

Gender differences in superior-memory SuperAgers and associated factors in an Australian cohort

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Abstract

Background: Despite expectations of deterioration in memory function with age, some older adults demonstrate superior memory performance and have been defined as SuperAgers. **Method:** SuperAgers were identified in a population-based prospective cohort in Australia ($n = 1,679$; 49.4% female; mean age = 70.6 ± 1.5 years) as participants who, over a 12-year period, consistently scored at or above the median of participants 40 years younger on recall tasks. Chi-square and t tests and logistic regression models measured associations between risk factors and being a SuperAger. **Results:** The prevalence of SuperAgers was higher in women (8.6%) than men (5.3%). Education was associated with being a SuperAger for women (adjusted odds ratio [OR] = 1.13, 95% confidence interval [CI] = [1.01, 1.26]) and men (adjusted OR = 1.22, 95% CI = [1.05, 1.40]). Other associated factors were investigative activities and alcohol consumption for women and social activities and depressive symptoms for men. **Conclusion:** Adults over 60 can sustain superior memory recall; however, associated factors may vary between genders.

Keywords

cognition, gender, memory, risk factors, SuperAger

Introduction

As populations age worldwide, the concept of “successful aging” is of increasing interest, although it is not without controversy. This stems, first, from a lack of consensus surrounding what the term means and how it should be measured (Cosco et al., 2014; Martin et al., 2015) and, second, from debate regarding whether it is an appropriate and useful concept or a harmful and limiting one (Martinson & Berridge, 2015). An alternative construct that has emerged from the literature in recent years, particularly in the domain of cognitive aging, is that of the SuperAger. A SuperAger has been defined as a person who, when tested for memory recall in older age, demonstrates superior memory performance by scoring as high as, or higher than, normative values of people aged decades younger (Gefen et al., 2014). The existence of SuperAgers is important because it demonstrates not only the possibility of high functioning in later life, but also that it is not just young people who have excellent memory, thus challenging assumptions and negative stereotypes about aging.

With memory impairment being one of the most common cognitive complaints in older age and a potential precursor to conditions such as Alzheimer’s disease (Arvanitakis et al.,

2018), there is considerable interest in risk and protective factors for exceptional memory in later life. To date, being a SuperAger has been linked to lower likelihood of having the APOE-ε4 allele (Rogalski et al., 2013), greater cortical thickness (Gefen et al., 2015; Harrison et al., 2012; Rogalski et al., 2019), lower frequency of Alzheimer pathology plaques and tangles (Rogalski et al., 2013), and greater density of von Economo neurons (Gefen et al., 2015; Rogalski et al., 2013), albeit in a small volunteer-recruited sample. Other investigations of maintained or superior memory in older age have reported links to youthful epigenetic age (Degerman et al., 2017), increased hippocampal volume

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(Dekhtyar et al., 2017), and specific metabolites (Mapstone et al., 2017). Associations with lifestyle and psychosocial factors are less established, although Maher found SuperAgers had greater levels of positive relations with others than their cognitively average peers (Maher et al., 2017).

It is largely unknown whether factors associated with cognitive decline in later life, such as diabetes, hypertension, and smoking, are also inversely associated with superior cognitive performance. It can be hypothesized that factors that are protective for memory decline in older age, such as education and other cognitively stimulating activities, might be positively associated with exceptional memory. Education has been reported as a marker of Successful Aging using a broad definition that included, but was not limited to, cognitive measures (Cosco et al., 2017). This analysis by Cosco et al. was unique in including stratification by gender. Despite evidence that memory recall scores differ by gender (Kramer et al., 2003; Munro et al., 2012; Sundermann et al., 2016) and that risk and protective factors for cognitive performance in later life also vary among men and women (McDermott et al., 2017), prior definitions of SuperAging have rarely taken these differences into account.

With the aim of adding to previous literature on SuperAging, the objectives of this article were to (a) apply a gender-specific definition of a SuperAger to a large community-based, randomly recruited cohort that allows direct comparison of memory recall test scores from older and younger participants within the same population; (b) measure the prevalence of male and female SuperAgers in this population; and (c) investigate gender-specific associations between being a SuperAger and various demographic, physical, genetic, lifestyle, and psychosocial factors previously associated with later-life cognition, including education.

Materials and Methods

The Personality and Total Health Through Life (PATH) Cohort Study

The data set originated from the PATH cohort study. Participants were randomly recruited from the sampling frame of the electoral rolls of the Australian Capital Territory and neighboring town Queanbeyan in three narrow age bands: 20 to 25 (the 20s cohort), 40 to 45 (the 40s cohort), and 60 to 65 (the 60s cohort) (Anstey et al., 2012). The original aim of the study was to collect longitudinal data on risk factors related to depression, anxiety, substance abuse, and cognitive ability. To date, there have been four completed waves of measurement, including baseline in 2000 and three waves of follow-up approximately 4 years apart. Measurements from the first three waves covering an average period of 12 years are included in this study, as a change in measurement technique rendered the outcome variable of interest (memory recall scores) for the fourth wave incomparable.

Participants

Participants were included in the SuperAger analysis if they were part of the 60s cohort (aged 68–74 at Wave 3) and had completed all three waves of the Mini-Mental-State Examination (MMSE) and the California Verbal Learning Tests (CVLT) of immediate and delayed recall, as the scores of these tests were used to define which participants were SuperAgers. As cognitively healthy older adults were the focus of this study, participants were excluded if they reported a history of stroke or had an MMSE score of less than 24 at any wave. Of the 2,551 (1,234 female and 1,317 male) participants enrolled in the study at baseline, 829 women and 850 men met eligibility criteria for this analysis ($N = 1,679$, participation rate of 65.8%). Figure 1 presents the flow of participants, including numbers of exclusions and loss to follow-up at each wave.

