

**Figure S1** Trial profile of all study participants. A $\beta$ , amyloid-beta; AD, Alzheimer’s disease; APOE, apolipoprotein E; CDR-SB, Clinical Dementia Rating-Sum of Boxes; HC, healthy control; MCI, mild cognitive impairment; MOCA, Montreal Cognitive Assessment; MMSE, Mini-Mental State Examination; PET, positron emission tomography; <sup>18</sup>F-AV-45, florbetapir; +, positive; –, negative.

**Table S1** Clinical ratings and demographic characteristics of longitudinal AD participants

Characteristics	AD (n=14)		P value
	A $\beta$ positive (n=13)	A $\beta$ negative (n=1)	
Sex (male/female)	9/4	1/0	1
Baseline age (years)	74.0 $\pm$ 5.6	81	–
Follow-up duration (years)	2.23 $\pm$ 0.83	2	–
Education (years)	16.5 $\pm$ 3.2	14	–
MMSE	-3.38 $\pm$ 3.52*	-3	–
MOCA	-5.23 $\pm$ 3.78*	1	–
CDR-SB	2.15 $\pm$ 2.23*	5	–
APOE $\epsilon$ 4 positivity (%)	100	0	–

\*,  $P < 0.05$ , 1-sample  $t$ -test. A $\beta$ , amyloid-beta; AD, Alzheimer's disease; APOE  $\epsilon$ 4 positivity, positive rate for the presence of at least 1  $\epsilon$ 4 apolipoprotein E; CDR-SB, Clinical Dementia Rating-Sum of Boxes; MOCA, Montreal Cognitive Assessment; MMSE, Mini-Mental State Examination.

**Table S2** Diagnostic ability of 4 semi-quantitative methods in the frontal lobe

Characteristics	Group	Whole cerebellum	MNI atlas-based WM	Subject-specific WM	PERSI-WM
SUVR (frontal lobe)	HC A $\beta$ -	1.16 $\pm$ 0.07	0.54 $\pm$ 0.06	0.53 $\pm$ 0.06	0.54 $\pm$ 0.06
	MCI A $\beta$ +	1.48 $\pm$ 0.15	0.72 $\pm$ 0.08	0.70 $\pm$ 0.08	0.71 $\pm$ 0.07
	AD A $\beta$ +	1.49 $\pm$ 0.12	0.72 $\pm$ 0.06	0.71 $\pm$ 0.06	0.79 $\pm$ 0.07
	HC A $\beta$ +	1.40 $\pm$ 0.12	0.63 $\pm$ 0.07	0.61 $\pm$ 0.07	0.62 $\pm$ 0.06
	MCI A $\beta$ -	1.12 $\pm$ 0.09	0.54 $\pm$ 0.05	0.52 $\pm$ 0.05	0.54 $\pm$ 0.05
	AD A $\beta$ -	1.13 $\pm$ 0.07	0.56 $\pm$ 0.09	0.56 $\pm$ 0.09	0.68 $\pm$ 0.10
AUC	AD & MCI A $\beta$ + vs. HC A $\beta$ -	0.975	0.961	0.966	0.975
	AD A $\beta$ + vs. HC A $\beta$ -	0.979	0.967	0.975	0.989
	MCI A $\beta$ + vs. HC A $\beta$ -	0.969	0.952	0.951	0.955
Effect size	AD & MCI A $\beta$ + vs. HC A $\beta$ -	2.55	2.57	2.64	3.07
	AD A $\beta$ + vs. HC A $\beta$ -	2.80	2.53	2.69	3.55
	MCI A $\beta$ + vs. HC A $\beta$ -	2.27	2.18	2.11	2.28

A $\beta$ , amyloid-beta; AD, Alzheimer's disease; AUC, area under the curve; HC, healthy control; MCI, mild cognitive impairment; MNI, Montreal Neurological Institute; PERSI, parametric estimation of reference signal intensity; SUVR, standardized uptake value ratio; WM, white matter; +, positive; -, negative.

