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Memory reserve and memory maintenance in SuperAgers

Paměťová rezerva a údržba paměti u paměťově superúspěšně stárnoucích osmdesátníků

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Abstract

Aim: Memory SuperAgers (SAs) are adults aged 80+ years whose episodic memory is as good as that of sexagenarians. The aim was to determine whether SAs are people with a higher memory reserve or more stable memory maintenance. *Sample and method:* We analyzed cognitive performance of 46 cognitively healthy older adults over 6 years, measuring them at three time points (T1, T2 and T3). All participants were aged 80+ years and had normal cognitive performance at T3. SAs were defined as persons whose Long Delayed Free Recall score of Philadelphia Verbal Learning Test (LDFR-PVLT) was ≥ nine words (the mean for healthy age group 60–64 years) at T3. Logical memory II (LM II-delayed recall) and PVLT sum of trial 1–5 were compared between and within the groups. *Results:* In our sample, we found 20 SAs (16 females) and 26 non-SAs (11 females) at T3, meaning more SAs were female than male. At T3, there were no significant differences between the two groups in age, education, or depressive symptoms. At T1, SAs performed significantly better on PVLT 1–5 but not in LM II; their cognitive reserve was thus higher for verbal learning but not for logical memory in non-SAs. Over time, SAs showed improvement in PVLT 1–5 but not in logical memory. *Conclusion:* We suggest that both memory reserve and memory maintenance play a role in SuperAging. The differences between SAs and non-SAs were more in verbal learning than in logical memory. Our data suggest that women SuperAge more frequently than men do.

Souhrn

Cíl: Dospělí ve věku 80 let a více s epizodickou pamětí jako průměrný šedesátník jsou nazýváni paměťově superúspěšně stárnoucími jedinci (PSÚSJ). Cílem práce je zjistit, zda PSÚSJ mají vyšší paměťovou rezervu nebo stabilnější paměťovou údržbu. *Soubor a metodika:* Analyzovali jsme kognitivní výkonnost u 46 kognitivně zdravých starších dospělých během 6 let ve 3 časových bodech (T1, T2 a T3). Všichni účastníci měli 80 a více let a měli normální kognitivní výkon v T3. PSÚSJ byli definováni výkonem ve spontánním oddáleném vybavení z paměti ve Filadelfském testu učení a paměti (LDFR-PVLT) ≥ devět slov (průměr zdravých osob ve věku 60–64 let) v T3. Logická paměť a PVLT suma pokusů 1–5 byly porovnávány mezi i v rámci skupin. *Výsledky:* V souboru bylo 20 PSÚSJ (16 žen) a 26 ne-PSÚSJ (11 žen) v T3, což znamená, že více PSÚSJ bylo mezi ženami než muži. V T3 nebyly zjištěny významné rozdíly mezi skupinami ve věku, vzdělání, depresivní symptomatice. PSÚSJ měli významně vyšší PVLT 1–5, ale nikoliv logickou paměť v T1. Jejich kognitivní rezerva byla vyšší pro verbální učení, nikoliv pro logickou paměť ve srovnání s ne-PSÚSJ. U PSÚSJ došlo během 6 let ke zlepšení v PVLT 1–5 ale nikoliv v logické paměti. *Závěr:* Naše výsledky naznačují, že paměťová rezerva i paměťová údržba hrají roli u PSÚSJ. Rozdíl mezi skupinami byl dán rozdílným učením nikoliv logickou pamětí. PSÚSJ jsou více mezi ženami než muži.

Key words

aging – cognitive maintenance – cognitive reserve – memory – resilience

Klíčová slova

stárnutí – kognitivní údržba – kognitivní rezerva – paměť – odolnost

Introduction

Pathological cognitive aging has been studied for over a century but resilience to cognitive aging started to be intensively studied only in the last decade [1–3]. Memory problems are a major complaint about cognitive functioning in older adults, which is why the concept of memory SuperAging and successful memory aging had attracted much attention [4]. According to Northwestern University criteria, memory SuperAgers (SAs) are defined as older adults aged 80 years and over who have episodic memory at least as good as the average 60-year-old [5]. Alternatively, we can say that the memory age of SAs is significantly lower than the memory age of their non-SuperAger (non-SAs) peers. What is novel in this defini-

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Tab. 1. Demographic and cognitive data of SuperAgers and non-SuperAgers at T3.

