Published in final edited form as:

JAMA. 2017 April 04; 317(13): 1373–1375. doi:10.1001/jama.2017.0627.

Rates of Cortical Atrophy in Adults 80 Years and Older With Superior vs Average Episodic Memory

Amanda H. Cook, MA, Jaishree Sridhar, MS, Daniel Ohm, BS, Alfred Rademaker, PhD, M.-Marsel Mesulam, MD, Sandra Weintraub, PhD, and Emily Rogalski, PhD

Cognitive Neurology and Alzheimer's Disease Center, Northwestern University, Chicago, Illinois (Cook, Sridhar, Ohm, Mesulam, Weintraub, Rogalski); Department of Preventive Medicine, Northwestern University, Chicago, Illinois (Rademaker)

“SuperAgers” have previously been defined as adults 80 years and older with episodic memory ability at least as good as that of average middle-age adults.¹ They have a significantly thicker brain cortex than their same-age peers with average-for-age memory,² which is unusual as age-related cortical atrophy is considered “normal” and often associated with cognitive decline in nondemented older adults.³ SuperAgers may experience similar atrophy rates as their cognitively average peers but start with larger brain volumes, or they may resist age-related cortical atrophy. To examine the latter possibility, we quantitated rates of cortical volume change over 18 months in SuperAgers and cognitively average elderly adults.

Methods

The study took place at Northwestern University following institutional review board approval between April 2010 and May 2015. Written informed consent was obtained. Strict inclusion criteria for SuperAgers were previously detailed.¹ Briefly, participants, recruited through the community, were adults 80 years and older with intact daily functioning. SuperAgers scored at or above average normative values for adults aged 50 to 65 years on a

Corresponding Author: Amanda H. Cook, MA, Northwestern University, 320 E Superior St, Searle 11, Chicago, IL 60611 (amandacook2017@u.northwestern.edu).

Conflict of Interest Disclosures: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.

Role of the Funder/Sponsor: The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Additional Contributions: We thank Adam Martersteck, BS, and Allison Rainford, BA (both from Northwestern University Feinberg School of Medicine), for their assistance with visual inspection and manual edits of the raw images. They were paid for their work as research assistants.

Author Contributions: Ms Cook and Dr Rogalski had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: Cook, Mesulam, Weintraub, Rogalski.

Acquisition, analysis, or interpretation of data: Cook, Sridhar, Ohm, Rademaker, Rogalski.

Drafting of the manuscript: Cook, Sridhar, Rogalski.

Critical revision of the manuscript for important intellectual content: Cook, Ohm, Rademaker, Mesulam, Weintraub, Rogalski.

Statistical analysis: Cook, Rademaker, Rogalski.

Obtained funding: Cook, Rogalski.

Administrative, technical, or material support: Sridhar, Ohm, Mesulam, Weintraub, Rogalski.

Supervision: Weintraub, Rogalski.

test of episodic memory and at least average-for-age normative values on tests in other cognitive domains. Cognitively average-for-age elderly adults scored within the average-for-age normative range on all cognitive tests, including episodic memory.

Participants were included if they had structural magnetic resonance imaging scans (3TMAGNETOMTrio, Siemens; using previously documented parameters²) at 2 consecutive study visits approximately 18 months apart and had stable cognitive status across visits to minimize inclusion of individuals with emerging dementia. Whole-brain cortical volumes were obtained using the FreeSurfer, version 5.1.0, longitudinal pipeline,⁴ reviewed primarily by 2 blinded technicians, manually corrected, and normalized to account for head circumference. Annual percent change (APC) in whole-brain cortical volume was compared between groups unadjusted and adjusted for sex, handedness, and education. SPSS Statistics, version 23, was used for analyses. Statistical tests were 2-tailed at a *P* value less than .05.