Exposure and Outcome Variables

Exposure variables. Risk and protective factors previously associated with cognition in later life (Anstey et al., 2015; Hersi et al., 2017) were tested for associations with being a SuperAger. All exposure variables were measured at Wave 3 except education and APOE- $\epsilon 4$ carrier status, which were collected at Wave 2 and baseline, respectively. Demographic exposure variables included age, education, and living with a partner. Education was measured as a participant's highest level of education converted to a number of years. The genetic exposure variable was APOE- $\epsilon 4$ carrier status (described in Andrews et al., 2016; Jorm et al., 2007), whereas physical variables included self-reported hypertension, cholesterol medication use, diabetes, and history of head injury. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in centimeters, using self-reported weight and height. Lifestyle variables were all self-reported and included exercise as none/mild, moderate, or vigorous as per the Whitehall II study (Stafford et al., 1998); current smoking; standard alcoholic drinks consumed per week; sleep problems; total positive and negative social exchanges per week; and frequency of participation in social activities, such as being on a committee, or investigative activities, such as solving maths or chess puzzles, in the last 6 months, using a shortened activity scale (RAISEC) based on the Holland code (Bielak et al., 2012; Kerby & Ragan, 2002). Psychosocial exposure variables were scores on the Goldberg depression and anxiety scales (Goldberg et al., 1988).

Outcome variables. Cognition was measured using standard tests, including the MMSE and the CVLT of immediate and delayed recall which were both used to identify SuperAgers. The MMSE is a validated cognitive screening test that includes items on memory recall as well as orientation, attention, and language (Folstein et al., 1975). The CVLT

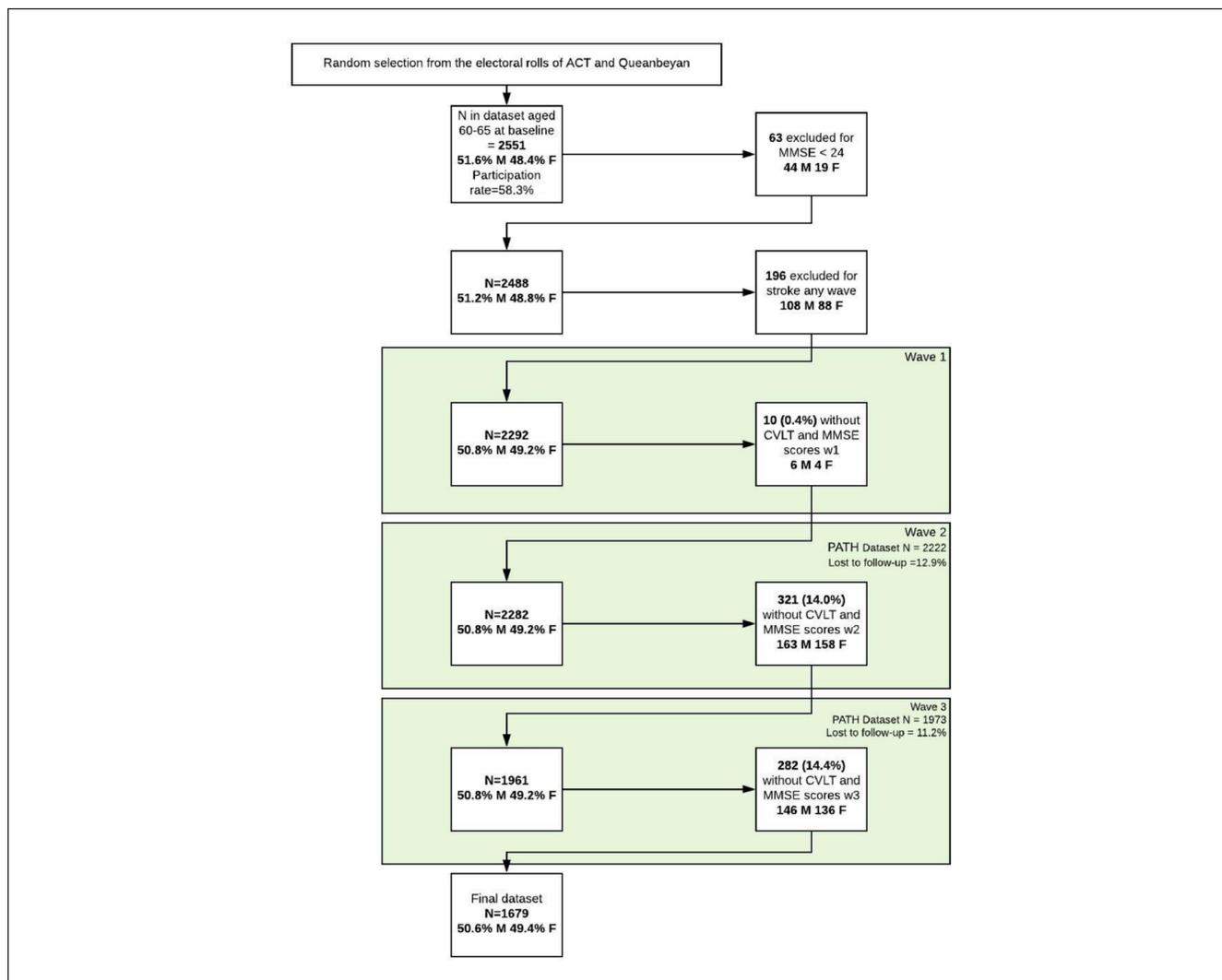


Figure 1. Flow of the 60s cohort participants (Anstey et al., 2012).

involves reading participants a list of 16 words and asking them to recall as many as they can, first immediately and then after some delay with other tasks intervening (Delis et al., 1987). Both the immediate and delayed recall measures used in this study were the result of single trials, meaning that participants did not get the chance to better their scores over repeated trials, thus avoiding ceiling effects associated with non-normally distributed test scores influencing results (Uttl, 2005).

