrophy subtype (LP)	0.30	0.52	1738.90	0.58	.564
Baseline atrophy stage (spline 1)	0.28	1.11	1749.30	0.25	.802
Baseline atrophy stage (spline 2)	-0.92	1.10	1727.06	-0.84	.403
Years (spline 1) × age at MRI	0.09	0.04	1399.07	2.23	.026*
Years (spline 2) × age at MRI	0.01	0.02	1426.04	0.27	.787
Years (spline 1) × sex (female)	-0.29	0.56	1412.83	-0.51	.612
Years (spline 2) × sex (female)	-0.64	0.31	1421.90	-2.08	.038*
Years (spline 1) × years of education	-0.03	0.10	1468.13	-0.28	.779
Years (spline 2) × years of education	-0.09	0.05	1414.41	-1.65	.099
Years (spline 1) × APOE ε4 carriership (carrier)	0.57	0.64	1400.28	0.89	.372
Years (spline 2) × APOE ε4 carriership (carrier)	-0.39	0.33	1417.00	-1.19	.234
Years (spline 1) × diagnosis (DAT)	3.21	0.62	1404.48	5.20	< .001***
Years (spline 2) × diagnosis (DAT)	1.44	0.52	1473.55	2.78	.005**
Years (spline 1) × baseline atrophy subtype (LP)	0.62	0.98	1397.12	0.63	.526
Years (spline 2) × baseline atrophy subtype (LP)	0.88	0.45	1400.09	1.97	.049*
Years (spline 1) × baseline atrophy stage (spline 1)	9.75	2.09	1400.86	4.66	< .001***
Years (spline 2) × baseline atrophy stage (spline 1)	8.20	1.10	1412.18	7.45	< .001***
Years (spline 1) × baseline atrophy stage (spline 2)	6.36	2.06	1412.38	3.09	.002**
Years (spline 2) × baseline atrophy stage (spline 2)	1.45	1.41	1432.67	1.03	.302
Baseline atrophy subtype (LP) × baseline atrophy stage (spline 1)	1.08	1.40	1742.45	0.77	.439
Baseline atrophy subtype (LP) × baseline atrophy stage (spline 2)	2.26	1.77	1743.41	1.28	.202
Years (spline 1) × baseline atrophy subtype (LP) × baseline atrophy stage (spline 1)	-1.44	2.65	1419.44	-0.55	.586
Years (spline 2) × baseline atrophy subtype (LP) × baseline atrophy stage (spline 1)	3.00	1.52	1421.61	1.98	.048*
Years (spline 1) × baseline atrophy subtype (LP) × baseline atrophy stage (spline 2)	-3.69	3.34	1404.66	-1.11	.269
Years (spline 2) × baseline atrophy subtype (LP) × baseline atrophy stage (spline 2)	1.61	2.52	1441.72	0.64	.525

Formula: CDR-SB ~ ns(years, $df = 2$) × age at MRI + ns(years, $df = 2$) × sex + ns(years, $df = 2$) × years of education + ns(years, $df = 2$) × APOE ε4 carriership + ns(years, $df = 2$) × baseline diagnosis + ns(years, $df = 2$) × baseline atrophy subtype × ns(baseline atrophy stage, knot = 3) + (1 | participant). R^2_{marginal} (REML/ML) = 0.48/0.49. * $p < .05$. ** $p < .01$. *** $p < .001$. Abbreviations: LP, limbic-predominant.

Supplementary Table 11 Summary statistics of LMMs predicting longitudinal PACC-5 scores using baseline atrophy subtype and stage in the preclinical AD sample, controlling for p-tau₂₁₇.