Results

Three SuperAgers and no cognitively average elderly adults were excluded for declining cognitive status. Excluded and included SuperAgers did not differ on baseline characteristics. Twenty-four SuperAgers (75% women; mean age, 83.3 years [SD, 3.5]) and 12 cognitively average elderly adults (42% women; mean age, 83.4 [SD, 3.8]) completed study procedures (Table 1). SuperAgers had significantly higher category fluency at visit 1 and episodic memory scores at both visits compared with cognitively average elderly adults. There were no other significant group differences in demographic or neuropsychological measures, including education, estimated premorbid intelligence, and between-visit interval (range: SuperAgers, 1.39–1.63 years; cognitively average elderly adults, 1.43–1.88 years).

Because there were no within-group differences in APC between left and right hemispheres, whole-brain cortical volume APC was analyzed. Both groups demonstrated statistically significant mean annual percent whole-brain cortical volume loss (SuperAgers, 1.06% [95% CI, 0.50%–1.63%], *P* < .001; cognitively average elderly, 2.24% [95% CI, 1.06%–3.42%], *P* = .002) (Table 2). However, the APC in whole-brain cortical volume loss was significantly greater in cognitively average elderly compared with SuperAgers (difference, 1.18% [95% CI, 0.08%–2.28%]; unadjusted *P* = .04; adjusted *P* = .02).

Discussion

Cognitively average elderly adults demonstrated greater annual whole-brain cortical volume loss compared with SuperAgers with similar levels of education and premorbid intellectual ability over 18 months. The possibility that SuperAgers were also constitutionally endowed with larger brains throughout life cannot be ruled out. As SuperAgers represent a rare cognitive phenotype,¹ study findings require validation in larger samples with broader representation of demographic and socioeconomic features. The functional effect of the lesser decline of cortical volume in SuperAgers over 18 months is difficult to surmise. However, the between-group unadjusted difference in APC of 1.2% is similar in magnitude to the difference demonstrated in previous studies between nondemented and demented adults older than 50 years (eg, range of APC differences of 0.5%–1.9%^{5,6}), suggesting that

differences of this magnitude may have functional consequences. The factors that underlie the rate of age-related cortical volume loss are unknown; however, research on SuperAgers provides unique opportunities for exploring their biological foundations.

Acknowledgments

Funding/Support: This work was funded by grants from the National Institutes of Health, including R01 AG045571 from the Alzheimer's Disease Core Center, P30 AG13854 from the National Institute on Aging, and training grant T32 NS047987 from the National Institute of Neurological Disorders and Stroke, as well as by a grant from the Davee Foundation.

References

1. Rogalski EJ, Gefen T, Shi J, et al. Youthful memory capacity in old brains. *J Cogn Neurosci*. 2013; 25(1):29–36. [PubMed: 23198888]
2. Harrison TM, Weintraub S, Mesulam MM, Rogalski E. Superior memory and higher cortical volumes in unusually successful cognitive aging. *J Int Neuropsychol Soc*. 2012; 18(6):1081–1085. [PubMed: 23158231]
3. Fleischman DA, Leurgans S, Arfanakis K, et al. Gray-matter macrostructure in cognitively healthy older persons. *Brain Struct Funct*. 2014; 219(6):2029–2049. [PubMed: 23955313]
4. Reuter M, Schmansky NJ, Rosas HD, Fischl B. Within-subject template estimation for unbiased longitudinal image analysis. *Neuroimage*. 2012; 61(4):1402–1418. [PubMed: 22430496]
5. Jack CR Jr, Shiung MM, Gunter JL, et al. Comparison of different MRI brain atrophy rate measures with clinical disease progression in AD. *Neurology*. 2004; 62(4):591–600. [PubMed: 14981176]
6. Cardenas VA, Du AT, Hardin D, et al. Comparison of methods for measuring longitudinal brain change in cognitive impairment and dementia. *Neurobiol Aging*. 2003; 24(4):537–544. [PubMed: 12714110]