SuperAger Definition

The definition of a SuperAger used in this study was informed by previous definitions in the literature that incorporated two components: the first being a comparison of memory recall scores of older participants with those of younger participants, and the second being a measure of overall cognition. The most-cited definition of SuperAgers recruited volunteer

participants aged 80+ and designated them as SuperAgers if their delayed recall scores on the Rey Auditory Verbal Learning Test (RAVLT) were equal to, or higher than, average normative scores of people in their 50s and 60s (Cook et al., 2017; Gefen et al., 2015, 2014; Harrison et al., 2012; Janeczek et al., 2018; Maher et al., 2017; Rogalski et al., 2013, 2019). Other definitions used different age ranges, for example, Sun et al. (2016) compared older participants aged 60 to 80 with younger participants aged 18 to 35. SuperAger and other definitions of superior cognitive performance in older age are summarized by Borelli et al. (2018) in a systematic review.

This study's definition of a SuperAger attempted to supplement the literature by using a randomly recruited sample and incorporating a cross-temporal component, in that recall test scores were compared across three waves of data collection. Furthermore, whereas previous SuperAger definitions predominantly used mean normative test scores of a younger age group as a comparison for an older age group, the PATH

Table 1. Median (and Interquartile Values) of Immediate and Delayed CVLT Recall Scores Across Waves for the 20s and 60s Cohorts, Overall and Stratified by Gender.

Recall test and wave	Both genders combined		Female		Male	
Immediate recall						
Wave	20s	60s	20s	60s	20s	60s
1	8 (6, 9)	7 (6, 9)	8 (7, 10)	8 (6, 9)	7 (6, 9)	7 (5, 8)
2	8 (7, 10)	7 (5, 8)	9 (7, 10)	7 (6, 9)	8 (6, 9)	6 (5, 8)
3	9 (7, 10)	6 (5, 8)	9 (7, 11)	7 (6, 9)	8 (7, 10)	6 (5, 8)
Delayed recall						
Wave	20s	60s	20s	60s	20s	60s
1	7 (6, 9)	6 (5, 8)	8 (6, 9)	7 (5, 8)	7 (5, 8)	6 (4, 7)
2	8 (6, 9)	6 (5, 8)	8 (6, 10)	7 (5, 8)	7 (6, 9)	5 (4, 7)
3	8 (6, 10)	6 (4, 7)	9 (7, 10)	6 (5, 8)	8 (6, 9)	5 (4, 7)

CVLT scores can range from 0 to 16. CVLT = California Verbal Learning Test.

study design included multiple narrow age-range cohorts, allowing direct comparison between test scores of participants recruited in their 20s and participants recruited in their 60s at each study wave.

SuperAgers were thus defined as participants from the 60s cohort who, for all three consecutive waves over a period of 12 years, maintained

1. principally, both immediate and delayed recall scores at or above the median of the immediate and delayed recall scores of participants of the same gender from the 20s cohort.
2. an MMSE score of 29 or 30 for that wave, as a supporting indicator of a good level of general overall cognition.

Median test scores were used as the point of comparison rather than mean test scores, because medians of CVLT scores are integers that can be easily compared with individual CVLT scores (which are also integers) without incorporating imprecision associated with rounding. The practical decision to use median test scores was supported by descriptive statistical analysis of CVLT scores, with histograms showing that scores approximated the normal distribution at all test waves for all age cohorts.

Analysis

Medians for immediate and delayed recall cognitive scores, stratified by age group and gender, were calculated and used to determine SuperAger cutoffs for each wave individually. Participants who met the criteria for being a SuperAger at all three waves were identified as SuperAgers. Chi-square tests for categorical variables and *t* tests for continuous variables were conducted to determine associations between potential risk factors and being a male or female SuperAger. Any variables that were found to have a significant association ($p < .05$) were used as input to gender-specific logistic regression

models to obtain adjusted odds ratios (ORs). Adjustments were made with one other associated variable at a time and then for all associated variables in the one model.

All analysis was performed using Stata version 15.1 (StataCorp LLC, Texas, US).

Results

Medians for immediate and delayed recall cognitive scores for the 20s and 60s cohorts in Waves 1 to 3 are presented in Table 1, overall and stratified by gender. While median scores were similar at Wave 1 for both age groups, scores for the 20s cohort increased over waves for both tests, whereas scores for the 60s cohort decreased.

Prevalence of SuperAgers

There was a higher prevalence of female SuperAgers (71 of 829 female participants, 8.6%) than male SuperAgers (45 of 850 male participants, 5.3%) ($p < .01$). Overall, 6.9% (116 of 1,679 participants) of the population were identified as SuperAgers.

Associated Risk and Protective Factors

Most factors previously identified as associated with older age cognitive decline were not found to be associated with being a SuperAger. As shown in Table 2, factors associated with being a female SuperAger were more years of education, more standard alcoholic drinks per week, and higher frequency of involvement in investigative activities. For male SuperAgers, more years of education, higher frequency of involvement in social activities, and a lower score on the Goldberg depression scale were the only factors associated with SuperAging. Cell sizes were small for some variables: There were very few SuperAgers (<10) who had suffered head injuries, had diabetes, had sleep problems, participated in vigorous exercise, or were current smokers.

Table 2. Gender-Stratified Comparison of SuperAgers and Non-SuperAgers in Terms of Risk and Protective Factors for Cognitive Decline.