**Table S3** Diagnostic ability of 4 semi-quantitative methods in the parietal lobe

Characteristics	Group	Whole cerebellum	MNI atlas-based WM	Subject-specific WM	PERSI-WM
SUVR (parietal lobe)	HC A $\beta$ -	1.13 $\pm$ 0.09	0.53 $\pm$ 0.06	0.51 $\pm$ 0.07	0.52 $\pm$ 0.06
	MCI A $\beta$ +	1.44 $\pm$ 0.16	0.70 $\pm$ 0.08	0.68 $\pm$ 0.08	0.69 $\pm$ 0.07
	AD A $\beta$ +	1.42 $\pm$ 0.14	0.68 $\pm$ 0.06	0.68 $\pm$ 0.06	0.75 $\pm$ 0.07
	HC A $\beta$ +	1.37 $\pm$ 0.13	0.62 $\pm$ 0.07	0.60 $\pm$ 0.07	0.60 $\pm$ 0.07
	MCI A $\beta$ -	1.07 $\pm$ 0.10	0.52 $\pm$ 0.05	0.50 $\pm$ 0.05	0.52 $\pm$ 0.05
	AD A $\beta$ -	1.08 $\pm$ 0.07	0.54 $\pm$ 0.08	0.54 $\pm$ 0.08	0.65 $\pm$ 0.10
AUC	AD & MCI A $\beta$ + vs. HC A $\beta$ -	0.965	0.948	0.955	0.971
	AD A $\beta$ + vs. HC A $\beta$ -	0.956	0.946	0.958	0.983
	MCI A $\beta$ + vs. HC A $\beta$ -	0.978	0.949	0.949	0.951
Effect size	AD & MCI A $\beta$ + vs. HC A $\beta$ -	2.36	2.23	2.32	2.76
	AD A $\beta$ + vs. HC A $\beta$ -	2.40	2.12	2.29	3.06
	MCI A $\beta$ + vs. HC A $\beta$ -	2.27	2.00	1.95	2.07

A $\beta$ , amyloid-beta; AD, Alzheimer's disease; AUC, area under the curve, HC, healthy control; MCI, mild cognitive impairment; MNI, Montreal Neurological Institute; PERSI, parametric estimation of reference signal intensity; SUVR, standardized uptake value ratio; WM, white matter; +, positive; -, negative.

**Table S4** Diagnostic ability of 4 semi-quantitative methods in the temporal lobe

Characteristics	Group	Whole cerebellum	MNI atlas-based WM	Subject-specific WM	PERSI-WM
SUVR (temporal lobe)	HC A $\beta$ -	1.21 $\pm$ 0.07	0.57 $\pm$ 0.06	0.55 $\pm$ 0.05	0.56 $\pm$ 0.05
	MCI A $\beta$ +	1.46 $\pm$ 0.15	0.71 $\pm$ 0.08	0.69 $\pm$ 0.07	0.71 $\pm$ 0.07
	AD A $\beta$ +	1.49 $\pm$ 0.13	0.72 $\pm$ 0.06	0.72 $\pm$ 0.06	0.75 $\pm$ 0.07
	HC A $\beta$ +	1.44 $\pm$ 0.13	0.64 $\pm$ 0.07	0.63 $\pm$ 0.07	0.60 $\pm$ 0.06
	MCI A $\beta$ -	1.17 $\pm$ 0.08	0.57 $\pm$ 0.05	0.55 $\pm$ 0.06	0.52 $\pm$ 0.06
	AD A $\beta$ -	1.16 $\pm$ 0.07	0.57 $\pm$ 0.08	0.58 $\pm$ 0.08	0.66 $\pm$ 0.09
AUC	AD & MCI A $\beta$ + vs. HC A $\beta$ -	0.968	0.951	0.954	0.971
	AD A $\beta$ + vs. HC A $\beta$ -	0.975	0.956	0.965	0.988
	MCI A $\beta$ + vs. HC A $\beta$ -	0.958	0.940	0.936	0.943
Effect size	AD & MCI A $\beta$ + vs. HC A $\beta$ -	2.37	2.38	2.43	2.89
	AD A $\beta$ + vs. HC A $\beta$ -	2.66	2.41	2.57	3.59
	MCI A $\beta$ + vs. HC A $\beta$ -	2.07	2.01	1.92	2.09

A $\beta$ , amyloid-beta; AD, Alzheimer's disease; AUC, area under the curve, HC, healthy control; MCI, mild cognitive impairment; MNI, Montreal Neurological Institute; PERSI, parametric estimation of reference signal intensity; SUVR, standardized uptake value ratio; WM, white matter; +, positive; -, negative.

