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Caregiving is associated with lower brain age in humans

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Abstract

Middle-aged adults who are parents have better average cognitive performance and lower average brain age compared with middle-aged adults without children, raising the possibility that caregiving slows brain aging. Here, we investigate this hypothesis in two additional groups of caregivers: grandmothers and caregivers for people living with dementia (PLWD). Demographic, questionnaire, and structural Magnetic Resonance Imaging (MRI) data were acquired from $n = 50$ grandmothers, $n = 24$ caregivers of PLWD, and $n = 37$ non-caregiver controls, and BrainAGE was estimated. BrainAGE estimation results suggest that after controlling for relevant covariates, grandmothers had a brain age that was 5.5 years younger than non-grandmother controls, and caregivers of PLWD had brains that were 4.7 years younger than non-caregiver controls. Women who became grandmothers at a later age had lower brain age than those who became grandmothers at an earlier age. Among caregivers of PLWD, stress and caregiving burden were associated with increased brain age, such that the beneficial effect of caregiving on brain age was reduced in caregivers reporting more burden. Our findings suggest that caring for dependents may slow brain aging.

Keywords: MRI; aging; neurobiology; grandmother; dementia caregiver

Introduction

Parity has been linked with decreased mortality in humans (Zeng et al. 2016). There are many possible explanations for this association. One possibility is that older adults receive care and attention from their adult children that helps them live longer. Another possibility is that people with more health challenges are both less likely to ultimately become parents and less likely to survive in old age. However, a third possibility is that parental caregiving slows the aging process. This possibility is supported by evidence showing that middle-aged parents have better average cognitive performance and a younger average brain age compared with middle-aged nonparents (de Lange et al. 2019, Ning et al. 2020). The relationship appears to be nonlinear insofar as parents with two to three children have the greatest benefit, with lesser effects for parents with either fewer or more children. Since this association is found in both men and women, it cannot be attributed to the experience of pregnancy.

Conceptually, why might caregiving slow aging? One possibility is that caregivers are more physically active and this contributes to improved health and greater longevity (Okun et al. 2013). Another possibility is that interactions with care recipients, as well as the coordination of their care, provide caregivers with cognitive stimulation that slows brain aging (La Rue 2010). It is also possible that the affective bonding and attachment facilitated by caring for another person promotes longevity by buffering against stress (Brown et al. 2008, Poulin et al. 2013). Caregiving might also increase one's overall sense of social integration or social connectedness, both of which are strongly associated with longevity (Holmes and Joseph 2011, Chen and Liu 2012, Yang et al. 2016). Finally, caregiving might also enhance meaning and purpose in life, which is associated with decreased mortality (Gruenewald et al. 2007, Hill and Turiano 2014).

If parental caregiving slows the aging process, we might expect the same to be true of other forms of caregiving including caring

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for grandchildren and perhaps even caring for dependent adults when the caregiving is not too burdensome. There are multiple types of grandparental roles, including custodial grandparents, grandparents who live with the grandchild, and day-care grandparents. While day-care grandparents often provide care voluntarily, custodial grandparents often have caregiving responsibilities thrust upon them due to duress in the nuclear family (Jendrek 1994). Other grandparents may be involved despite not providing hands-on care. Grandparental involvement is a multidimensional construct that includes not only instrumental care (e.g. feeding, bathing, and transporting) but also positive engagement activities (e.g. reading, playing, and conversing), sharing experiences and mental perspectives, emotional closeness, and financial support (Sadruddin et al. 2019, Danielsbacka et al. 2022). Among non-custodial grandparents, those who provide care to their grandchildren have lower mortality than both non-grandparents and grandparents who do not provide care to their grandchildren (Hilbrand et al. 2017). Although grandmothers who provide more care tend to have better health (Di Gessa et al. 2016), this relationship also appears to be nonlinear at the extremes (Coall and Hertwig 2010). For example, custodial grandparental care can be burdensome and is associated with decreased well-being (Ross and Aday 2006, Chen and Liu 2012, Danielsbacka et al. 2022). Several studies also suggest a positive impact of grandparenting on cognition (Rafael et al. 2021), raising the prospect that noncustodial grandparenting, like parenting, may be neuroprotective and may slow brain aging.

As our population ages and the number of people living with dementia (PLWD) grows, an increasing number of family members are providing care for relatives who are living with dementia ("2022 Alzheimer's disease facts and figures," 2022). Dementia caregiving can be stressful, and caregivers suffer increased rates of both depression and anxiety (Pinquart and Sorensen 2003, Bin Sallim et al. 2015, Joling et al. 2015). An initial study showed that caregivers who experience strain have a 63% higher mortality rate compared with non-caregivers (Schulz and Beach 1999). Several studies also report that spousal caregivers perform more poorly than non-caregivers across multiple cognitive domains (Vitaliano et al. 2003, de Vugt et al. 2006, Mackenzie et al. 2009, Oken et al. 2011, Palma et al. 2011). These findings suggest that, in contrast to parental and grandparental caregiving, dementia caregiving may accelerate aging. On the other hand, several recent studies have shown caregivers to have lower mortality than non-caregivers (O'Reilly et al. 2008, 2015, Brown et al. 2009, Ramsay et al. 2013, Fredman et al. 2015, Caputo et al. 2016). In addition, one study found that despite higher levels of stress and depression, caregivers were three times less likely to be physically inactive and also outperformed controls on processing speed, reaction time, and free recall (O'Sullivan et al. 2019). Findings like these have given rise to the Healthy Caregiver Hypothesis which posits that more physically robust older adults tend to become caregivers due to a selection effect, and further, that they stay active and therefore maintain good health due to their role of performing caregiving tasks (Fredman 2008). However, new research shows that even caregivers with the poorest initial health status have a decreased mortality risk compared with non-caregivers (Ramsay et al. 2013, Leggett et al. 2020). Many caregivers report benefits and rewards from the caregiving role (Fisher et al. 2011), and caregiving often provides a sense of meaning and purpose. This could conceivably slow the aging process, as older adults who feel useful experience reduced mortality (Gruenewald et al. 2007).