Risk factor	Female				Male					
	SuperAger M (SD) or %	Normal M (SD) or %	p value	Odds ratio ^a (95% CI)	N	SuperAger M (SD) or %	Normal M (SD) or %	p value	Odds ratio (95% CI)	N
<i>Demographic</i>										
Age	70.42 (1.58)	70.68 (1.52)	.18	0.90 [0.76, 1.05]	829	70.24 (1.35)	70.55 (1.48)	.17	0.86 [0.70, 1.07]	850
Education	14.52 (2.22)	13.52 (2.52)	<.01	1.18 [1.07, 1.31]	827	15.79 (1.91)	14.44 (2.67)	<.001	1.26 [1.09, 1.45]	849
Partnered	70.4%	61.6%	.14	1.48 [0.87, 2.52]	829	86.7%	86.9%	.96	0.98 [0.40, 2.36]	849
<i>Physical</i>										
BMI	26.89 (5.6)	26.74 (5.5)	.82	1.01 [0.96, 1.05]	816	26.03 (3.28)	26.82 (4.23)	.22	0.95 [0.87, 1.03]	845
Hypertension	77.5%	76.9%	.92	1.03 [0.58, 1.84]	825	75.6%	79.0%	.59	0.82 [0.41, 1.66]	848
On cholesterol meds	29.6%	39.8%	.09	0.63 [0.37, 1.08]	829	35.6%	42.0%	.39	0.76 [0.41, 1.42]	849
Diabetes	8.5% ^b	10.2%	.65	0.82 [0.34, 1.95]	829	11.1% ^b	15.4%	.43	0.69 [0.27, 1.77]	849
History of head injury	4.2% ^b	4.0%	.93	1.06 [0.31, 3.56]	821	6.7% ^b	11.2%	.34	0.56 [0.17, 1.86]	846
<i>Genetic</i>										
APOE ε4 carrier	21.7%	28.1%	.26	0.71 [0.39, 1.29]	788	29.55%	26.30%	.64	1.18 [0.60, 2.29]	812
<i>Lifestyle</i>										
Exercise	None/mild 50.7% Moderate 39.4% Vigorous 9.9% ^b	None/mild 51.3% Moderate 39.5% Vigorous 9.2%	.98	1.03 [0.71, 1.49]	821	None/mild 28.89% Moderate 55.56% Vigorous 15.56% ^b	None/mild 37.58% Moderate 43.95% Vigorous 18.48%	.31	1.11 [0.74, 1.69]	836
Current smoker	7.0% ^b	5.3%	.53	1.36 [0.52, 3.56]	829	4.4% ^b	4.9%	.90	0.91 [0.21, 3.90]	849
Alcoholic drinks per week	6.01 (5.54)	4.24 (4.99)	<.01	1.06 [1.02, 1.10]	828	9.18 (7.66)	9.01 (9.10)	.90	1.00 [0.97, 1.04]	847
Sleep problems	40.9%	37.4%	.56	1.16 [0.70, 1.90]	828	17.8% ^b	28.6%	.12	0.54 [0.25, 1.18]	845
Total positive exchanges	23.96 (3.52)	23.74 (3.78)	.68	1.02 [0.94, 1.10]	511	24.67 (2.96)	24.50 (2.73)	.71	1.02 [0.90, 1.16]	729
Total negative exchanges	8.63 (3.93)	8.11 (5.01)	.49	1.02 [0.96, 1.08]	499	8.32 (4.10)	8.19 (4.77)	.87	1.01 [0.94, 1.08]	718
Social activities in a week	2.66 (1.13)	2.41 (1.14)	.08	1.21 [0.97, 1.51]	820	2.78 (1.04)	2.21 (1.21)	<.01	1.54 [1.17, 2.03]	844
Investigative activities in a week	2.03 (1.06)	1.63 (1.08)	<.01	1.39 [1.11, 1.74]	821	2.56 (1.03)	2.26 (1.23)	.11	1.23 [0.95, 1.59]	844
<i>Psychosocial</i>										
Goldberg depression score	1.87 (1.78)	1.63 (1.80)	.28	1.07 [0.94, 1.22]	826	0.87 (1.16)	1.46 (1.71)	.02	0.76 [0.59, 0.97]	845
Goldberg anxiety score	2.32 (2.12)	2.30 (2.17)	.93	1.01 [0.90, 1.12]	826	1.31 (1.76)	1.86 (2.00)	.07	0.85 [0.71, 1.01]	846

Note. All variables were measured at wave 3 except education and ε4 carrier status. Values in bold indicate findings where chi-square or t tests resulted in a p value <.05. CI = confidence interval; BMI = body mass index.

^aOdds ratios for continuous variables represent the increase or decrease in odds of being a SuperAger for each unit increase of a risk factor variable, and odds ratios for dichotomous variables represent the overall increase or decrease in odds of being a SuperAger if the variable = "yes."

^bSmall cell size <10 participants.

Adjusted ORs for Being a SuperAger

As demonstrated in Table 3, all three factors associated with being a SuperAger for women remained significantly associated in a combined adjusted model. According to the model, each year of education increased the odds of being a female SuperAger by 13% (95% confidence interval [CI] = [1%, 26%]), each increase in investigative activity level increased odds by 27% (95% CI = [0, 61%]), and each drink per week increased odds by 5% (95% CI = [1%, 10%]). For male SuperAgers, all three associated factors also remained robust to adjustment. Each year of education increased the odds of being a male SuperAger by 22% (95% CI = [5%, 40%]), each increase in social activity level increased odds by 45% (95% CI = [9%–93%]), and each unit increase on the Goldberg

depression scale decreased the odds of being a male SuperAger by 23% (95% CI = [2%, 40%]).

Missing Data

As candidates for SuperAging were defined as those who had scores for all three waves of immediate and delayed recall and MMSE, there were few missing data within this sample, as can be seen in the N values in Table 2.

Comparison of Eligible and Excluded Participants

Of all participants in the 60s cohort not excluded for low MMSE or a history of stroke, only 73.2% had complete data

Table 3. Adjusted Odds Ratios of Being a Female or Male SuperAger, Using Logistic Regression Models Adjusting for One Variable at a Time and Then All Associated Variables Together.