**Table S5** Diagnostic ability of 4 semi-quantitative methods in the occipital lobe

Characteristics	Group	Whole cerebellum	MNI atlas-based WM	Subject-specific WM	PERSI-WM
SUVR (occipital lobe)	HC A $\beta$ -	1.30 $\pm$ 0.08	0.61 $\pm$ 0.05	0.59 $\pm$ 0.06	0.60 $\pm$ 0.06
	MCI A $\beta$ +	1.53 $\pm$ 0.16	0.74 $\pm$ 0.07	0.73 $\pm$ 0.11	0.74 $\pm$ 0.07
	AD A $\beta$ +	1.55 $\pm$ 0.14	0.75 $\pm$ 0.06	0.75 $\pm$ 0.08	0.82 $\pm$ 0.07
	HC A $\beta$ +	1.49 $\pm$ 0.15	0.67 $\pm$ 0.06	0.65 $\pm$ 0.09	0.66 $\pm$ 0.07
	MCI A $\beta$ -	1.25 $\pm$ 0.08	0.61 $\pm$ 0.05	0.58 $\pm$ 0.07	0.61 $\pm$ 0.05
	AD A $\beta$ -	1.27 $\pm$ 0.08	0.63 $\pm$ 0.08	0.63 $\pm$ 0.09	0.76 $\pm$ 0.10
AUC	AD & MCI A $\beta$ + vs. HC A $\beta$ -	0.935	0.906	0.921	0.943
	AD A $\beta$ + vs. HC A $\beta$ -	0.952	0.912	0.933	0.972
	MCI A $\beta$ + vs. HC A $\beta$ -	0.909	0.896	0.901	0.896
Effect size	AD & MCI A $\beta$ + vs. HC A $\beta$ -	2.01	1.72	1.82	2.14
	AD A $\beta$ + vs. HC A $\beta$ -	2.20	1.76	1.95	2.62
	MCI A $\beta$ + vs. HC A $\beta$ -	1.81	1.53	1.51	1.58

A $\beta$ , amyloid-beta; AD, Alzheimer's disease; AUC, area under the curve; HC, healthy control; MCI, mild cognitive impairment; MNI, Montreal Neurological Institute; PERSI, parametric estimation of reference signal intensity; SUVR, standardized uptake value ratio; WM, white matter; +, positive; -, negative.

**Table S6** Diagnostic ability of 4 semi-quantitative methods in the anterior cingulate

Characteristics	Group	Whole cerebellum	MNI atlas-based WM	Subject-specific WM	PERSI-WM
SUVR (anterior cingulate)	HC A $\beta$ -	1.35 $\pm$ 0.13	0.63 $\pm$ 0.07	0.62 $\pm$ 0.07	0.63 $\pm$ 0.07
	MCI A $\beta$ +	1.74 $\pm$ 0.28	0.85 $\pm$ 0.11	0.83 $\pm$ 0.11	0.84 $\pm$ 0.10
	AD A $\beta$ +	1.78 $\pm$ 0.21	0.86 $\pm$ 0.08	0.85 $\pm$ 0.08	0.94 $\pm$ 0.09
	HC A $\beta$ +	1.67 $\pm$ 0.20	0.74 $\pm$ 0.08	0.73 $\pm$ 0.08	0.73 $\pm$ 0.08
	MCI A $\beta$ -	1.30 $\pm$ 0.15	0.63 $\pm$ 0.06	0.62 $\pm$ 0.06	0.63 $\pm$ 0.06
	AD A $\beta$ -	1.32 $\pm$ 0.21	0.65 $\pm$ 0.12	0.65 $\pm$ 0.13	0.79 $\pm$ 0.09
AUC	AD & MCI A $\beta$ + vs. HC A $\beta$ -	0.946	0.951	0.956	0.968
	AD A $\beta$ + vs. HC A $\beta$ -	0.963	0.965	0.972	0.990
	MCI A $\beta$ + vs. HC A $\beta$ -	0.919	0.929	0.927	0.935
Effect size	AD & MCI A $\beta$ + vs. HC A $\beta$ -	2.18	2.58	2.64	3.02
	AD A $\beta$ + vs. HC A $\beta$ -	2.48	2.66	2.83	3.68
	MCI A $\beta$ + vs. HC A $\beta$ -	1.84	2.16	2.11	2.26

A $\beta$ , amyloid-beta; AD, Alzheimer's disease; AUC, area under the curve; HC, healthy control; MCI, mild cognitive impairment; MNI, Montreal Neurological Institute; PERSI, parametric estimation of reference signal intensity; SUVR, standardized uptake value ratio; WM, white matter; +, positive; -, negative.