One possible explanation for these inconsistencies in the dementia caregiving literature is that, similar to parental and grandparental caregiving, the benefits of caregiving are nonlinear and depend on caregiving intensity and amount of associated burden (Schulz et al. 2020). Caregiving may be particularly burdensome for spousal caregivers, who are often older, provide more hours of care, and are more likely to be the sole care provider as compared with other informal caregivers (Christian et al. 2023).

In this study, we examine the effect of both grandparental and dementia caregiving on brain aging. Human brain aging involves well-characterized, region-specific, nonlinear changes in gray matter (GM) and white matter (WM) that can be detected with structural MRI scans. The "Brain Age Gap Estimation (BrainAGE)" method is the first and most widely applied concept for predicting and evaluating brain age based on the structural MRI (Franke et al. 2010). BrainAGE is equivalent to the difference between estimated brain age and chronological age (Franke and Gaser 2019). We test the following three hypotheses. First, that noncustodial grandmaternal caregiving decreases BrainAGE. Second, that the effect of grandmaternal caregiving on BrainAGE is moderated by the amount of time spent with the grandchild, the degree of positive engagement with the grandchild, and the quality of the emotional bond with the grandchild. Our third hypothesis is that the effect of dementia caregiving on BrainAGE will be moderated by caregiving burden such that caregiving is associated with lower BrainAGE in those with low levels of burden and greater BrainAGE in those reporting high levels of caregiving burden. A corollary is that spousal caregivers, who tend to experience more burden, will have higher brain age than non-spousal caregivers.

Materials and methods

All procedures were approved by the Emory University Institutional Review Board (caregiver IRB number: STUDY00001824 and grandmother IRB number: STUDY00000006).

Grandmothers

Participants were 50 women ($M = 59.26$, s.d. $= 7.80$, range 45–75 years) from the Greater Atlanta area who had at least one biological grandchild between 3 and 12 years of age. We restricted to this grandchild age range because the measures of grandmaternal involvement that we collected apply to children of these ages. A different set of measures would have been needed for infants/toddlers. Participants were recruited for a larger study aimed at investigating grandmaternal neural responses to viewing grandchild photographs (Rilling et al. 2021). Grandmothers were recruited through Facebook advertisements and physical flyers posted in and around the Emory University community.

Exclusion criteria: Grandmothers were excluded if they had conditions that could be associated with abnormal brain function such as a history of psychiatric illnesses (other than depression and anxiety disorders), a history of seizures or other neurological disorders, or a history of alcoholism or any other substance abuse. Subjects with a history of head trauma were excluded based on severity. Subjects with MRI contraindications were also excluded. The exclusion of participants based on COVID was dictated by Emory COVID policies at the time.

A subset of caregiver controls (see below) who were female and also not grandmothers ($N = 25$: age $M = 56.56$, s.d. $= 6.76$, range 37–71 years) were used as controls for comparison with the grandmothers.

Grandmothers provided information on their age, race, body mass index (BMI), household annual income, years of education, hours per week exercise, and also completed several questionnaires online via Research Electronic Data Capture (REDCap).

These measured grandmaternal involvement with and attachment to the grandchild. The Amended Parental Responsibility Scale is a 14-item scale measuring perceived parenting responsibility (McBride and Mills 1993, Montague and Walker-Andrews 2002) that has been modified to compare primary responsibilities between grandmother and parent. Respondents designate who has the primary responsibility for a given task using a 5-point Likert scale ranging from 1 (almost always completed by grandparent) to 5 (almost always completed by parent). The Amended Positive Affect Index is a 10-item scale (Bengtson 1982) that has been modified to measure the grandmother's assessment of the degree of positive feelings between the grandmother and grandchild. It measures understanding, fairness, trust, respect, and affection within the relationship. This scale was initially created to reflect a parent–child relationship. The Amended Supportive Engagement Behaviors Index is a modified version of a 10-item subscale of the Parent Behavior Inventory (Lovejoy et al. 1999). These questions measure grandmaternal warmth and involve behaviors demonstrating acceptance through affection, shared activities, and emotional and instrumental support to a child. While these measures were not originally developed to study grandmaternal caregiving, previous theoretical and empirical studies have suggested the utility and validity of these adapted measures for studying supportive social transactions exchanged among family members, including grandmothers and elderly parents (Bengtson and Roberts 1991, Smith et al. 2015).

One grandmother did not provide data on hours per week exercise.

After providing this information, grandmothers participated in a neuroimaging session that included both a structural MRI scan and a functional MRI scan to measure their neural response to viewing photographs of their grandchild and others. Only the demographic, questionnaire, and structural MRI data are considered here. Analyses of the functional MRI data were previously published (Rilling et al. 2021).