Females								
Associated risk factor	Adjusted for						All associated variables combined: education, investigative activities, drinks per week	
	Years of education only	p value	Investigative activities only	p value	Drinks per week only	p value	per week	p value
Years of education	1.18 [1.07, 1.31]	.001	1.14 [1.02, 1.28]	.017	1.17 [1.05, 1.30]	.004	1.13 [1.01, 1.26]	.034
Investigative activities	1.27 [1.00, 1.61]	.051	1.39 [1.11, 1.74]	.004	1.37 [1.10, 1.72]	.006	1.27 [1.00, 1.61]	.052
Drinks per week	1.05 [1.01, 1.09]	.025	1.06 [1.02, 1.11]	.007	1.06 [1.02, 1.10]	.006	1.05 [1.01, 1.10]	.017
Males								
Associated risk factor	Adjusted for						All associated variables combined: education, social activities, depression	
	Years of education only	p-value	Social activities only	p-value	Depression only	p-value	depression	p-value
Years of education	1.26 [1.09, 1.45]	.001	1.23 [1.06, 1.41]	.005	1.25 [1.09, 1.43]	.002	1.22 [1.05, 1.40]	.007
Social activities	1.43 [1.08, 1.89]	.012	1.54 [1.17, 2.03]	.002	1.55 [1.17, 2.06]	.002	1.45 [1.09, 1.93]	.010
Depression	0.77 [0.60, 0.98]	.037	0.75 [0.59, 0.96]	.024	0.76 [0.59, 0.97]	.025	0.77 [0.60, 0.98]	.033

for all three outcomes for all three waves. Table 4 presents a comparison of baseline data for eligible versus excluded participants, demonstrating that eligible participants had higher levels of education, more participation in moderate or vigorous exercise and social and investigative activities, less symptoms of depression and anxiety, and higher cognitive test scores overall.

Discussion/Conclusion

Despite the use of gender-specific cutoffs for being a SuperAger, there was a higher prevalence of female SuperAgers than male in this Australian population. As hypothesized, years of education was associated with SuperAging for both men and women, with more years of education increasing the odds of being a SuperAger. Education was the only factor associated with SuperAging for both men and women. For women, other associated risk factors were more participation in investigative activities and more alcohol consumption. For men, more social activities and a lower score for depressive symptoms were also associated. Interestingly, many risk factors linked to cognitive decline such as APOE-ε4 carrier status, history of head injury, and diabetes were not associated with being a SuperAger, perhaps due to small cell sizes or, alternatively, suggesting that factors related to decline may be different from factors related to sustained superior performance.

Our findings are comparable with, but not entirely confirmatory of, other studies of risk factors for exceptional memory or SuperAging. In a sample of 1,558 participants aged 35 to 85 at baseline, Josefsson et al. (2012) found that years of education was associated with being a memory “maintainer” rather than “average” in terms of memory decline (OR = 1.15, 95% CI = [1.09, 1.20]). Investigating memory resilience in the presence of genetic risk factors, McDermott et al. (2017) also found education to be a strong predictor for both sexes in a sample of 642 adults from the Victoria Longitudinal Study (VLS). In that study, age was an additional strong demographic predictor; however, the age range included (53–95) was not as narrow as ours (68–74).

In terms of gender-specific findings, the association we found between a lower score for depressive symptoms and being a male SuperAger complements another finding from the VLS—that fewer depressive symptoms acted as a genetically robust predictor of memory resilience in men only (McDermott et al., 2017). Although the gender-specific association we report between alcohol consumption and being a female SuperAger is possibly controversial, it replicates a finding from an entirely different cohort linguistically, geographically, and temporally—that of the Epidemiology of Vascular Aging (EVA) Study of 1,389 participants born between 1922 and 1932 and living in Nantes, France. This study also found that women who consumed more alcoholic drinks per day were more likely to be high cognitive performers (defined as in the

Table 4. Comparison of Baseline Data for Those Participants Who Were Eligible for Inclusion in the Study (Having Immediate and Delayed CVLT Recall and MMSE Scores for All Three Waves) and Those Who Were Not.

Variable	Eligible for inclusion M (SD) or %	Not eligible for inclusion M (SD) or %	p value	N
Female	49.4%	48.6%	.75	2,292
Age	62.50 (1.51)	62.48 (1.51)	.75	2,291
Education	14.12 (2.63)	13.33 (2.93)	<.001	2,174
Partnered	79.3%	75.2%	.04	2,289
BMI	26.78 (5.08)	26.80 (5.63)	.92	2,080
Hypertension	61.6%	65.6%	.09	2,258
On cholesterol meds	22.8%	20.0%	.15	2,288
Diabetes		Baseline comparisons unavailable		
History of head injury	5.3%	6.1%	.43	2,198
APOE ε4 carrier	27.0%	29.1%	.33	2,149
Exercise	None/mild 50.4% Moderate 35.0% Vigorous 14.6%	None/mild 61.3% Moderate 29.1% Vigorous 9.6%	<.001	2,015
Current smoker		Baseline comparisons unavailable		
Alcoholic drinks per week	6.94 (8.28)	6.31 (8.93)	.12	2,284
Sleep problems	31.6%	31.4%	.91	2,285
Total positive exchanges	24.09 (3.43)	23.96 (3.78)	.48	1,784
Total negative exchanges	10.64 (5.17)	10.72 (5.24)	.78	1,773
Social activities in a week	2.53 (1.07)	2.30 (1.08)	<.001	2,281
Investigative activities in a week	1.68 (1.12)	1.51 (1.17)	<.01	2,282
Goldberg depression score	1.49 (1.72)	1.87 (2.00)	<.001	2,284
Goldberg anxiety score	2.07 (2.21)	2.36 (2.43)	<.01	2,284
Immediate recall	7.35 (2.17)	6.74 (2.35)	<.001	2,292
Delayed recall	6.28 (2.42)	5.85 (2.53)	<.001	2,292

BMI = body mass index.

top 10% on a global score derived from 10 neuropsychological tests; Dufouil et al., 1997). Nevertheless, this counterintuitive finding of the consumption of more alcoholic drinks per week being associated with being a female SuperAger must be interpreted with caution. Methodological challenges in measuring the association between alcohol consumption and later-life cognition have been reported, including the problems with self-reported measurements, the lack of information regarding alcohol type, and the important role of confounding factors such as socioeconomic status and health (Anstey & Peters, 2018).