**Table S7** Diagnostic ability of 4 semi-quantitative methods in the posterior cingulate

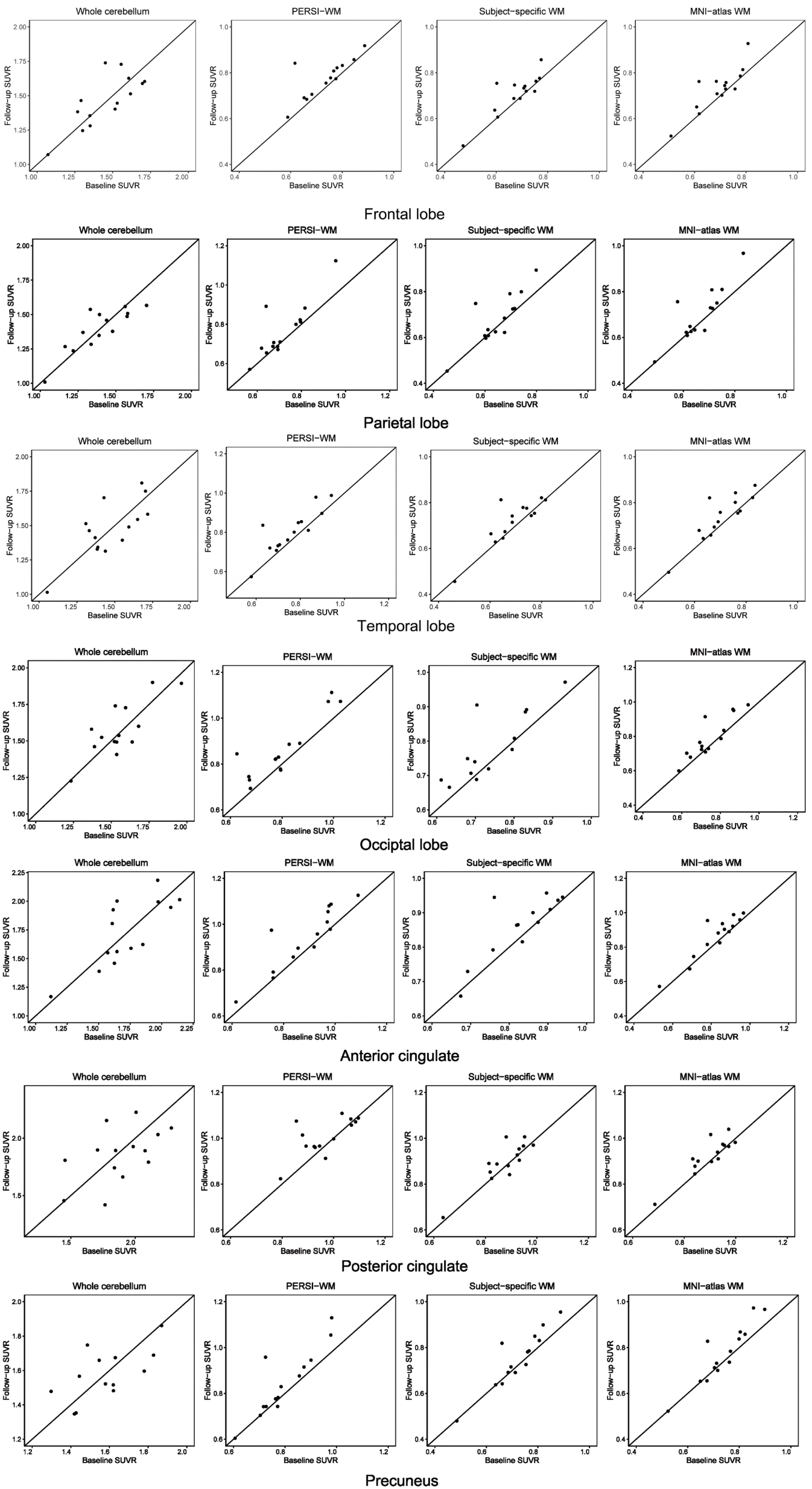
Characteristics	Group	Whole cerebellum	MNI atlas-based WM	Subject-specific WM	PERSI-WM
SUVR (posterior cingulate)	HC A $\beta$ -	1.58±0.15	0.74±0.05	0.71±0.06	0.73±0.07
	MCI A $\beta$ +	1.86±0.24	0.91±0.05	0.88±0.06	0.90±0.10
	AD A $\beta$ +	1.89±0.19	0.91±0.06	0.91±0.06	1.00±0.09
	HC A $\beta$ +	1.88±0.18	0.84±0.06	0.82±0.07	0.83±0.08
	MCI A $\beta$ -	1.51±0.18	0.73±0.07	0.70±0.07	0.73±0.07
	AD A $\beta$ -	1.55±0.16	0.76±0.08	0.76±0.08	0.89±0.14
AUC	AD & MCI A $\beta$ + vs. HC A $\beta$ -	0.875	0.971	0.975	0.987
	AD A $\beta$ + vs. HC A $\beta$ -	0.891	0.968	0.977	0.996
	MCI A $\beta$ + vs. HC A $\beta$ -	0.850	0.973	0.972	0.973
Effect size	AD & MCI A $\beta$ + vs. HC A $\beta$ -	1.62	2.79	2.84	3.21
	AD A $\beta$ + vs. HC A $\beta$ -	1.73	2.62	2.81	3.94
	MCI A $\beta$ + vs. HC A $\beta$ -	1.37	2.42	2.28	2.41