Caregivers

Participants were 24 caregivers of PLWD from the Greater Atlanta area (21 female, age $M = 55.54$, s.d. $= 10.75$, range 25–80 years). Caregivers were recruited via word of mouth, physical flyers, Facebook advertisements and online recruitment (Schlesinger Group | Qualitative & Quantitative Research Services). Caregivers were recruited as part of a larger study aimed at investigating the effect of a cognitive empathy intervention on caregiver mental health and brain function (Rilling et al. 2024). This larger aim influenced the specific study measures that were collected as described below. All dementia caregivers were their care recipient's primary caregiver. Hours caregiving per week ranged widely, from 15 up to 168 for those who were providing full-time care ($M = 91.5$, s.d. $= 60.8$). An additional group of 37 non-caregiver control participants (33 female, age $M = 54.95$, s.d. $= 8.96$, range 32–71 years) were also recruited via word of mouth, physical flyers, and Facebook advertisements. Controls were selected to be of similar age and gender as the caregiver population.

Exclusion criteria: Caregivers and non-caregiver controls were excluded if they had conditions that could be associated with abnormal brain function such as a history of psychiatric illnesses (other than depression and anxiety disorders), history of seizures or other neurological disorders, or a history of alcoholism or any other substance abuse. Subjects with a history of head trauma were excluded based on the severity. Subjects with MRI contraindications were also excluded. Additionally, caregivers and controls were excluded if over the age of 80. Caregivers who cared for their PLWD for an average of <2 h/day were also excluded. The exclusion of participants based on COVID was dictated by the Emory COVID policies at the time.

Caregivers provided data on their age, race, gender, BMI, household annual income, years of education, hours per week exercise, number of alcoholic drinks per week, number of children, number of grandchildren, and the presence/absence of heart disease, diabetes, and hypertension. They also completed several questionnaires via REDCap, including: (i) The Perceived Stress Scale (Cohen et al. 1983), (ii) The Center for Epidemiological Studies Depression Scale (Radloff 1977), (iii) The State/Trait Anxiety Index (limited to the 20 items assessing state anxiety) (Spielberger 1983), (iv) the Zarit Burden Scale (Zarit et al. 1980), which is a measure of caregiving burden, (v) The Interpersonal Reactivity Index (Davis 1983), (vi) the Barrett-Lennard Empathy Scale (Barrett-Lennard 1978), and (vii) the Purpose in Life Scale, a subscale of the Scales of Psychological Well-being (Ryff and Keyes 1995). Caregivers were also asked to rate their overall sleep quality in the past month on a 4-point Likert scale [1 (very bad), 2 (fairly bad), 3 (fairly good) to 4 (very good)]. All of these measures have been used extensively and are known to be valid and reliable instruments. Our own assessment of the internal consistency also confirmed that psychological questionnaires used for the current study had adequate reliability across different groups of subjects, with Cronbach's alpha ranging from 0.703 to 0.963 (Supplementary Table 3).

After providing this information, caregivers participated in a neuroimaging session that included both a structural MRI scan and a functional MRI scan to measure their neural response to viewing photographs of their PLWD and others. Only the structural MRI scans were used to calculate BrainAGE. The functional MRI data were published previously (Rilling et al. 2024). Although both pre- and post-intervention questionnaires and neuroimaging data were collected, only baseline pre-intervention data are analyzed here.

Control participants provided the same data as the caregivers but did not receive a functional MRI scan and only completed a subset of the questionnaires: Perceived Stress Scale, Center for Epidemiological Studies Depression Scale, State/Trait Anxiety Index, and the Purpose in Life Scale. Only the demographic, questionnaire, and structural MRI data are considered here.

For caregivers, questions regarding the history of hypertension, hours per week of exercise, number of alcoholic drinks per week, sleep quality, household income, years of education, number of children and grandchildren, and the Purpose in Life Scale were added part way through the study, so that many participants had to be recontacted to provide these data. Five caregivers could not be reached, and those data are therefore missing. In addition, one caregiver and one control did not provide income data, and one control did not provide their BMI.

Neuroimaging

Participants were positioned in the Siemens Trio 3T MRI scanner. Subjects lay motionless in a supine position in the scanner with a padded head restraint to minimize head movement during scanning. Each scanning session began with a 15 s localizer, followed by a 5-min T1-weighted Magnetization-Prepared Rapid Gradient Echo anatomical scan (TR = 1900 ms, TE = 2.27 ms, matrix = 256 × 256, in-plane resolution 1.00 mm × 1.00 mm, FOV = 250 mm, slice thickness = 1.00 mm, gap = 0 mm). After collecting the anatomical scan, functional scans were acquired.

BrainAGE calculation

T1-weighted images were segmented into GM and WM and affinely normalized using standard preprocessing procedures available in the CAT12.8 toolbox (Gaser et al. 2024, https://neuro-jena.github.io/cat) within Matlab 2019b and SPM12 (Wellcome Centre for Human Neuroimaging, https://www.fil.ion.ucl.ac.uk/spm/). Preprocessing included a unified segmentation (Ashburner and Friston 2005) to remove B0 inhomogeneities and generate an initial segmentation. This initial segmentation was subjected to (local) intensity scaling and adaptive nonlocal mean denoising (Manjon et al. 2010). Subsequently, an adaptive maximum *a posteriori* segmentation (Rajapakse et al. 1997) incorporating a partial volume effect model (Tohka et al. 2004) was used to generate the final segmentation.

