

Supplemental Table e-1.
Baseline demographics, PET, CSF, and MRI values in three-category ATN classification in SCD

		Normal AD biomarkers N=385 (55.6%)	Non-AD pathologic change N=186 (26.8%)	Alzheimer's continuum N=122 (17.6%)	P-value
Demographic	Age, mean (SD)	57.2 (8.3)	60.6 (8.7)	65.4 (7.6)	0.00*
	Sex, n female (%)	155 (40.3%)	70 (37.6%)	58 (47.5%)	0.21
	Education, mean (SD)	5.4 (1.3)	5.5 (1.2)	5.5 (1.3)	0.57
	MMSE, mean (SD)	28 (2)	28 (2)	28 (1)	0.91
Amyloid PET	APOE E4 carriers, n (%)	103 (27.2%)	67 (36.0%)	75 (61.5%)	0.00*
	Amyloid PET, n positive/total (N=105)	0/54	0/27	24/24	0.00*
	CSF Abeta, mean (SD) (N=688)	1125.2 (154.9)	1191.1 (208.7)	671.5 (107.5)	0.00*
	P-tau, mean (SD)	38.1 (8.6)	60.4 (19.2)	65.5 (37.0)	0.00*
MRI	Total Tau, mean (SD)	215.8 (74.0)	367.4 (166.9)	442.9 (314.6)	0.00*
	MTA, mean (SD)\$	0.2 (0.3)	0.5 (0.5)	0.5 (0.6)	0.00*
	GCA, mean (SD)	0.2 (0.4)	0.5 (0.6)	0.4 (0.6)	0.00*
	PA, mean (SD)\$	0.4 (0.6)	0.6 (0.7)	0.6 (0.6)	0.00*
	Fazekas, mean (SD)	0.5 (0.6)	0.7 (0.7)	0.9 (0.7)	0.00*
	Lacunes, n (%)#	12 (3.1%)	11 (5.9%)	6 (4.9%)	0.24
	Microbleeds, n (%)#	39 (10.3%)	24 (12.9%)	29 (23.8%)	0.00*

Analyses were performed using ANOVA and Fisher's exact test. *: p-value <0.05. \$: average between left and right side. #: values are dichotomized into 0 counts and ≥ 1 counts. N shown is number of participants with ≥ 1 counts.

MMSE=mini-mental state examination; PET=positron emission tomography; CSF=cerebrospinal fluid; MRI=magnetic resonance imaging; MTA=medial temporal atrophy; GCA=global cortical atrophy; PA=parietal atrophy

Normal AD biomarkers: A-T-N-; *Non-AD pathologic change:* A-T-N+, A-T+N-, A-T+N+;
Alzheimer's continuum: A+T-N-, A+T-N+, A+T+N-, A+T+N

Supplemental Table e-2.Baseline demographics, PET, CSF, and MRI values of control group without SCD

		A-T-N- N=71 (57.3%)	A-T-N+ N=21 (16.9%)	A-T+N- N=12 (9.7%)	A-T+N+ N=3 (2.4%)	A+T-N- N=0 (0%)	A+T-N+ N=0 (0%)	A+T+N- N=12 (9.7%)	A+T+N+ N=5 (4.0%)	P-value
Demo-graphics	Age, mean (SD)	66.4 (4.9)	69.0 (7.0)	69.7 (4.5)	84.7 (8.0)	NA	NA	71.6 (6.9)	79.3 (5.7)	0.00*
	Sex, n female (%)	39 (54.9%)	7 (33.3%)	5 (41.7%)	3 (100%)	NA	NA	8 (66.7%)	3 (60%)	0.19
	Education, mean (SD)	5 (1)	5 (1)	5 (2)	5 (2)	NA	NA	5 (1)	6 (1)	0.07
	MMSE, mean (SD)	29 (1)	29 (1)	29 (2)	27 (1)	NA	NA	28 (2)	29 (1)	0.01*
	APOE E4 carriers, n (%)	21 (29.6%)	6 (30%)	5 (41.7%)	1 (33.3%)	NA	NA	8 (66.7%)	3 (60%)	0.14

Analyses were performed using ANOVA and Fisher's exact test. *: p-value <0.05.

MMSE=mini-mental state examination

NA: not applicable.