A $\beta$ , amyloid-beta; AD, Alzheimer's disease; AUC, area under the curve; HC, healthy control; MCI, mild cognitive impairment; MNI, Montreal Neurological Institute; PERSI, parametric estimation of reference signal intensity; SUVR, standardized uptake value ratio; WM, white matter; +, positive; -, negative.

**Table S8** Diagnostic ability of 4 semi-quantitative methods in the precuneus

Characteristics	Group	Whole cerebellum	MNI atlas-based WM	Subject-specific WM	PERSI-WM
SUVR (precuneus)	HC A $\beta$ -	1.17±0.09	0.55±0.06	0.53±0.06	0.54±0.06
	MCI A $\beta$ +	1.54±0.18	0.76±0.07	0.73±0.07	0.75±0.07
	AD A $\beta$ +	1.55±0.15	0.75±0.06	0.74±0.06	0.82±0.07
	HC A $\beta$ +	1.47±0.15	0.66±0.08	0.64±0.08	0.65±0.08
	MCI A $\beta$ -	1.13±0.11	0.54±0.06	0.52±0.06	0.54±0.05
	AD A $\beta$ -	1.17±0.08	0.58±0.09	0.58±0.09	0.70±0.11
AUC	AD & MCI A $\beta$ + vs. HC A $\beta$ -	0.981	0.973	0.977	0.986
	AD A $\beta$ + vs. HC A $\beta$ -	0.977	0.974	0.980	0.993
	MCI A $\beta$ + vs. HC A $\beta$ -	0.985	0.972	0.973	0.975
Effect size	AD & MCI A $\beta$ + vs. HC A $\beta$ -	2.78	2.88	2.97	3.35
	AD A $\beta$ + vs. HC A $\beta$ -	2.93	2.77	2.81	3.78
	MCI A $\beta$ + vs. HC A $\beta$ -	2.58	2.55	2.49	2.63

A $\beta$ , amyloid-beta; AD, Alzheimer's disease; AUC, area under the curve; HC, healthy control; MCI, mild cognitive impairment; MNI, Montreal Neurological Institute; PERSI, parametric estimation of reference signal intensity; SUVR, standardized uptake value ratio; WM, white matter; +, positive; -, negative.



**Figure S2** Fewer individual variations in tracking of increase in candidate regions of interest standardized uptake value ratios (SUVRs) with parametric estimation of reference signal intensity-white matter (PERSI-WM) than with other reference regions. MNI, Montreal Neurological Institute.

**Table S9** Correlations between clinical cognitive scores and standardized uptake value ratio of the frontal lobe

Frontal lobe	PERSI-WM	Subject-specific WM	MNI atlas-based WM	Whole cerebellum
MMSE	-0.426	-0.325	-0.298	-0.144 <sup>†</sup>
MOCA	-0.373	-0.271	-0.256	-0.093 <sup>†</sup>
CDR-SB	0.447	0.403	0.397	0.241

<sup>†</sup>, insignificant correlation, P value with correction for multiple comparisons >0.05. CDR-SB, Clinical Dementia Rating-Sum of Boxes; MMSE, Mini-Mental State Examination; MNI, Montreal Neurological Institute; MOCA, Montreal Cognitive Assessment; PERSI, parametric estimation of reference signal intensity; WM, white matter.