Eight configurations of single tissue class models (GM/WM) were generated, varying in spatial resolution (4 mm/8 mm) and Gaussian smoothing (FWHM: 4 mm/8 mm). Principal component analysis using singular value decomposition was applied to all models to orthogonalize the data. We used a Gaussian process regression (GPR) model with a linear covariance function, a constant mean function, and a Gaussian likelihood function. The hyperparameters were set to 100 for the constant mean function and −1 for the likelihood function (Rasmussen and Williams 2006). The GPR used a conjugate gradient method for numerical optimization. Estimates from all eight models were averaged. A linear trend correction was then used to correct for age bias.

The BrainAGE model was trained on a large sample of healthy subjects from five databases (IXI, OASIS-3, Cam-CAN, SALD, and NKI Enhanced), following the methodology outlined in Kalc et al. (2024). The training dataset included subjects aged between 20 and 75 years and consisted of 1894 individuals (mean age: 50.11 ± 13.54 years, including 767 males and 1127 females).

Statistical analysis

For both caregivers and grandmothers, we collected data on potential confounding variables that are known or suspected to affect brain aging (Franke and Gaser 2019). For grandmothers, this included data on age, BMI, years of education, annual household income, hours per week exercise, and race. For caregivers, we collected data on age, gender, BMI, years of education, annual household income, race, number of children, number of grandchildren, hours per week exercise, number of alcoholic drinks per week, sleep quality, depressive symptomology (Center for Epidemiological Studies Depression Scale), Purpose in Life, stress (The Perceived Stress Scale), anxiety (The State/Trait Anxiety Index), and the presence/absence of heart disease, diabetes, and hypertension. Both caregivers and grandmothers were compared with their respective control groups on these variables using two sample *t*-tests. Variables that differed between the two groups were included as covariates, along with caregiver or grandmaternal status, in multiple linear regression models to predict BrainAGE.

Among grandmothers, scores on the Parental Responsibility Scale, the Positive Affect Index, the Supportive Engagement Behaviors Index, and Time Spent With Grandchild were all non-normally distributed. Therefore, we used the nonparametric Kendall's Tau-b correlation coefficient to test for associations between BrainAGE and these variables. We also tested for correlations between BrainAGE and the total number of grandchildren, the age of the youngest grandchild, and the age of becoming a grandmother for the first time using the Pearson Product–Moment Correlation.

Among caregivers of PLWD, we used the Pearson correlation coefficient to test for associations between BrainAGE and self-reported caregiver burden (Zarit Burden Scale). We also compared BrainAGE between spousal and non-spousal caregivers with a two-sample *t*-test.

Results

Grandmothers

Compared with the non-grandmother controls, grandmothers were of similar age ($t(73) = 1.48$; $P = .144$; $d = 0.36$), had less education ($t(73) = -2.86$; $P = .006$; $d = -0.70$), had marginally lower household income ($t(35.62) = -1.95$; $P = .059$; $d = -0.54$), had higher BMI ($t(72) = 3.18$; $P = .002$; $d = 0.79$), and exercised more ($t(54.92) = 4.48$; $P < .001$; $d = 0.81$). With respect to race, grandmothers were also more likely to be Black than controls ($X^2(1, N = 75) = 7.68$, $P = .006$) (Table 1). Whereas all of the grandmothers were necessarily also mothers, only 72% of grandmother controls were mothers. However, there was no significant difference in BrainAGE between grandmother controls who were ($M = 1.23$, s.d. = 6.07) and were not mothers ($M = -2.13$, s.d. = 6.00; $t(23) = 1.25$; $P = .22$; $d = 0.56$). Three grandmothers were the primary caregiver for their grandchild and are referred to as custodial grandmothers.

Multiple linear regression revealed that BrainAGE was associated with grandmaternal status and BMI, but not with household income, exercise level, education, or race. On average, grandmother brains were 5.5 years younger than control brains after accounting for covariates. For comparison, the unadjusted BrainAGE of grandmothers was 3.0 years younger than controls. In addition, BMI was positively associated with BrainAGE (Supplementary Table 1a). Similarly, when we excluded the three custodial grandmothers from our sample, BrainAGE was associated with grandmaternal status and BMI, but not household income, exercise level, education, or race (Supplementary Table 1b).

On average, grandmothers spent 32.1 h/week with their grandchild, but with substantial variance (s.d. = 48.4; range = 0–168), as those who lived with their grandchild were recorded as spending 168 h/week with them. According to the Amended Parental Responsibility Scale, grandmothers were typically less involved in instrumental caregiving than parents were ($M = 25.1$, s.d. = 11.6; scale ranges from 12 to 60, 36 is equal involvement), and their degree of involvement closely matched their preferred level of involvement ($M = 25.4$, s.d. = 7.2). Grandmothers also reported very high levels of positive affect and supportive engagement toward their grandchild (Positive Affect Scale: 0 min, 40 max; $M = 37.0$, s.d. = 4.2; Supportive Engagement Scale: 0 min, 50 max; $M = 47.4$, s.d. = 4.5).

Table 1. Comparison of grandmothers and controls.

