

AD Brain Signature and Regional Patterns of Brain Atrophy in SuperAgers



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Background

- SuperAgers are oldest individuals (ages 80+) whose exceptional memory performance tests resemble those of adults in their mid 50s to 60s
- Previous neuroimaging research suggests that SuperAgers exhibit preserved brain volume in regions associated with memory and executive function despite advanced aged

Aim and Hypothesis

We aimed to analyze the association of SuperAging with regional brain volume and brain signatures of aging and Alzheimer's disease. We hypothesized that SuperAgers would demonstrate superior brain volume in memory regions and lower SPARE-AD scores, compared to AD cases and controls.

Participant Characteristics

Table 1. Participant characteristics by diagnostic group

	All	SuperAgers	Controls	AD Cases
No. participants	1132	323	262	461
Baseline Age, mean (SD), y	81.1 (6)	77.7 (6)	81.5 (6)	83.0 (4)
Age at T1 Scan, mean (SD), y	83.6 (3)	82.6 (4)	83.6 (4)	84.3 (3)
Scan to Cognitive Interval, mean (SD), y	0.03 (0.09)	0.03 (0.11)	0.02 (0.09)	0.03 (0.07)
Education, mean (SD), y	16 (3)	17 (3)	16 (3)	15 (3)
Female Sex, No. (%)	620 (55)	213 (66)	179 (57)	228 (46)
Non-Hispanic White Race/Ethnicity, No. (%)	1010 (89)	278 (86)	282 (90)	450 (91)
SPARE-AD, mean (SD)	0.18 (0.66)	-0.25 (0.46)	-0.11 (0.48)	0.65 (0.56)

Cohorts: Alzheimer's Disease Neuroimaging Initiative (ADNI); Knight Alzheimer's Disease Research Center at Washington University (Knight ADRC); National Alzheimer's Coordinating Center (NACC); Religious Orders Study/Memory and Aging Project/Minority Aging Research Study (ROS/MAP/MARS); Wisconsin Registry for Alzheimer's Prevention (WRAP)

Results

Table 3. Linear regression model results comparing AD brain signatures and regional volumetric measures of SuperAgers to AD cases and controls