**Table S10** Correlations between clinical cognitive scores and standardized uptake value ratio of the parietal lobe

Parietal lobe	PERSI-WM	Subject-specific WM	MNI atlas-based WM	Whole cerebellum
MMSE	-0.387	-0.294	-0.243	-0.124 <sup>†</sup>
MOCA	-0.355	-0.248	-0.231	-0.078 <sup>†</sup>
CDR-SB	0.437	0.383	0.375	0.221

<sup>†</sup>, insignificant correlation, P value with correction for multiple comparisons >0.05. CDR-SB, Clinical Dementia Rating-Sum of Boxes; MMSE, Mini-Mental State Examination; MNI, Montreal Neurological Institute; MOCA, Montreal Cognitive Assessment; PERSI, parametric estimation of reference signal intensity; WM, white matter.

**Table S11** Correlations between clinical cognitive scores and standardized uptake value ratio of the temporal lobe

Temporal lobe	PERSI-WM	Subject-specific WM	MNI atlas-based WM	Whole cerebellum
MMSE	-0.415	-0.317	-0.291	-0.134 <sup>†</sup>
MOCA	-0.364	-0.263	-0.243	-0.007 <sup>†</sup>
CDR-SB	0.402	0.347	0.338	0.187 <sup>†</sup>

<sup>†</sup>, insignificant correlation, P value with correction for multiple comparisons >0.05. CDR-SB, Clinical Dementia Rating-Sum of Boxes; MMSE, Mini-Mental State Examination; MNI, Montreal Neurological Institute; MOCA, Montreal Cognitive Assessment; PERSI, parametric estimation of reference signal intensity; WM, white matter.

**Table S12** Correlations between clinical cognitive scores and standardized uptake value ratio of the occipital lobe

Occipital lobe	PERSI-WM	Subject-specific WM	MNI atlas-based WM	Whole cerebellum
MMSE	-0.454	-0.372	-0.339	-0.217
MOCA	-0.409	-0.309	-0.288	-0.127 <sup>†</sup>
CDR-SB	0.482	0.422	0.406	0.294

<sup>†</sup>, insignificant correlation, P value with correction for multiple comparisons >0.05. CDR-SB, Clinical Dementia Rating-Sum of Boxes; MMSE, Mini-Mental State Examination; MNI, Montreal Neurological Institute; MOCA, Montreal Cognitive Assessment; PERSI, parametric estimation of reference signal intensity; WM, white matter.

**Table S13** Correlations between clinical cognitive scores and standardized uptake value ratio of the anterior cingulate

Anterior cingulate	PERSI-WM	Subject-specific WM	MNI atlas-based WM	Whole cerebellum
MMSE	-0.402	-0.302	-0.281	-0.154 <sup>†</sup>
MOCA	-0.356	-0.268	-0.255	-0.114 <sup>†</sup>
CDR-SB	0.398	0.355	0.346	0.229

<sup>†</sup>, insignificant correlation, P value with correction for multiple comparisons >0.05. CDR-SB, Clinical Dementia Rating-Sum of Boxes; MMSE, Mini-Mental State Examination; MNI, Montreal Neurological Institute; MOCA, Montreal Cognitive Assessment; PERSI, parametric estimation of reference signal intensity; WM, white matter.

**Table S14** Correlations between clinical cognitive scores and standardized uptake value ratio of the posterior cingulate

Posterior cingulate	PERSI-WM	Subject-specific WM	MNI atlas-based WM	Whole cerebellum
MMSE	-0.338	-0.209	-0.175	-0.012 <sup>†</sup>
MOCA	-0.341	-0.223	-0.199	-0.05 <sup>†</sup>
CDR-SB	0.368	0.271	0.255	0.08 <sup>†</sup>

<sup>†</sup>, insignificant correlation, P value with correction for multiple comparisons >0.05. CDR-SB, Clinical Dementia Rating-Sum of Boxes; MMSE, Mini-Mental State Examination; MNI, Montreal Neurological Institute; MOCA, Montreal Cognitive Assessment; PERSI, parametric estimation of reference signal intensity; WM, white matter.

**Table S15** Correlations between clinical cognitive scores and standardized uptake value ratio of the precuneus

Precuneus	PERSI-WM	Subject-specific WM	MNI atlas-based WM	Whole cerebellum
MMSE	-0.394	-0.295	-0.273	-0.131 <sup>†</sup>
MOCA	-0.356	-0.247	-0.231	-0.09 <sup>†</sup>
CDR-SB	0.427	0.382	0.375	0.227

<sup>†</sup>, insignificant correlation, P value with correction for multiple comparisons >0.05. CDR-SB, Clinical Dementia Rating-Sum of Boxes; MMSE, Mini-Mental State Examination; MNI, Montreal Neurological Institute; MOCA, Montreal Cognitive Assessment; PERSI, parametric estimation of reference signal intensity; WM, white matter.