Supplemental Table e-3.
Clinical progression in three ATN categories in SCD

	N	Details clinical progression			Cox proportional hazard models		
		Total, n (%)	MCI, n	AD, n	Other dementia, n	Progression to dementia [□]	Progression to MCI or dementia [□]
<i>Normal AD biomarkers</i>	175	9 (5%)	7	0	2	1 (reference)	1 (reference)
<i>Non-AD pathologic change</i>	90	6 (7%)	2	2	2	3.2 (0.6- 17.8)	0.9 (0.3-2.6)
<i>Alzheimer's continuum</i>	77	31 (40%)	15	14	2	17.0 (3.6- 79.0)	7.5 (3.4- 16.5)

[□]: Cox proportional hazard models, adjusted for age, sex and education. Data is presented as Hazard Ratio (HR) (95% CI).

MCI=mild cognitive impairment; AD=Alzheimer's disease

Supplemental Table e-4.

Relationship between three-category ATN classification and baseline and longitudinal cognition in SCD

	<i>Baseline</i>		<i>Longitudinal</i>	
	<i>Non-AD pathologic change</i>	<i>Alzheimer's continuum</i>	<i>Non-AD pathologic change</i>	<i>Alzheimer's continuum</i>
VAT-A	-0.05 (0.08)	-0.12 (0.09)	-0.04 (0.08)	-0.54 (0.08)*
RAVLT immediate recall	0.90 (0.79)	-1.15 (0.95)	-0.94 (0.45)	-2.16 (0.45)*
RAVLT delayed recall	0.16 (0.26)	-0.86 (0.31)*	-0.36 (0.14)*	-0.75 (0.14)*
Digit span forward	0.23 (0.25)	0.32 (0.30)	-0.08 (0.08)	-0.10 (0.08)
Digit span backward	0.41 (0.22)	0.26 (0.27)	-0.03 (0.09)	-0.22 (0.09)*
Animal fluency	0.45 (0.50)	0.07 (0.60)	-0.07 (0.21)	-0.68 (0.22)*
TMT-A	-0.01 (0.03)	-0.04 (0.04)	-0.01 (0.02)	-0.04 (0.02)*
TMT-B	-0.04 (0.03)	-0.06 (0.04)	-0.02 (0.01)	-0.07 (0.02)*
Stroop I	-0.00 (0.02)	-0.00 (0.02)	0.00 (0.01)	-0.02 (0.01)*
Stroop II	-0.01 (0.02)	-0.04 (0.02)	-0.00 (0.01)	-0.03 (0.01)*
Stroop III	-0.01 (0.02)	-0.04 (0.03)	-0.01 (0.01)	-0.04 (0.01)*

Values given are Beta (SE), corrected for age, sex, education, as estimated by Linear Mixed Models (reference category: *normal AD biomarkers*). Beta baseline = association between ATN category and baseline test result. Beta longitudinal = association with annual decline. Note that TMT-A, TMT-B, Stroop I, Stroop II, Stroop III are log transformed and inversed.

* p-value remaining significant after FDR correction with q set at 0.05

VAT=Visual Association Test; RAVLT=Rey Auditory Verbal Learning Test; TMT=Trail Making Test

Supplemental Table e-5.Relationship between ATN categories and cognition in control group without SCD

	<i>Baseline</i>		<i>Longitudinal</i>	
	<i>Non-AD pathologic change</i>	<i>Alzheimer's continuum</i>	<i>Non-AD pathologic change</i>	<i>Alzheimer's continuum</i>
VAT-A	0.05 (0.17)	-0.55 (0.23)	0.02 (0.11)	0.01 (0.15)
RAVLT immediate recall	0.31 (1.57)	-2.44 (2.12)	-1.24 (0.79)	-1.78 (1.10)
RAVLT delayed recall	-0.18 (0.51)	-0.66 (0.70)	-0.19 (0.27)	-0.57 (0.38)
Digit span forward	-0.31 (0.38)	-0.09 (0.51)	0.08 (0.19)	-0.06 (0.26)
Digit span backward	-0.33 (0.34)	-0.05 (0.45)	-0.29 (0.18)	-0.33 (0.25)
Animal fluency	-2.48 (1.27)	0.88 (1.70)	0.14 (0.73)	-0.96 (1.00)
TMT-A	-0.03 (0.06)	0.02 (0.08)	-0.01 (0.03)	-0.08 (0.04)
TMT-B	-0.01 (0.07)	-0.03 (0.09)	-0.07 (0.03)	-0.05 (0.04)

Values given are Beta (SE), corrected for age, sex, education, as estimated by Linear Mixed Models (reference category: *normal AD biomarkers*). Beta baseline = association between ATN category and baseline test result. Beta longitudinal = association with annual decline. Note that TMT-A and TMT-B are log transformed and inverted.

* p-value remaining significant after FDR correction with q set at 0.05

VAT=Visual Association Test; RAVLT=Rey Auditory Verbal Learning Test; TMT=Trail Making Test