Predictor	Estimate	SE	df	t value	p
Intercept	-2.33	1.06	1350.95	-2.21	.028*
Years (spline 1)	14.29	3.59	755.73	3.99	<.001***
Years (spline 2)	3.76	2.34	784.22	1.60	.109
Age at MRI	0.03	0.01	1345.13	1.89	.059
Sex (female)	0.07	0.13	1298.23	0.51	.612
APOE ε4 carriership (carrier)	-0.03	0.13	1310.95	-0.22	.823
Treatment (solanezumab)	0.07	0.13	1308.15	0.56	.574
Years of education	-0.01	0.02	1355.58	-0.28	.776
Version B: Martha Jackson	-0.25	0.04	4627.91	-5.84	<.001***
Version SC: Anna Thompson	-0.76	0.17	5037.48	-4.50	<.001***
Version SC: Robert Miller	-0.93	0.05	4657.16	-19.35	<.001***
Baseline atrophy subtype (LP)	0.14	0.15	1312.20	0.94	.349
Baseline atrophy stage	0.08	0.05	1384.64	1.53	.126
p-tau ₂₁₇	0.35	0.42	1288.57	0.84	.404
Years (spline 1) × age at MRI	-0.13	0.05	753.81	-2.77	.006**
Years (spline 2) × age at MRI	-0.03	0.03	798.83	-0.88	.377
Years (spline 1) × sex (female)	0.26	0.45	729.13	0.57	.566
Years (spline 2) × sex (female)	0.34	0.28	718.80	1.21	.228
Years (spline 1) × APOE ε4 carriership (carrier)	-0.75	0.44	734.50	-1.71	.087
Years (spline 2) × APOE ε4 carriership (carrier)	-0.68	0.28	730.97	-2.45	.015*
Years (spline 1) × treatment (solanezumab)	0.06	0.42	731.65	0.15	.878
Years (spline 2) × treatment (solanezumab)	0.13	0.27	724.27	0.50	.620
Years (spline 1) × years of education	-0.05	0.08	748.81	-0.57	.566
Years (spline 2) × years of education	0.03	0.05	781.30	0.58	.561
Years (spline 1) × baseline atrophy subtype (LP)	-0.65	0.51	730.78	-1.27	.205
Years (spline 2) × baseline atrophy subtype (LP)	-0.98	0.33	738.26	-3.01	.003**
Years (spline 1) × p-tau ₂₁₇	-0.75	0.17	753.31	-4.39	<.001***
Years (spline 2) × p-tau ₂₁₇	-0.53	0.11	836.62	-4.62	<.001***
Years (spline 1) × baseline atrophy stage	0.15	0.14	1315.87	1.05	.294
Years (spline 2) × baseline atrophy stage	-9.29	1.39	727.14	-6.69	<.001***
Baseline atrophy subtype (LP) × baseline atrophy stage	-8.77	0.90	777.61	-9.75	<.001***
Years (spline 1) × baseline atrophy subtype (LP) × baseline atrophy stage	-1.82	0.45	730.46	-4.02	<.001***
Years (spline 2) × baseline atrophy subtype (LP) × baseline atrophy stage	-1.21	0.30	800.55	-4.11	<.001***

N = 601. Formula: PACC-5 ~ ns(years, $df = 2$) × age at MRI + ns(years, $df = 2$) × sex + ns(years, $df = 2$) × APOE ε4 carriership + ns(years, $df = 2$) × treatment + ns(years, $df = 2$) × years of education + ns(years, $df = 2$) × baseline p-tau₂₁₇ + version + ns(years, $df = 2$) × baseline atrophy subtype × baseline atrophy stage + (years | participant). R^2_{marginal} (REML/ML) = 0.34/0.22. * $p < .05$. ** $p < .01$. *** $p < .001$. Abbreviations: LP, limbic-predominant.

Supplementary Table 12 Summary statistics of LMMs predicting longitudinal CDR-SB scores using baseline atrophy subtype and stage in the mild symptomatic AD sample, controlling for p-tau₂₁₇/Aβ₄₂ ratios.

Predictor	Estimate	SE	df	t value	p
Intercept	3.04	3.10	98.36	0.98	.329
Years	1.04	1.23	223.34	0.85	.399
Age at MRI	0.01	0.03	97.02	0.22	.826
Sex (female)	-0.46	0.48	100.93	-0.95	.346
Years of education	-0.07	0.09	94.98	-0.77	.446
APOE ε4 carriership (carrier)	-0.58	0.54	97.56	-1.08	.281
Diagnosis (DAT)	2.34	0.51	97.17	4.55	<.001***
Baseline atrophy subtype (LP)	-0.07	0.72	96.79	-0.09	.925
Baseline atrophy stage	-0.06	0.11	90.42	-0.55	.587
p-tau ₂₁₇ /Aβ ₄₂	0.24	0.50	87.14	0.49	.623
Years × age at MRI	0.00	0.01	222.01	-0.36	.716
Years × sex (female)	-0.29	0.21	223.15	-1.40	.163
Years × years of education	-0.01	0.03	219.08	-0.42	.678
Years × APOE ε4 carriership (carrier)	-0.14	0.23	225.28	-0.61	.544
Years × diagnosis (DAT)	0.87	0.22	225.14	3.91	<.001***
Years × baseline atrophy subtype (LP)	0.35	0.27	216.21	1.29	.198
Years × baseline atrophy stage	0.14	0.04	219.22	3.57	<.001***
Baseline atrophy subtype (LP) × baseline atrophy stage	0.14	0.14	91.41	1.04	.303
Years × p-tau ₂₁₇ /Aβ ₄₂	-0.17	0.17	215.04	-0.96	.339
Years × baseline atrophy subtype (LP) × baseline atrophy stage	0.04	0.07	226.31	0.54	.589

N = 80. Formula: CDR-SB ~ years × age at MRI + years × sex + years × years of education + years × APOE ε4 carriership + years × diagnosis + years × p-tau₂₁₇/Aβ₄₂ + years × baseline atrophy subtype × baseline atrophy stage + (1 | participant). R^2_{marginal} (REML/ML) = 0.48/0.51. * $p < .05$. ** $p < .01$. *** $p < .001$. Abbreviations: LP, limbic-predominant.