	Grandmothers (N)	Controls (N)	P
Age	59.26 ± 7.80 (50)	56.56 ± 6.76 (25)	.144
BMI	**30.53 ± 6.19 (50)**	**26.07 ± 4.21 (24)**	**.002**
Exercise (hours/week)	**17.56 ± 18.24 (49)**	**5.44 ± 3.59 (25)**	**<.001**
Income	\$68 944 ± 49 449 (50)	\$100 218 ± 72 198 (25)	.059
Education (years)	**14.92 ± 2.02 (50)**	**16.4 ± 2.29 (25)**	**.006**
Race			
Black	**44% (22)**	**12% (3)**	**.006**
Nonblack	**56% (28)**	**88% (22)**	

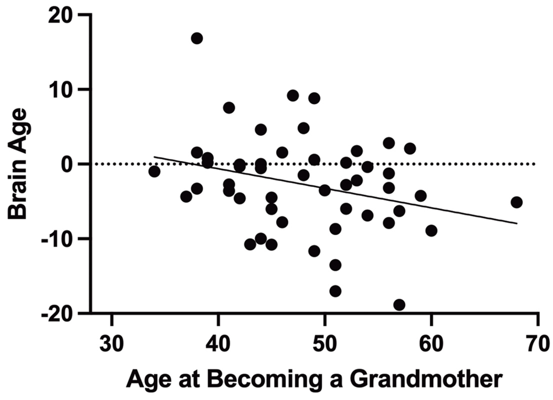

Figure 1. Scatterplot of the relationship between grandmaternal BrainAGE and age at becoming a grandmother for the first time.

BrainAGE was not associated with measures of grandmaternal investment, such as the Parental Responsibility Scale ($\tau b = -0.06$, $P = .51$) and the Positive Affect Index ($\tau b = -0.04$, $P = .73$), but it was negatively associated with the Supportive Engagement Behaviors Index ($\tau b = -0.24$, $P = .02$). It was also negatively associated with the amount of time spent with the grandchild per week when the three custodial grandmothers were excluded from analysis ($\tau b = -0.21$, $P = .04$). BrainAGE was not associated with the total number of grandchildren ($r(48) = 0.16$, $P = .27$) or the age of the youngest grandchild ($r(48) = -0.26$, $P = .07$). On the other hand, BrainAGE was negatively associated with age at becoming a grandmother for the first time ($r(48) = -0.29$, $P = .04$), such that women who became a grandmother later in life derived more benefits in terms of reduced BrainAGE (Fig. 1).

Caregivers for people living with dementia

Caregivers and non-caregiver controls did not differ in age ($t(59) = 0.23$, $P = .82$), the proportion of female/male participants ($X^2(1, N = 61) = 0.041$, $P = .84$), years of education ($t(54) = -0.29$, $P = .773$), household income ($t(52) = 0.771$, $P = .44$), number of children ($t(54) = -0.58$, $P = .56$), or number of grandchildren ($t(54) = 0.63$, $P = .53$), percentage who were parents ($X^2(1, N = 56) = 0.\ 34$, $P = .56$), or percentage who were grandparents ($X^2(1, N = 56) = 0.66$, $P = .42$). In terms of health status, caregivers and controls did not differ in their likelihood of having heart disease ($X^2(1, N = 61) = 3.19$, $P = .07$), diabetes ($X^2(1, N = 61) = 2.28$, $P = .13$), or hypertension ($X^2(1, N = 57) = 1.70$, $P = .19$). Nor did they differ in terms of alcohol consumption ($t(54) = 0.50$, $P = .62$), amount of exercise ($t(54) = -0.42$, $P = .67$), or sleep quality ($t(28.66) = -0.97$, $P = .34$). Psychologically, they did not differ in self-reported depressive symptomology ($t(35.47) = 0.159$, $P = .88$) or Purpose in Life ($t(54) = -0.12$, $P = .91$). On the other hand, caregivers had a higher BMI ($t(58) = 2.58$, $P = .013$; $d = 0.68$) and reported higher levels of stress ($t(36.32) = 2.60$, $P = .013$; $d = 0.74$) and anxiety ($t(36.16) = 2.51$, $P = .017$; $d = 0.72$) compared with controls. Caregivers were also more likely to be non-white compared with controls ($X^2(1, N = 61) = 7.17$, $P = .007$) (Table 2).

Multiple linear regression revealed that BrainAGE was associated with caregiver status ($t = -2.98$, $P = .004$) and stress ($t = 3.20$, $P = .002$), but not with race ($t = 0.23$, $P = .82$), anxiety ($t = -0.03$, $P = .97$), or BMI ($t = -0.74$, $P = .46$). On average, caregiver brains were 4.7 years younger than control brains after accounting for covariates. For comparison, the unadjusted BrainAGE of caregivers was 2.4 years younger than controls. In addition, more self-reported stress was associated with greater BrainAGE (Supplementary Table 2; Fig. 2).

Table 2. Comparison of caregivers and controls.