	SuperAgers median (25%; 75%)	Non-SuperAgers median (25%; 75%)	P-level
participants	20	26	
age (T3)	83 (81; 87.5)	85.5 (83; 88.25)	0.221
sex (f : m)	16 : 4	11 : 15	**0.016**
education (years)	12 (11; 15.75)	15 (12; 19)	0.053
MMSE (T3)	28 (27; 29.75)	27.5 (25.5; 29.0)	0.070
GDS (T3)	2.5 (1; 3)	2 (1; 3.25)	0.831
FAQ (T3)	1 (0; 2)	1 (0; 4)	0.255
PVLT-LDFR (T1)	10 (7.25; 11)	7.5 (6; 10)	
PVLT-LDFR (T3)	10 (9; 11)	6.5 (5; 8)	

f – female; FAQ – Functional Activities Questionnaire; GDS – Geriatric Depression Scale; m – male; MMSE – Mini-Mental State Examination; PVLT-LDFR – Philadelphia Verbal Learning Test – Long Delayed Free Recall; T1 – assessment in 2012; T3 – assessment in 2018

tion is the use of a new reference group. The usual normative approach compares peers within the appropriate age groups but such design cannot compare different age groups with respect to one reference group. Several studies tried to discover what is behind the phenomenon of SuperAging. To date, at least four neuroimaging cross-sectional studies found that the SAs' cerebral cortex was thicker than that of typical older adults [5–8]. In fact, SAs were anatomically indistinguishable from young adults [8]: their hippocampal volume [8–10] and anterior cingulate [7,10] were likewise preserved. These studies confirmed intact brain structure in SAs and confirmed the validity of the concept of memory SuperAging. On the other hand, longitudinal studies found that the longitudinal rate of hippocampal volume atrophy and thinning of the entire cortex did not significantly differ between successful agers and typical older adults [10,11]. In theory, high memory reserve or memory maintenance may both play a significant role in how one becomes a SA.

Cognitive reserve is defined as individual differences in how people process tasks which "allow some to cope better than others with brain pathology" [12,13]. In other words, cognitive reserve can be understood as cognitive resilience to brain pathology, a buffer that can emerge due to academic background (level of education) or the type of occupation. Consequently, the number of years of education completed, the type of occupation, or a measure of general cognitive ability (IQ) are common proxies for cognitive reserve [14]. It is unclear whether cognitive reserve is a general psychological characteristic or whether it is domain-specific. For the purpose of this study, let us assume that memory performance at the beginning of the study is equivalent to the memory reserve and the years of education characterize the general cognitive reserve.

As a concept complementary to cognitive reserve "brain maintenance" was introduced [13,15]. Nyberg et al. [13] define brain maintenance as follows: "Individual differences in the manifestation of age-related brain changes and pathology allow some people to show little or no age-related cognitive decline." Further research in aging cognition and resilience has led to introduction of "cognitive maintenance", which is "the degree to which cognitive decline over time is minimized " and pertains to specific cognitive abilities [16]. We use the term memory maintenance for the degree to which episodic memory decline over time is minimized.

Various studies described maintenance of memory function in sexagenarians [17,18] and octogenarians [19], or the maintenance of executive function in septuagenarians [20], but none used the definition of SuperAging. Recently, a longitudinal observational study found that a group of SuperAging octogenarians showed a trend toward increasing memory performance over a five-year period [10]. So far, no study documented what the main episodic memory characteristic is that predicts if one becomes a SA in their late life. Thus, we ask whether it is solely due to the very high level of memory performance they reached in earlier years (memory reserve) or mainly due to their memory maintenance or whether SAs do show both superior memory reserve and memory maintenance.