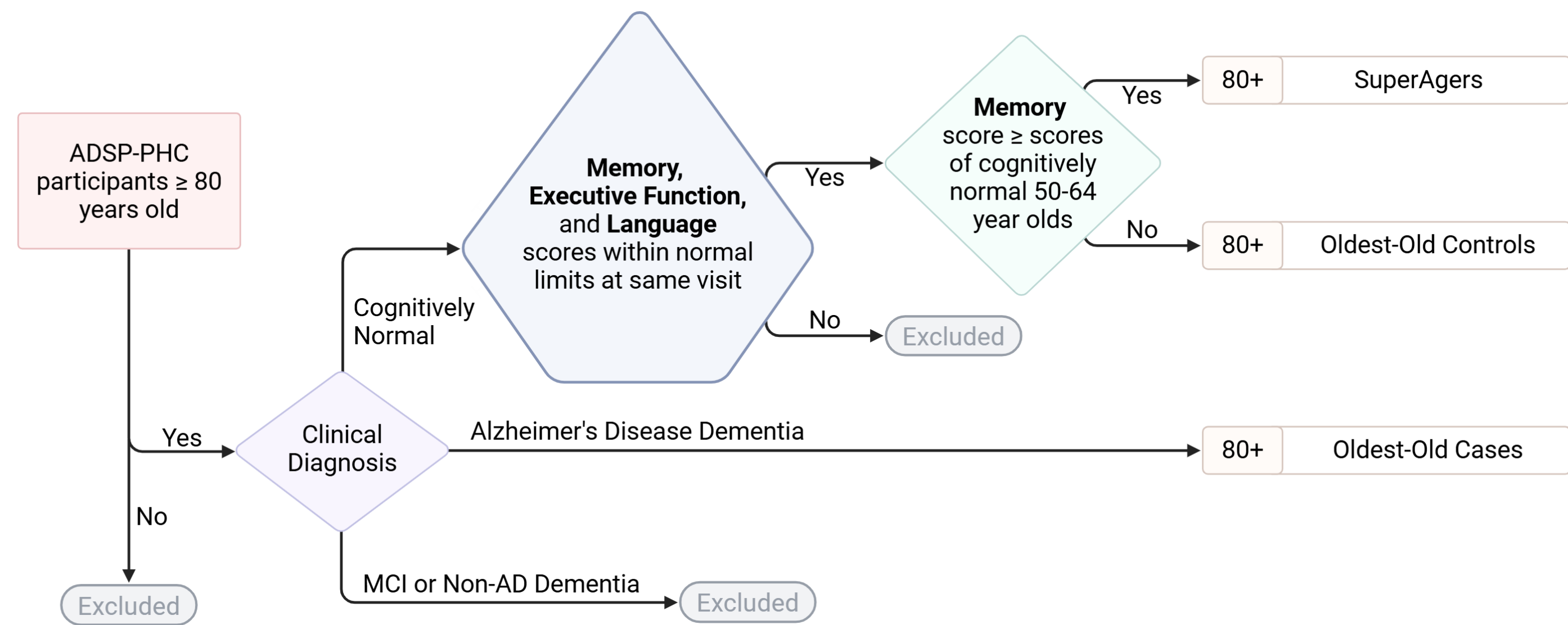
	SuperAgers vs Controls			SuperAgers vs AD Cases		
	β	CI	P_{FDR}	β	CI	P_{FDR}
Brain Signature						
SPARE Alzheimer's Disease Score	-0.09	[-0.17, -0.02]	0.0127	-0.99	[-1.07, -0.91]	<0.0001
SPARE Brain Age Score	-0.81	[-2.13, 0.52]	0.0273	-7.53	[-8.82, -6.25]	<0.0001
Total Brain Volumes						
White Matter Volume	-2172.50	[-5897.10, 1552.09]	0.0408	-3602.13	[-7401.27, 197.01]	0.0026
Gray Matter Volume	2000.64	[-2060.06, 6061.33]	0.4591	22981.0	[18851.7, 27110.4]	<0.0001
Intracranial Volume	-5.79	[-6950.67, 6939.09]	0.0127	-20585.4	[-28146.0, -13024.8]	<0.0001
White Matter Lobe Volumes						
Frontal Lobe White Matter Volume	-585.77	[-2340.26, 1168.73]	0.1739	-2015.95	[-3832.19, -199.71]	0.0106
Temporal Lobe White Matter Volume	-302.10	[-1246.55, 642.35]	0.0445	-164.83	[-1105.25, 775.59]	0.0215
Parietal Lobe White Matter Volume	-669.24	[-1656.96, 318.48]	0.0445	-688.34	[-1660.12, 283.44]	0.0106
Occipital Lobe White Matter Volume	-369.28	[-1028.57, -290.01]	0.0585	-769.65	[-1412.31, -126.98]	0.0005
Regional Volumes						
Hippocampal Volume	28.60	[-22.59, 79.79]	0.4240	426.61	[371.32, 481.90]	<0.0001
Anterior Insula Volume	77.44	[13.92, 140.96]	0.0445	331.17	[265.20, 397.14]	<0.0001
Anterior Cingulate Gyrus Volume	103.32	[8.52, 198.12]	0.1056	253.32	[161.18, 345.45]	<0.0001

β = Beta estimate, CI = Confidence Interval (95%) of β , P_{FDR} = FDR-corrected P-value