	Caregivers (N)	Controls (N)	P
Age	55.54 ± 10.75 (24)	54.95 ± 8.96 (37)	.815
Education (years)	16.00 ± 2.31 (19)	16.19 ± 2.32 (37)	.773
Combined income	$108 611.11 ± 61 160.48 (18)	$94 470.56 ± 64 642.58 (36)	.444
Parenthood			
# children	1.53 ± 1.31 (19)	1.81 ± 1.91 (37)	.564
Is a parent	68.42% (13)	75.68% (28)	.562
Is not a parent	31.58% (6)	24.32% (9)	
Grandparenthood			
# grandchildren	1.42 ± 2.93 (19)	0.97 ± 2.67 (37)	.529
Is a grandparent	31.58% (6)	21.62% (8)	.415
Is not a grandparent	68.42% (14)	78.38 (29)	
Alcohol (drinks/week)	2.11 ± 2.62 (19)	1.78 ± 2.11 (37)	.622
Exercise (hours/week)	5.32 ± 3.96 (19)	5.81 ± 4.23 (37)	.673
Sleep quality	1.68 ± 0.82 (19)	1.89 ± 0.61 (37)	.339
Depression (0–60)	17.04 ± 12.96 (24)	16.57 ± 8.37 (37)	.875
Purpose in life	39.00 ± 7.06 (19)	39.23 ± 6.04 (37)	.905
BMI	**29.70 ± 6.58 (24)**	**26.05 ± 4.41 (36)**	**.013**
Stress	**17.54 ± 8.34 (24)**	**12.51 ± 5.58 (37)**	**.013**
Anxiety (20–80)	**38.92 ± 14.56 (24)**	**30.46 ± 9.67 (37)**	**.017**
Gender			
Female	87.5% (21)	89.19% (33)	.84
Male	12.5% (3)	10.81% (4)	
Heart disease			
Has heart disease	8.33% (2)	0% (0)	.074
No heart disease	91.67% (22)	100% (37)	
Diabetes			
Has diabetes	12.5% (3)	2.70% (1)	.131
No diabetes	87.5% (21)	97.30% (36)	
Hypertension			
Has hypertension	20% (4)	8.11% (3)	.192
No hypertension	80% (16)	91.98% (34)	
Race			
White	**41.67% (10)**	**75.68% (28)**	**.007**
Nonwhite	**58.33% (14)**	**24.32% (9)**	

Among caregivers, self-reported caregiving burden was positively associated with BrainAGE ($r(22) = 0.58$, $P = .003$), such that the beneficial effect of caregiving was attenuated, or even reversed, with increasing burden (Fig. 3).

Spousal caregivers ($n = 7$, $M = -7.9$ years, s.d. $= 6.4$) also had lower unadjusted BrainAGE than non-spousal caregivers ($n = 17$, $M = -0.14$ years, s.d. $= 4.73$; $t(22) = -3.30$, $P = .003$).

Discussion

Parental caregiving has been associated with slower brain aging, but the generalizability of this finding to other forms of caregiving has not yet been explored. Here we show that after controlling for relevant covariates, both grandmothers and dementia caregivers

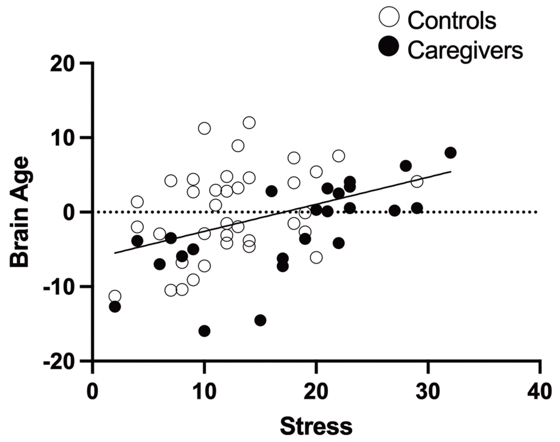

Figure 2. Scatterplot of BrainAGE vs. perceived stress in caregivers and controls.

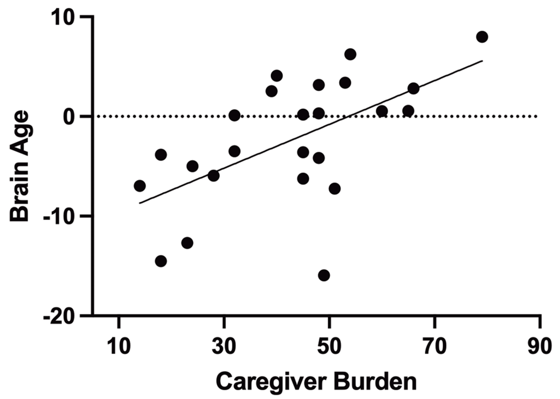

Figure 3. Scatterplot of BrainAGE vs. caregiver burden among caregivers.

have lower brain age than a control group. Both grandmothers and dementia caregivers commonly provide care for a dependent. The same is true of parents, who by middle-age, have also been shown to have a lower brain age compared with nonparents (de Lange et al. 2019, Ning et al. 2020). In both males and females, the largest effect of parity was found for parents with three children, who had a brain age that was 0.7 years younger than childless adults (Ning et al. 2020). In comparison, the unadjusted BrainAGE of grandmothers and caregivers in our study were 3.0 and 2.6 years younger than controls, respectively. After accounting for relevant covariates, the adjusted BrainAGE of grandmothers and caregivers were 5.5 and 4.7 years younger than controls, respectively. The average age of the grandmothers and caregivers in our sample was in the mid- to late 50s. Parents in the above studies were studied at a similar age (i.e. average in the late 50s) but likely provided their most intensive childcare decades earlier. Thus, it may be that caregiving later in life has a larger impact on brain aging compared with care provided in young adulthood. Indeed, among grandmothers, we found that those who took on that role later in life derived more benefits in terms of reduced brain age compared with those who became grandmothers at a younger age. Further support is provided by a study showing that becoming a grandmother lowered mortality only when it occurred after 50 years of age (Christiansen 2014). The grandmothers in our study were likely at various stages of the menopausal transition, including premenopause, perimenopause, and postmenopause. Neuroimaging studies show that this transition involves substantial changes in brain structure, connectivity, and energy metabolism (Mosconi et al. 2021). Therefore, older postmenopausal female brains are in a different state and could potentially be differentially impacted by a caregiving experience. Although men do not experience menopause, our caregiving sample was highly skewed toward women, such that the sample was likely composed of mostly postmenopausal females as well. Future studies with grandfathers and male caregivers would help determine the importance of menopause for our findings.