To answer the questions, we present three models: i) If only memory reserve plays a role, the differences between SAs and non-SAs identified at the end of the study (T3) will be detected already at the beginning of the observation (T1); ii) If memory maintenance is solely responsible for the differences between SAs and non-SAs, we should observe that memory performance of SAs did not decrease between T1 and T2 resp. T3; iii) A combination of both processes is at work. The answer will help us better understand the general principles of SuperAging. Further, we explore possible differences in demographic variables between the SAs and non-SAs.

Patients and methods

Study design and sample

The current study is based on the data from the Cognitive SuperAging (CoSA) project, conducted in 2018–2020, and the data from the first (T1) and fourth waves (T2) of the National Normative Study of Cognitive Determinants of Healthy Aging (NANOK), its predecessor, which was implemented in 2012–2015 [21]. Only NANOK participants were invited to CoSA. Inclusion criteria for NANOK were: age ≥ 60 years, Czech as the first language, willingness to participate in a four-year study, and absence of cognitively relevant issues in the medical history (e.g., a diagnosis/treatment for a serious neurological disorder, stroke, traumatic brain injury, acute phase of a serious mental disorder, hospitalization for substance abuse, or chemotherapeutic treatment). In 2018 (T3), 113 participants (60% female) who met the inclusion criteria (age ≥ 80 years) and provided informed consent were recruited from NANOK into the CoSA project. For this study, five participants were excluded due to suspected dementia (Mini-Mental State Examination < 23 [22]), four persons were excluded due to age (they declared at recruitment to be 80 years old when they were only nearly 80 years old at the assessment), and one participant was excluded due to the inability to finish the protocol. Additionally, at T3, we excluded 57 participants due to suspected pathological aging, which was defined as –1.5 standard deviation below

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the mean for age and education band in one of the following areas: memory (Philadelphia Verbal Learning Test – Long Delayed Free Recall [PVLT-LDFR]) [23], executive functions (Trail Making test, part B [TMT-B]) [24], confrontation picture-naming (Boston Naming Test [BNT]) [25,26] or Categorical Verbal Fluency – Animals [27, 28]. The final dataset included 46 participants who were over 80 years old in 2018 (T3) and their performance in neuropsychological tests did not indicate cognitive impairment (Tab. 1).

Procedure and instruments

Memory was assessed with a Story recall from the Wechsler Memory Scale-Revised subtest of Logical Memory II (LM II delayed recall) [29,30] at T1 and T2 (over 3 years). In the LM II, subjects are asked to recall the passages after a 30-min delay.

Episodic memory was measured by Philadelphia Verbal Learning Test (PVLT) at T1, T2 and T3 (over 6 years). In the learning part of PVLT, probands listen and recall a 12-words list five times. The sum of five trials of PVLT (PVLT 1–5) reflects the verbal learning. Short and Long Delayed Free Recall score of Philadelphia Verbal Learning Test (PVLT-LDFR) give us information how many correct words is a participant able to recall immediately after interference of a new 12-words list (short), or after a 30-min delay (long).

Changes (delta) in memory (PVLT-LDFR) and learning performance (PVLT 1–5) were calculated by subtracting the scores from the 2018 and 2012 assessments (T3–T1) or 2015 and 2012 assessments (T2–T1).

The mean Long Delayed Free Recall score of Philadelphia Verbal Learning Test (PVLT-LDFR) was nine words for age group 60–64 in the Czech normative study [23]. The cut score of nine words is concidentally equal to the score in another verbal list delayed recall test (Rey Auditory Verbal learning Test) used in the previous studies on SuperAging [5,10]. In a further step, additional criteria for SuperAging were applied in line with previous studies on the subject: performance on non-memory tasks such as the BNT-30, TMT-B, and Category Fluency – Animals, must be better than –1 standard deviation below the mean for the relevant age and education band [5–8,31]. General cognitive abilities were tested using the Mini-Mental State Examination (MMSE) [21,32]. Depressive symptoms were evaluated by the Geriatric Depression Scale-15 [33,34] and instrumental functional activities by the Functional Activities Questionnaire (FAQ) [35,36].

