Supplementary Material

Self- and Partner-reported Subjective Memory Complaints: Association with Objective Cognitive Impairment and Risk of Decline

Supplementary Table 1. Measures of Cognitive Domains in the Uniform Dataset versions 2 and 3

Cognitive Domain	UDS V2	UDS V3
Global Cognition	MMSE [1]	MoCA [2]
Processing Speed	Trail Making Test A [3]	Trail Making Test A [3]
Working Memory	Trail Making Test B [3]	Trail Making Test B [3]
Attention	Digit Span [4]	Number Span [5]
Episodic Memory	Logical Memory, Immediate Recall Logical Memory, Delayed Recall [4]	Craft Story, Immediate Recall Craft Story, Delayed Recall [6]
Verbal Fluency	Letter and Category Fluency [7]	Letter and Category Fluency [7]

Supplementary Table 2. Subject Demographic Data for Neuroimaging Subgroups

	MTL Subgroup			Amyloid PET Subgroup			SPARE-AD/BA Subgroup			Plasma Biomarker Subgroup			
	Total Cohort (N=224)	NC (N=171)	MCI (N=53)	Total Cohort (N=121)	NC (N=71)	MCI (N=50)	Total Cohort (N=222)	NC (N=166)	MCI (N=56)	Total Cohort (N=339)	NC (N=227)	MCI (N=79)	AD (N=33)
Age, Mean (SD)[a]	72.74 (7.0)	72.59 (7.0)	73.21 (6.9)	69.06 (6.6)	68.31 (6.5)	70.12 (6.6)	73.11 (7.1)	72.87 (7.1)	73.81 (7.0)	72.30 (7.9)	71.87 (7.7)	73.50 (7.9)	72.33 (8.7)
Sex, (% Female)[b]	61.6%	67.3%	43.4%*	58.7%	64.8%	50.0%	61.3%	66.3%	46.4%*	62.7%	66.2%*	47.5%	33.3%
Race, (%)[b]													
White	74.6%	71.4%	84.9%	74.8%	68.1%	84.0%	73.9%	70.5%	84.0%	75.3%	71.1%	85.0%	81.8%
Black	22.3%	24.6%	15.1%	23.5%	30.4%	14.0%	23.0%	25.3%	16.0%	22.6%	26.8%	15.0%	12.1%
Other	3.12%	4.09%	0%	1.7%	1.5%	2.0%	3.1%	4.2%	0%	2.1%	2.2%	0%	6.1%
Education Mean (SD)[a]	16.4 (2.5)	16.3 (2.6)	16.8 (2.5)	16.2 (2.9)	16.1 (2.8)	16.3 (2.9)	16.4 (2.6)	16.2 (2.7)	16.8 (2.4)	16.4 (2.7)	16.5 (2.7)	16.4 (2.8)	15.6 (2.9)

MCI, mild cognitive impairment; MTL, medial temporal lobe; NC, normal cognition; SPARE, spatial patterns of atrophy of brain atrophy. Demographic variables were compared across diagnostic groups using

[a] Kruskal-Wallis test with Dunn's post-test

[b] Pearson's chi-squared test.

* $p < 0.01$.

Supplementary Table 3. Mean (SD) scores on Cognitive Domain Measures in the Uniform Dataset Versions 2 and 3

Cognitive Domain	UDS V2				UDS V3			
	Measure	NC	MCI	AD	Measure	NC	MCI	AD
Global Cognition	MMSE	29.0 (1.2)	26.7 (2.7)	21.0 (4.6)	MMSE Conversion	29.1 (0.73)	27.3 (1.7)	21.6 (4.8)
Processing Speed	Trails A	33.4 (13.1)	41.7 (19.5)	67.6 (37.9)	Trails A	29.6 (8.4)	39.0 (17.3)	69.6 (43.9)
Executive Function	Trails B	88.8 (47.1)	132.3 (78.6)	209.3 (85.8)	Trails B	73.9 (30.9)	111.3 (65.1)	193.7 (93.2)
Episodic Memory	LM, Immediate Recall	14.2 (3.6)	7.2 (3.5)	3.8 (2.9)	Craft, Immediate Recall	22.7 (4.8)	12.1 (5.7)	5.7 (4.4)
	LM, Delayed Recall	13.0 (3.9)	4.6 (3.5)	1.1 (1.9)	Craft, Delayed Recall	19.6 (6.1)	6.0 (5.5)	1.4 (2.0)
Verbal Fluency	F Words	14.0 (4.4)	11.2 (4.3)	10.1 (5.5)	F Words	16.2 (4.7)	13.1 (4.7)	9.5 (4.5)
Category Fluency	Animals	21.2 (5.4)	15.9 (5.4)	10.7 (4.6)	Animal	23.1 (5.7)	16.7 (4.6)	12.0 (5.1)

AD, Alzheimer's disease; LM, Logical Memory; MCI, Mild Cognitive Impairment; MMSE, Mini-Mental State Examination; NC, Normal Cognition; UDS, Uniform Dataset

Supplementary Table 4. Median (IQR) SMCs by *APOE4* carrier status.