Regarding lifestyle factors, Maher et al. (2017) found that SuperAgers (defined using a similar episodic memory-based definition to ours but using an older sample recruited in their 80s) reported more positive social relations with others than cognitively average participants of similar ages. The sample size for this study was small, and the authors recommended further study with a larger community-based sample such as ours. We did confirm an association between social activities and SuperAging for men only. The association we found between investigative activities and being a female SuperAger contributes to the lively debate regarding activity engagement in later life that is summarized in the adage “use it or lose it.” In our study, more participation in investigative activities—defined using questions regarding reading scientific books or

magazines, reading about special subjects, solving maths or chess puzzles, or doing troubleshooting of software packages on a PC (Bielak et al., 2012)—was associated with being a SuperAger for women but not for men. Hypothesizing possible explanations for a similar finding in Swedish twins, Crowe suggests that traditional gender roles having women in the home and men in the intellectually stimulating workforce may underlie the fact that women might appear to gain more benefit from cognitively stimulating activities in later life (Bielak, 2010; Crowe et al., 2003). As our study did not include measurement of gender roles, it is not possible to speculate on this assumption.

This article has attempted to add to the SuperAging literature in five ways: (a) by using a large population-based, randomly recruited cohort of naturally evolving SuperAgers rather than volunteers, facilitating what is to our knowledge the first measurement of the prevalence of SuperAgers in a longitudinal cohort and also improving the generalizability of the findings and the power to detect statistically significant associations; (b) by directly comparing memory recall scores of participants from the same cohort aged 40 years apart, minimizing the effect of unmeasured demographic confounders and maximizing comparability of cultural background and also test conditions; (c) by using gender-specific cutoffs for

being a SuperAger, thus avoiding any inherent gender bias in the definition of SuperAging that could result in an underrepresentation of men given the known higher recall test scores of women; (d) by performing gender-stratified analysis of factors associated with SuperAging so as to reveal any gender differences that may be masked by a combined analysis; and, finally, (e) by investigating a number of demographic, physical, genetic, lifestyle, and psychosocial risk factors.

It is possible that this analysis adds weight to the cognitive reserve hypothesis, which suggests that resilience to age-related cognitive decline can be developed through activities that stimulate neural activity, such as education and investigative activities (Stern, 2002, 2012). However, without neuroimaging data or analysis of a longitudinal slope, we do not know whether these SuperAgers are truly resilient to decline or are merely consistently high performers across all life stages. Although our study did include a cross-temporal component, in that SuperAgers had to maintain their status across three waves of data collection over a 12-year period, the analysis was not strictly longitudinal in nature and is thus constrained in terms of etiological implications.

Reverse causality is a plausible explanation for some of the risk and protective factors found to be associated with superior memory performance, especially for men—it may be that older men with excellent memory are more likely to feel social and less likely to report feelings associated with depression. A further limitation is the risk that unmeasured confounders, specifically socioeconomic factors, may also have influenced associated factors, particularly for women. A final consideration is that our SuperAgers, with a mean age around 70, are relatively young compared with other SuperAgers reported in the literature, who are mostly aged 80 or older (Borelli et al., 2018). Given that risks of cognitive impairment increase with increasing age, it may be that the superior memory performance evidenced in this cohort will not be sustained as participants approach their 80s; however, we hope to be able to examine this possibility with further waves of data collection and a longitudinal approach.

This research showed that factors associated with being a SuperAger differ for men and women, with the exception of years of education, which appears to have a strong association with SuperAging for both genders. Investigations of predictors of being a SuperAger could be improved in future analyses—a first step would be to examine longitudinal trajectories as this cohort ages, but there is also potential to add other cognitive measures to the definition of SuperAging and to consider prevalence in cohorts with more diversity in educational and socioeconomic backgrounds.

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Author Contributions

J.M. conceived the definition of a SuperAger presented and related research questions, with input from K.J.A. and R.P. J.M. performed data analysis and interpretation and wrote the first draft of the manuscript in consultation with K.J.A. and R.P. K.J.A. is the lead investigator of the PATH project. K.J.A. and R.P. supervised the work and assisted in data interpretation and manuscript evaluation. All authors provided critical feedback and approved the final manuscript.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Statement of Ethics

All participants provided written informed consent for each wave of data collection. The PATH study has received approval from the Australian National University's Human Research Ethics Committee.