According to the well-known grandmother hypothesis, there has been selection for postmenopausal longevity in human females to permit investment in grandchildren that increases grandmaternal inclusive fitness (Hawkes et al. 1998, Hawkes and Coxworth 2013). The hypothesis is supported by evidence that modern-day grandmaternal investment often improves grandchild health and survival and can increase maternal fertility by shortening maternal interbirth intervals (Hawkes et al. 1997, Lahdenpera et al. 2004, Sear and Mace 2008, Chung et al. 2020). In addition to explaining our species' postmenopausal longevity, grandmaternal investment may also help explain longevity at the level of individuals. For example, caregiving grandparents have been shown to have lower mortality than either non-caregiving grandparents or non-grandparents (Hilbrand et al. 2017). Our results suggest that grandmaternal involvement may actually slow the aging process, which would allow simultaneous selection on both caregiving and longevity. A similar process operating in our evolutionary past could explain the current state in which postmenopausal females often provide considerable care to their grandchildren.

If grandmaternal involvement reduces brain age, one might expect more involved grandmothers to have lower brain age than less involved grandmothers. However, in the extreme, grandmaternal caregiving can become burdensome. For example, custodial grandparental care can have negative health consequences (Ross and Aday 2006, Chen and Liu 2012). As with parental care, this might result in a nonlinear relationship between grandmaternal involvement and brain aging. While time (hours per week) spent with the grandchild was negatively correlated with brain age when custodial grandmothers were excluded, that association becomes nonsignificant when custodial grandmothers are included. This is because custodial grandmothers, who spend maximum time with their grandchild, tend to have higher brain age. Specifically, the three custodial grandparents in our sample had an average unadjusted brain age of 0.56 years (s.d. = 0.86) compared with –2.95 years (s.d. = 6.70) for the noncustodial grandmothers ($t(48) = 0.90$, $P = .37$). While hours per week with the grandchild is one measure of grandmaternal involvement, the frequency of contact between grandmother and grandchild is a related but different measure since some grandmothers have frequent but short visits and others have infrequent but long visits. Examining the relationship between brain age and frequency of contact revealed neither a significant linear nor quadratic relationship. However, average brain age tended to be lower among grandmothers who saw their grandchildren once per week ($M = -3.61$) or once per month ($M = -4.62$) compared with daily ($M = -0.98$) or only once per year ($M = -1.14$) or less ($M = -2.74$). While these effects were not statistically significant, they raise the possibility that a significant nonlinear effect may emerge with a larger sample size.

There are a number of potential mechanisms by which caregiving could affect brain aging. One possibility is that the mental and physical activity required by caregiving slows the aging process. One study found that dementia caregivers were three times less likely to be physically inactive compared with non-caregiver controls (O'Sullivan et al. 2019). Caring for another person also likely involves cognitive demands that could slow brain aging. Dementia caregivers, e.g. typically have to plan and coordinate the activities of their care recipient. They also have to be nimble in the moment in responding to their care recipient's behaviors, and they have to adopt a long-term analytic view of the progression of the illness and its effects on the care recipient. Another possible mechanism is that caregivers are more socially connected and have stronger support networks, which could slow brain aging by buffering against life stress (House et al. 1988). For example, grandparents may have more contact with their children than non-grandparents and may be drawn into social networks via their caregiving activities. On the other hand, dementia caregivers often suffer from social isolation (Kovaleva et al. 2018, Lee et al. 2022). It is also possible that emotional bonding with the care recipient decreases BrainAGE. One candidate in such a mechanism is the hormone and neuropeptide oxytocin, which is both involved in allomaternal care (Madden and Clutton-Brock 2011, Saito and Nakamura 2011, Weisman et al. 2012, Finkenwirth et al. 2016, Yuan et al. 2019) and known to have neuroprotective effects (Kamrani-Sharif et al. 2023). A final possible mechanism is that the meaning and purpose afforded by successfully helping a relative in need triggers continued physiological and behavioral investment in self-maintenance, which has the advantage of keeping oneself alive longer to provide future care. In the strict Darwinian sense, this mechanism would be maladaptive when care is directed at debilitated, post-reproductive individuals. However, this type of caregiving may have been rare in our evolutionary past, and therefore not impacted by natural selection.

While our study was not designed to systematically evaluate the mechanism by which caregiving influences BrainAGE, our covariate analyses are relevant to this question. Whereas neither grandmaternal positive affect nor grandmaternal involvement in instrumental care was associated with BrainAGE among grandmothers, grandmaternal supportive engagement was negatively correlated with BrainAGE. Additionally, time spent with the grandchild was negatively correlated with BrainAGE when the three custodial grandmothers were excluded from the analysis. Thus, grandmothers who spend more time with their grandchild and who engage in more positive behaviors with them may derive more benefits in terms of BrainAGE reduction. This might afford the opportunity for more physical activity, greater mental stimulation, stronger emotional bonding, greater social integration, or greater meaning and purpose, any of which could conceivably mediate the effect. These results should be interpreted cautiously, however, because the significant correlations are weak and do not survive correction for multiple comparisons. Furthermore, our sample of grandmothers reported very high levels of both positive affect and supportive engagement toward their grandchild (Positive Affect Scale: 0 min, 40 max; $M = 37.0$, s.d. $= 4.2$; Supportive Engagement Scale: 0 min, 50 max; $M = 47.4$, s.d. $= 4.5$), such that there was limited variation for these analyses. In contrast to grandmothers, time spent caregiving was not correlated with BrainAGE among dementia caregivers, but we may have lacked adequate statistical power to detect such an effect in our sample of 24 dementia caregivers.