	PRMQ Self			PRMQ Proxy		
	e4 -	**e4 +**	**p**	**e4 -**	**e4 +**	**p**
NC (N = 324)	37 (32 – 42)	39 (32 – 43)	0.201	26 (21 – 31)	25 (21 – 32)	0.604
MCI (N = 190)	43 (35 – 49)	41 (36 – 50)	0.861	38 (27 – 43)	38 (30 – 45)	0.419
AD (N = 210)	40 (32 – 45)	38 (32 – 45)	0.997	51 (43 – 60)	51 (42 – 60)	0.903

IQR, Interquartile range; AD, Alzheimer's disease; MCI, mild cognitive impairment; NC, normal cognition; PRMQ, Prospective Retrospective Memory Questionnaire

Supplementary Table 5. Median (IQR) plasma biomarker concentration by diagnostic category

	NC	MCI	AD	*p*
GFAP (pg/mL)	120.0 (89.7 – 154.9)	145.8 (112.9 – 188.6)	184.2 (156.0 – 306.2)	0.0001
NfL (pg/mL)	16.56 (12.5 – 21.7)	20.75 (14.9 – 28.6)	25.10 (19.7 – 28.8)	0.0001
p-tau181 (pg/mL)	2.15 (1.59 – 2.97)	3.08 (2.19 – 4.09)	4.43 (3.49 – 5.88)	0.0001

Comparisons across diagnostic groups were performed using Kruskal-Wallis test with Dunn's post-test. AD, Alzheimer's disease; GFAP, glial fibrillary acidic protein; IQR, Interquartile range; MCI, mild cognitive impairment; NC, normal cognition; NfL, neurofilament light chain; PRMQ, Prospective Retrospective Memory Questionnaire; p-tau, phosphorylated tau.

Supplementary Table 6. SMCs and baseline factors affecting cognitive decline in NC & MCI subjects

Fixed Terms in final model	Estimate	Std. Err.	p	95% Confidence Interval	
				Lower Bound	Upper Bound
NC					
PRMQ <u>Self</u> x Time (y)	0.0015	0.005	0.749	-0.0076	0.0106
MMSE at baseline	0.7732	0.035	<0.001	0.7043	0.8420
PRMQ Self	-0.0047	0.006	0.401	-0.0158	0.0063
Time (y)	-0.1423	0.179	0.427	-0.4933	0.2087
Education	0.0638	0.014	<0.001	0.0367	0.0908
MCI					
PRMQ <u>Self</u> x Time (y)	0.0013	0.015	0.928	-0.0274	0.0301
MMSE at baseline	0.8630	0.043	<0.001	0.7789	0.9471
PRMQ Self	0.0086	0.011	0.421	-0.0123	0.0294
Time (y)	-0.0828	0.647	0.201	-2.0965	0.4399
NC					
PRMQ <u>Proxy</u> x Time (y)	-0.0009	0.005	0.863	-0.0109	0.0091
MMSE at baseline	0.7771	0.036	<0.001	0.7070	0.8474
PRMQ Proxy	0.0035	0.006	0.556	-0.0082	0.0153
Time (y)	-0.0735	0.141	0.602	-0.3494	0.2024
Education	0.0683	0.014	<0.001	0.0412	0.0954
MCI					
PRMQ <u>Proxy</u> x Time (y)	-0.0219	0.014	0.114	-0.0492	0.0053
MMSE at baseline	0.8627	0.046	<0.001	0.7733	0.9521
PRMQ Proxy	-0.0022	0.011	0.838	-0.0231	0.0187
Time (y)	0.1234	0.564	0.827	-0.9826	1.2295

The above fixed effects remained in the final model following optimization with backward selection. Random effects include a random intercept for each subject and a random slope for time in years, for which model statistics are not shown. MCI, mild cognitive impairment; MMSE, Mini-Mental State Examination; NC, normal cognition; PRMQ, Prospective Retrospective Memory Questionnaire.

Supplementary Table 7. SMCs and baseline factors affecting functional decline in NC & MCI subjects

Fixed Terms in final model	Estimate	Std. Err.	*p*	95% Confidence Interval	
				Lower Bound	Upper Bound
MCI					
PRMQ <u>Self</u> x Time (y)	-0.0114	0.005	0.028	-0.0216	-0.0012
FRS at baseline	0.8428	0.031	<0.001	0.7825	0.9031
PRMQ Self	0.0009	0.006	0.876	-0.0106	0.0125
Time (y)	0.5139	0.200	0.010	0.1226	0.9052
NC					
PRMQ <u>Proxy</u> x Time (y)	0.0023	0.006	0.684	-0.0099	0.0134
FRS at baseline	0.8352	0.034	<0.001	0.7682	0.9022
PRMQ Proxy	-0.0006	0.007	0.929	-0.0140	0.0127
Time (y)	0.0310	0.137	0.844	-0.2766	0.3385
MCI					
PRMQ <u>Proxy</u> x Time (y)	-0.0029	0.023	0.927	-0.0444	0.0405
FRS at baseline	0.7963	0.058	<0.001	0.6834	0.9094
PRMQ Proxy	0.0413	0.022	0.059	-0.0016	0.0842
Time (y)	1.1667	0.875	0.182	-0.5482	2.8816

The above fixed effects remained in the final model following optimization with backward selection. Random effects include a random intercept for each subject and a random slope for time in years, for which model statistics are not shown. FRS, Functional Rating Scale; MCI, Mild Cognitive Impairment; PRMQ, Prospective Retrospective Memory Questionnaire.

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