References

- Andrews, S. J., Das, D., Cherbuin, N., Anstey, K. J., & Eastaale, S. (2016). Association of genetic risk factors with cognitive decline: The PATH through life project. *Neurobiology of Aging, 41*, 150–158. <https://doi.org/10.1016/j.neurobiolaging.2016.02.016>
- Anstey, K. J., Christensen, H., Butterworth, P., Eastaale, S., Mackinnon, A., Jacomb, T., . . . Jorm, A. F. (2012). Cohort Profile: The PATH through life project. *International Journal of Epidemiology, 41*(4), 951–960. <https://doi.org/10.1093/ije/dyr025>
- Anstey, K. J., Eramudugolla, R., Hosking, D. E., Lautenschlager, N. T., & Dixon, R. A. (2015). Bridging the translation gap: From dementia risk assessment to advice on risk reduction. *The Journal of Prevention of Alzheimer's Disease, 2*(3), 189–198.
- Anstey, K. J., & Peters, R. (2018). Alcohol and dementia—Risk or protective factor? *Nature Reviews Neurology, 14*(11), 635–636. <https://doi.org/10.1038/s41582-018-0073-0>

- Arvanitakis, Z., Leurgans, S. E., Fleischman, D. A., Schneider, J. A., Rajan, K. B., Pruzin, J. J., . . . Bennett, D. A. (2018). Memory complaints, dementia, and neuropathology in older blacks and whites. *Annals of Neurology*, *83*(4), 718–729. <https://doi.org/10.1002/ana.25189>
- Bielak, A. A. M. (2010). How can we not “lose it” if we still don’t understand how to “use it”? Unanswered questions about the influence of activity participation on cognitive performance in older age—A mini-review. *Gerontology*, *56*(5), 507–519. <https://doi.org/10.1159/000264918>
- Bielak, A. A. M., Anstey, K. J., Christensen, H., & Windsor, T. D. (2012). Activity engagement is related to level, but not change in cognitive ability across adulthood. *Psychology and Aging*, *27*(1), 219–228. <https://doi.org/10.1037/a0024667>
- Borelli, W. V., Schilling, L. P., Radaelli, G., Ferreira, L. B., Pisani, L., Portuguese, M. W., & da Costa, J. C. (2018). Neurobiological findings associated with high cognitive performance in older adults: A systematic review. *International Psychogeriatrics*, *30*, 1813–1825. <https://doi.org/10.1017/S1041610218000431>
- Cook, A. H., Sridhar, J., Ohm, D., Rademaker, A., Mesulam, M.-M., Weintraub, S., & Rogalski, E. (2017). Rates of cortical atrophy in adults 80 years and older with superior vs average episodic memory. *Journal of the American Medical Association*, *317*(13), 1373–1375. <https://doi.org/10.1001/jama.2017.0627>
- Cosco, T. D., Prina, A. M., Perales, J., Stephan, B. C. M., & Brayne, C. (2014). Operational definitions of successful aging: A systematic review. *International Psychogeriatrics*, *26*(3), 373–381. <https://doi.org/10.1017/S1041610213002287>
- Cosco, T. D., Stephan, B. C. M., Brayne, C., Muniz, G., & MRC CFAS. (2017). Education and successful aging trajectories: A longitudinal population-based latent variable modelling analysis. *Canadian Journal on Aging / La Revue Canadienne Du Vieillessement*, *36*, 427–434. <https://doi.org/10.1017/S0714980817000344>
- Crowe, M., Andel, R., Pedersen, N. L., Johansson, B., & Gatz, M. (2003). Does participation in leisure activities lead to reduced risk of Alzheimer’s disease? A prospective study of Swedish twins. *The Journals of Gerontology, Series B: Psychological Sciences and Social Sciences*, *58*(5), P249–P255. <https://doi.org/10.1093/geronb/58.5.P249>
- Degerman, S., Josefsson, M., Nordin Adolfsson, A., Wennstedt, S., Landfors, M., Haider, Z., . . . Adolfsson, R. (2017). Maintained memory in aging is associated with young epigenetic age. *Neurobiology of Aging*, *55*, 167–171. <https://doi.org/10.1016/j.neurobiolaging.2017.02.009>
- Dekhtyar, M., Papp, K. V., Buckley, R., Jacobs, H. I. L., Schultz, A. P., Johnson, K. A., . . . Rentz, D. M. (2017). Neuroimaging markers associated with maintenance of optimal memory performance in late-life. *Neuropsychologia*, *100*, 164–170. <https://doi.org/10.1016/j.neuropsychologia.2017.04.037>
- Delis, D., Kramer, J., Kaplan, E., & Ober, B. (1987). *California Verbal Learning Test*. Psychological Corp.
- Dufouil, C., Ducimetiere, P., & Alperovitch, A. (1997). Sex differences in the association between alcohol consumption and cognitive performance. *American Journal of Epidemiology*, *146*(5), 405–412. <https://doi.org/10.1093/oxfordjournals.aje.a009293>
- Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). “Mini-mental state”: A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research*, *12*(3), 189–198.
- Gefen, T., Peterson, M., Papastefan, S. T., Martersteck, A., Whitney, K., Rademaker, A., . . . Geula, C. (2015). Morphometric and histologic substrates of cingulate integrity in elders with exceptional memory capacity. *The Journal of Neuroscience*, *35*(4), 1781–1791. <https://doi.org/10.1523/JNEUROSCI.2998-14.2015>
- Gefen, T., Shaw, E., Whitney, K., Martersteck, A., Stratton, J., Rademaker, A., . . . Rogalski, E. (2014). Longitudinal neuropsychological performance of cognitive SuperAgers. *Journal of the American Geriatrics Society*, *62*(8), 1598–1600. <https://doi.org/10.1111/jgs.12967>
- Goldberg, D., Bridges, K., Duncan-Jones, P., & Grayson, D. (1988). Detecting anxiety and depression in general medical settings. *BMJ (Clinical Research Ed.)*, *297*(6653), 897–899.
- Harrison, T. M., Weintraub, S., Mesulam, M.-M., & Rogalski, E. (2012). Superior memory and higher cortical volumes in unusually successful cognitive aging. *Journal of the International Neuropsychological Society*, *18*(6), 1081–1085. <https://doi.org/10.1017/S1355617712000847>
- Hersi, M., Irvine, B., Gupta, P., Gomes, J., Birkett, N., & Krewski, D. (2017). Risk factors associated with the onset and progression of Alzheimer’s disease: A systematic review of the evidence. *NeuroToxicology*, *61*, 143–187. <https://doi.org/10.1016/j.neuro.2017.03.006>
- Janecek, M., Gefen, T., Samimi, M., Kim, G., Weintraub, S., Bigio, E., . . . Geula, C. (2018). Variations in acetylcholinesterase activity within human cortical pyramidal neurons across age and cognitive trajectories. *Cerebral Cortex*, *28*(4), 1329–1337. <https://doi.org/10.1093/cercor/bhx047>
- Jorm, A. F., Mather, K. A., Butterworth, P., Anstey, K. J., Christensen, H., & Easteal, S. (2007). APOE genotype and cognitive functioning in a large age-stratified population sample. *Neuropsychology*, *21*(1), 1–8. <https://doi.org/10.1037/0894-4105.21.1.1>
- Josefsson, M., de Luna, X., Pudas, S., Nilsson, L.-G., & Nyberg, L. (2012). Genetic and lifestyle predictors of 15-Year longitudinal change in episodic memory. *Journal of the American Geriatrics Society*, *60*(12), 2308–2312. <https://doi.org/10.1111/jgs.12000>
- Kerby, D. S., & Ragan, K. M. (2002). Activity interests and Holland’s RIASEC system in older adults. *The International Journal of Aging and Human Development*, *55*(2), 117–139.
- Kramer, J. H., Yaffe, K., Lengsfelder, J., & Delis, D. C. (2003). Age and gender interactions on verbal memory performance. *Journal of the International Neuropsychological Society*, *9*(01). <https://doi.org/10.1017/S1355617703910113>
- Maher, A. C., Kielb, S., Loyer, E., Connelley, M., Rademaker, A., Mesulam, M.-M., . . . Rogalski, E. (2017). Psychological well-being in elderly adults with extraordinary episodic memory. *PLOS ONE*, *12*(10), Article e0186413.
- Mapstone, M., Lin, F., Nalls, M. A., Cheema, A. K., Singleton, A. B., Fiandaca, M. S., & Federoff, H. J. (2017). What success can teach us about failure: The plasma metabolome of older adults with superior memory and lessons for Alzheimer’s disease. *Neurobiology of Aging*, *51*, 148–155. <https://doi.org/10.1016/j.neurobiolaging.2016.11.007>
- Martin, P., Kelly, N., Kahana, B., Kahana, E., Willcox, B. J., Willcox, D. C., & Poon, L. W. (2015). Defining successful aging: A tangible or elusive concept? *The Gerontologist*, *55*(1), 14–25. <https://doi.org/10.1093/geront/gnu044>