Methods

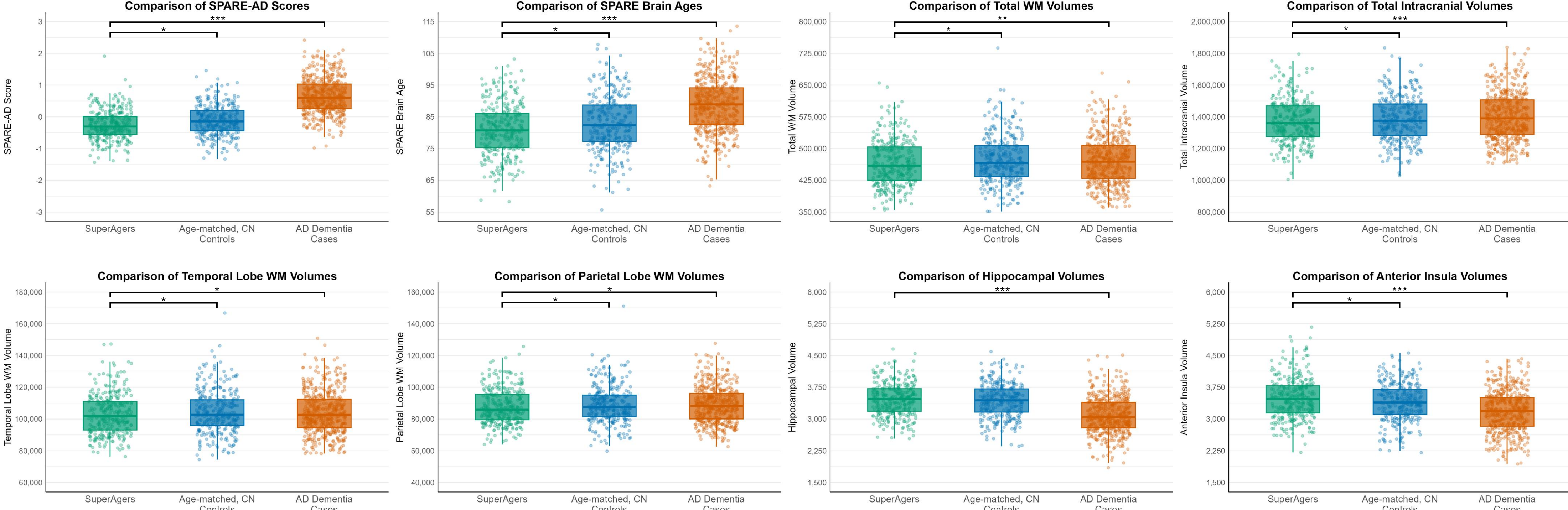
- Data were collected from non-Hispanic White (NHW) and non-Hispanic Black (NHB) participants across six well-established longitudinal cohorts of aging
- Harmonized T1-weighted magnetic resonance imaging (MRI) scans and cognitive scores were obtained through the Alzheimer's Disease Sequencing Project Phenotype Harmonization Consortium (ADSP-PHC)
 - Cognitive domain scores were estimated using latent variable modeling
 - Regional brain volume was obtained using Multi-atlas region Segmentation using Ensembles (MUSE)
 - Machine learning was used to derive brain signatures of AD (Spatial Pattern of Abnormality for Recognition of Early Alzheimer's Disease, or SPARE-AD) and brain aging (SPARE-BA)
- Linear regression analyses were used to compare regional brain volume and signatures of AD and brain aging across SuperAgers and their counterparts

Figure 1. Flow diagram for participant classification of SuperAgers, cases, and controls



Results

Figure 2. Boxplots of SPARE-AD and regional brain volumes of SuperAgers compared to AD cases and controls



Conclusions

SPARE Findings

- SuperAgers demonstrated significantly lower SPARE-AD values compared to both cognitively normal controls and AD dementia cases
- SuperAgers also showed significantly younger SPARE-Brain Age values compared to both AD dementia cases and cognitively normal controls
- Findings suggest that, through lower SPARE AD and BA values, SuperAgers exhibit a more favorable AD-related neuroanatomical profile despite advanced age

The findings also suggest that structural brain integrity across distributed cortical and medial temporal systems may support exceptional memory performance in advanced aging. Future work will expand to additional image processing methods to solidify regions of interest relevant in SuperAging.

Regional Brain Volume Findings

- SuperAgers showed greater temporal, parietal, and total white matter volume compared to both cognitively normal controls and AD dementia cases
- SuperAgers demonstrated larger anterior insula volumes compared to AD dementia cases and cognitively normal controls
- Aligned with previous studies, SuperAgers demonstrated larger anterior cingulate gyrus and hippocampal volumes than AD dementia cases

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