Caregivers of PLWD had lower brain age even though they reported more stress and anxiety compared with controls. This result parallels another study showing better cognitive function in caregivers despite increased stress and depression (O'Sullivan et al. 2019). These findings suggest that any negative effects of stress and anxiety on brain aging can be more than compensated by positive effects of caregiving.

One potential explanation that has been offered for increased longevity in dementia caregivers is that healthy people are more likely to adopt and continue in a caregiving role (Fredman et al. 2015), which would argue against a causal impact of caregiving on brain aging. However, in our sample, there were no differences between caregivers and controls in any health measures. Additionally, a recent longitudinal study (Leggett et al. 2020) found that the least healthy caregivers actually experienced the greatest mortality reduction from caregiving. These observations support the possibility that dementia caregiving can actually reduce cognitive and brain aging.

It is important to emphasize that the association between dementia caregiving and lower brain age was attenuated when caregiving burden was high. Moreover, both stress and caregiving burden were associated with increased BrainAGE. Conceivably, stress could accelerate brain aging by increasing stress hormone levels and/or by increasing levels of proinflammatory cytokines (MohanKumar et al. 2023). This modulatory effect of caregiver burden might help to explain the inconsistent findings in the literature with respect to whether dementia caregiving has positive or negative effects on caregivers. That is, caregiving is more likely to have positive effects when the burden level is low (Schulz et al. 2020). In fact, the seminal study by Schulz and Beach (1999) found that increased mortality in dementia caregivers was specific to caregivers who were experiencing strain. Our finding that burden is positively correlated with BrainAGE also emphasizes the importance of efforts to reduce burden among caregivers of PLWD, and of reducing stress levels in older people more generally. When burden is low, dementia caregiving can be a rewarding (Fisher et al. 2011) and, it seems, even a rejuvenating experience.

Finally, our data suggest that dementia caregiving spouses may derive more benefits in terms of brain aging than caregivers who are not spouses, as evidenced by spousal caregivers having a significantly lower BrainAGE. Although spousal caregiving has been posited to be more burdensome (Christian et al. 2023), this was not the case in our data (spouse $M = 37.00$, s.d. $= 17.32$; non-spouse $M = 45.00$, s.d. $= 16.26$; $t(22) = -1.08$, $P = .29$). Since spousal caregivers were significantly older ($M = 64.57$ years, s.d. $= 8.77$) than other caregivers ($M = 51.82$, s.d. $= 9.32$) in our study ($t(22) = 3.09$, $P = .005$), this finding raises the possibility that, similar to grandmothers, having a caregiving experience later in life provides more benefits in terms of brain aging.

There are important limitations to our study that should be acknowledged. First, this is a cross-sectional study. While we controlled for several variables that may affect brain aging, we cannot exclude the possibility that group differences in some unmeasured confounding variables drive these effects. Longitudinal studies that follow participants across the transition to caregiving will be needed to definitively test our hypothesis. Second, we had limited statistical power to evaluate our hypotheses due to small sample sizes. In contrast to previous studies that showed modest effects of parenthood on brain age in samples of thousands of participants (de Lange et al. 2019, Ning et al. 2020), our larger effect size estimates for grandmothers and dementia caregivers could be due to our smaller sample sizes. Third, our sample of grandmothers and caregivers may not be representative of the general population of grandmothers and caregivers. As we noted in a previous publication (Rilling et al. 2021), our sample of grandmothers was mentally and physically very healthy and highly positively engaged with their grandchildren. Future studies should determine if BrainAGE is also reduced among less healthy and less positively engaged grandmothers. Our dementia caregivers were selected to be high in self-reported caregiver burden; however, this did not preclude detecting salutary effects of caregiving and a significant positive correlation between caregiver burden and BrainAGE. Again, it would be interesting to extend this research to caregivers experiencing lower levels of caregiving burden. A fourth limitation is that grandmothers were not asked if they happened to also be dementia caregivers so we could not account for this potential influence in our analysis. Fifth, our study was not designed to evaluate potential mechanisms to explain the relationship between caregiving status and lower brain age. Future studies should be designed and powered to do so. Finally, we included several variables as covariates in our analysis that had previously been linked with brain aging (Franke and Gaser 2019). While we replicated an effect of BMI on BrainAGE in our grandmother sample, we did not detect significant effects of either exercise or education. We assume that this is due to the limited statistical power afforded by our sample size.

In sum, we find that interacting with a dependent relative, whether adult or child, is associated with lower BrainAGE among adults, raising the possibility that such interactions slow brain aging. Thus, caring for others may support healthy brain and cognitive aging. Future studies should investigate whether the effects observed in grandmothers also apply to grandfathers, whose longevity may be attributable to different selection pressures (Lahdenperä et al. 2007, 2011). Future studies might also investigate if the putative benefits of caregiving extend to caring for nonrelatives, which also seems to reduce mortality (Hilbrand et al. 2017), and even potentially caring for nonhuman species such as domesticated pets.

Supplementary data

Supplementary data is available at SCAN online.

Conflict of interest: The authors have no conflict of interest to declare.

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Data availability

This study was not preregistered. Data are available at: https://osf.io/qa4hr/.

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