- Martinson, M., & Berridge, C. (2015). Successful aging and its discontents: A systematic review of the social gerontology literature. *The Gerontologist, 55*(1), 58–69. <https://doi.org/10.1093/geront/gnu037>
- McDermott, K. L., McFall, G. P., Andrews, S. J., Anstey, K. J., & Dixon, R. A. (2017). Memory resilience to Alzheimer's genetic risk: Sex effects in predictor profiles. *The Journals of Gerontology, Series B: Psychological Sciences and Social Sciences, 72*, 937–946. <https://doi.org/10.1093/geronb/gbw161>
- Munro, C. A., Winicki, J. M., Schretlen, D. J., Gower, E. W., Turano, K. A., Muñoz, B., . . . West, S. K. (2012). Sex differences in cognition in healthy elderly individuals. *Aging, Neuropsychology, and Cognition, 19*(6), 759–768. <https://doi.org/10.1080/13825585.2012.690366>
- Rogalski, E. J., Gefen, T., Mao, Q., Connelly, M., Weintraub, S., Geula, C., . . . Mesulam, M.-M. (2019). Cognitive trajectories and spectrum of neuropathology in SuperAgers: The first 10 cases. *Hippocampus, 29*(5), 458–467. <https://doi.org/10.1002/hipo.22828>
- Rogalski, E. J., Gefen, T., Shi, J., Samimi, M., Bigio, E., Weintraub, S., . . . Mesulam, M.-M. (2013). Youthful memory capacity in old brains: Anatomic and genetic clues from the Northwestern SuperAging Project. *Journal of Cognitive Neuroscience, 25*(1), 29–36. https://doi.org/10.1162/jocn_a_00300
- Stafford, M., Hemingway, H., Stansfeld, S. A., Brunner, E., & Marmot, M. (1998). Behavioural and biological correlates of physical functioning in middle aged office workers: The UK Whitehall II study. *Journal of Epidemiology and Community Health, 52*(6), 353–358. <https://doi.org/10.1136/jech.52.6.353>
- Stern, Y. (2002). What is cognitive reserve? Theory and research application of the reserve concept. *Journal of the International Neuropsychological Society, 8*(3), 448–460. <https://doi.org/10.1017/S1355617702813248>
- Stern, Y. (2012). Cognitive reserve in ageing and Alzheimer's disease. *The Lancet Neurology, 11*(11), 1006–1012. [https://doi.org/10.1016/S1474-4422\(12\)70191-6](https://doi.org/10.1016/S1474-4422(12)70191-6)
- Sun, F. W., Stepanovic, M. R., Andreano, J., Barrett, L. F., Touroutoglou, A., & Dickerson, B. C. (2016). Youthful brains in older adults: Preserved neuroanatomy in the default mode and salience networks contributes to youthful memory in superaging. *Journal of Neuroscience, 36*(37), 9659–9668. <https://doi.org/10.1523/JNEUROSCI.1492-16.2016>
- Sundermann, E. E., Maki, P. M., Rubin, L. H., Lipton, R. B., Landau, S., & Biegon, A. (2016). Female advantage in verbal memory: Evidence of sex-specific cognitive reserve. *Neurology, 87*(18), 1916–1924.
- Uttl, B. (2005). Measurement of individual differences: Lessons from memory assessment in research and clinical practice. *Psychological Science, 16*(6), 460–467. <https://doi.org/10.1111/j.0956-7976.2005.01557.x>