Supplementary Table 13 Summary statistics of LMMs predicting longitudinal CDR-SB scores using baseline MTA scores in the mild symptomatic AD sample with available MTA scores.

Predictor	Estimate	SE	df	t value	p
Intercept	-1.76	5.59	30.58	-0.31	.755
Years	-2.27	1.79	55.81	-1.27	.210
Years of education	-0.05	0.15	31.82	-0.34	.735
Age at MRI	0.04	0.06	30.90	0.67	.510
Sex (female)	0.39	0.84	32.13	0.47	.644
APOE ε4 carriership (carrier)	0.44	0.99	31.86	0.44	.661
MTA score	0.60	0.63	32.06	0.95	.348
Years × years of education	0.01	0.05	54.59	0.15	.880
Years × age at MRI	0.02	0.02	56.04	0.86	.392
Years × sex (female)	0.41	0.29	55.29	1.43	.159
Years × APOE ε4 carriership (carrier)	0.76	0.34	55.57	2.27	.027*
Years × MTA score	0.56	0.21	54.86	2.72	.009**

$N = 29$. Formula: $\text{CDR-SB} \sim \text{years} \times \text{age at MRI} + \text{years} \times \text{sex} + \text{years} \times \text{years of education} + \text{years} \times \text{APOE } \epsilon 4 \text{ carriership} + \text{years} \times \text{baseline diagnosis} + \text{years} \times \text{baseline MTA score} + (1 \mid \text{participant})$. R^2_{marginal} (REML/ML) = 0.26/0.30. * $p < .05$. ** $p < .01$. *** $p < .001$. Abbreviations: LP, limbic-predominant.

Supplementary Table 14 Summary statistics of LMMs predicting longitudinal CDR-SB scores using baseline atrophy subtype and stage in the mild symptomatic AD sample with available MTA scores.

Predictor	Estimate	SE	df	t value	p
Intercept	0.21	5.62	25.39	0.04	.970
Years	-1.78	1.84	51.02	-0.97	.339
Years of education	0.01	0.16	26.95	0.08	.933
Age at MRI	0.00	0.07	24.47	0.07	.945
Sex (female)	-0.18	0.82	26.50	-0.21	.832
APOE ε4 carriership (carrier)	-0.03	1.02	26.86	-0.03	.974
Baseline atrophy subtype (LP)	0.15	1.34	25.54	0.11	.912
Baseline atrophy stage (spline 1)	2.36	2.91	25.19	0.81	.425
Baseline atrophy stage (spline 2)	-1.10	1.84	26.93	-0.60	.554
Years × years of education	0.05	0.05	49.92	1.00	.325
Years × age at MRI	0.01	0.02	50.75	0.42	.676
Years × sex (female)	0.10	0.28	50.89	0.35	.726
Years × APOE ε4 carriership (carrier)	0.13	0.35	50.52	0.37	.714
Years × baseline atrophy subtype (LP)	0.40	0.41	49.76	0.98	.331
Years × baseline atrophy stage (spline 1)	2.77	0.87	49.74	3.17	.003**
Years × baseline atrophy stage (spline 2)	-1.57	0.64	49.77	-2.44	.018*
Baseline atrophy subtype (LP) × baseline atrophy stage (spline 1)	0.88	3.57	25.26	0.25	.808
Baseline atrophy subtype (LP) × baseline atrophy stage (spline 2)	0.45	2.97	28.19	0.15	.881
Years × baseline atrophy subtype (LP) × baseline atrophy stage (spline 1)	-1.52	1.12	49.81	-1.36	.179
Years × baseline atrophy subtype (LP) × baseline atrophy stage (spline 2)	1.16	1.08	49.31	1.08	.288

$N = 29$. Formula: $\text{CDR-SB} \sim \text{years} \times \text{age at MRI} + \text{years} \times \text{sex} + \text{years} \times \text{years of education} + \text{years} \times \text{APOE } \epsilon 4 \text{ carriership} + \text{years} \times \text{baseline diagnosis} + \text{years} \times \text{baseline atrophy subtype} \times \text{ns}(\text{baseline atrophy stage, knot} = 3) + (1 \mid \text{participant})$. R^2_{marginal} (REML/ML) = 0.38/0.47. * $p < .05$. ** $p < .01$. *** $p < .001$. Abbreviations: LP, limbic-predominant.