Table 1

Demographic and Neuropsychological Characteristics Among Adults 80 Years and Older With Superior vs Average Episodic Memory

	Visit 1		Visit 2	
	SuperAgers (n = 24)	Cognitively Average Elderly Adults (n = 12)	SuperAgers (n = 24)	Cognitively Average Elderly Adults (n = 12)
Women, No. (%)	18 (75)	5 (42)		
Right-handedness, No. (%)	23 (96)	10 (83)		
Education, mean (SD), y	15.0 (2.4)	15.6 (4.1)		
White race, No. (%) ^a	23 (96)	12 (100)		
Years between brain MRI scans, mean (SD)	1.53 (0.1)	1.56 (0.1)		
Age, mean (SD), y	83.3 (3.5)	83.4 (3.8)	85.0 (3.5)	84.9 (4.0)
Neuropsychological Measures				
WTAR Est. FSIQ, mean (SD) ^b	113.9 (7.4)	114.4 (9.5)		
RAVLT delay, mean raw score (SD) ^c	11.2 (1.9) ^d	6.2 (0.9)	11.0 (1.7) ^d	5.5 (1.7)
Category fluency (animals), mean raw score (SD) ^e	24.0 (5.1) ^f	20.0 (4.8)	23.1 (5.2)	19.7 (4.4)
BNT-30, mean raw score (SD) ^g	27.5 (3.7)	27.3 (3.1)	27.6 (3.3)	26.9 (4.1)
Phonemic fluency, mean raw score (SD) ^h	50.2 (16.3)	51.2 (16.1)	49.4 (15.5)	46.6 (12.8)
Trail-Making Test, mean (SD), s				
Part A ⁱ	34.6 (9.7)	33.9 (10.1)	38.5 (12.7)	32.9 (12.3)
Part B ^j	98.5 (42.6)	91.3 (36.4)	105.9 (48.3)	84.3 (26.1)

Abbreviations: BNT-30, 30-item Boston Naming Test; MRI, magnetic resonance imaging; RAVLT, Rey Auditory Verbal Learning Test; WTAR Est. FSIQ, Wechsler Test of Adult Reading Estimated Full-Scale Intelligence Quotient.

^aRace was self-reported.

^bAn estimate of premorbid intellectual ability. Scores are equivalent to the IQ scale (mean, 100 [SD, 15]).

^cA 15-item list learning test of episodic memory with possible scores ranging from 0 to 15. Mean normative raw score for adults 80 years and older is 6.

^dSignificant between-group differences were found at visits 1 and 2 ($P < .001$ for both visits).

^eSemantic fluency task in which individuals say as many items from a given category (ie, animals) as they can in 1 minute.

^fA significant between-group difference was found at visit 1 ($P = .03$). There was no significant between-group difference at visit 2.

^gMeasure of object naming with possible scores ranging from 0 to 30.

^hFluency task in which individuals say as many words as they can that begin with letters F, A, and S (allowed 1 minute per letter).

ⁱTimed test that assesses attention and processing speed. Test discontinued at 180 seconds if not completed.

^jTimed test that assesses executive attention. Test discontinued at 300 seconds if not completed.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table 2

Cortical Volumes in Adults 80 Years and Older With Superior vs Average Episodic Memory

	Mean (95% CI)	
	SuperAgers (n = 24)	Cognitively Average Elderly Adults (n = 12)
Visit 1 volume, mm ³	281.0 (275.8–286.3)	273.4 (264.4–282.5)
Visit 2 volume, mm ³	276.3 (270.7–281.9)	264.3 (253.6–274.9)
Volume loss between visit 1 and visit 2, mm ³	4.71 (2.26–7.17)	9.17 (4.34–13.99)
Annual percent change between visit 1 and visit 2, %	1.06 (0.50–1.63) ^a	2.24 (1.06–3.42)

^aUnadjusted $P = .04$; adjusted $P = .02$ (adjusted for sex, handedness, and years of education).