Tab. 2. Memory in SuperAgers and non-SuperAgers at T1, T2 and T3.

	SuperAgers M (SD)	Non-superAgers M (SD)	P-level	Effect size (Cohen d)
LM II (T1)	8.7 (3.5)	8.5 (3.7)	0.823	0.067
LM II (T2)	8.8 (3.9)	7.8 (3.3)	0.287	0.321
PVLT 1-5 (T1)	42.25 (6.0)	37.7 (6.8)	**0.018**	0.729
PVLT 1-5 (T2)	42.5 (7.0)	36.2 (6.8)	**0.005**	0.888
PVLT 1-5 (T3)	44.15 (6)	34.4 (5.8)	**0.001**	1.683

LM II – Logical Memory II (delayed recall); M – mean; PVLT 1-5 – the sum of five trials of Philadelphia Verbal Learning Test; SD – standard deviation; T1 – assessment in 2012; T2 – assessment in 2015; T3 – assessment in 2018

Tab. 3. Longitudinal changes within the SuperAger and non-SuperAger groups.

	Change within SuperAgers M (SD)	P-level	Change within non-SuperAgers M (SD)	P-level
Delta LM II (T2 – T1)	+0.05 (3.3)	0.947	–0.68 (3.3)	0.311
Delta PVLT 1-5 (T2 – T1)	+0.2 (4.5)	0.845	–1.48 (6.8)	0.287
Delta PVLT 1-5 (T3 – T1)	+1.9 (4.2)	0.059	–3.19 (7.2)	**0.032**

LM II – Logical Memory II (delayed recall); M – mean; PVLT 1-5 – the sum of five trials of Philadelphia Verbal Learning Test; SD – standard deviation; T1 – assessment in 2012; T2 – assessment in 2015; T3 – assessment in 2018

Statistics

We used parametric and nonparametric statistics based on the results of the Shapiro-Wilk and Kolmogorov-Smirnov tests. The independent sample t-test and the Mann-Whitney U test were used to compare quantitative variables between independent groups of SAs and non-SAs. Paired t-test was used to compare the change of pair variables within the groups and Fisher's exact test was applied to evaluate nominal variables such as sex. All tests were two-sided; the significance level of $P < 0.05$ was adopted. All analyses were performed using IBM SPSS 23 (Armonk, NY, USA).

Results

Twenty SAs (16 females) and 26 non-SAs (11 females) were found in our sample at T3. Using the Mann-Whitney U test, we determined that there were no significant differences in age, education, depressive symptoms), MMSE and FAQ between the two groups at T3 (Tab. 1). More females were SAs (80%) than males (Fisher's exact test; $P = 0.016$).

At T1, SAs performed significantly better on PVLT 1-5 (t-test, $t = 2.450$; $P = 0.018$) but not in LM II (t-test, $t = 0.225$; $P = 0.823$) (Tab. 2); their memory reserve was thus higher for verbal learning but not for logical memory in non-SAs. PVLT 1-5 was higher (t-test, $t = 2.985$; $P = 0.005$) in SAs at T2 and T3 (t-test, $t = 5.660$; $P = 0.001$). LM II was not different between the groups (t-test, $t = 1.078$; $P = 0.287$) at T2.

There were no significant changes in LM II ($P = 0.311$; $P = 0.947$) and PVLT 1–5 ($P = 0.287$; $P = 0.845$) performance within both groups between T1 and T2 (Tab. 3). A significant decline in PVLT 1-5 (paired t-test, $t = –2.273$; $P = 0.032$) was observed between T1 and T3 in non-SAs and no decline was detected in SAs (paired t-test, $t = 2.009$; $P = 0.059$).

Discussion

We assessed cognitively healthy adults aged 80+ years who met the criteria for memory SuperAging in 2018 (T3) and compared their memory performance with cognitively healthy peers (non-SAs) during assessments

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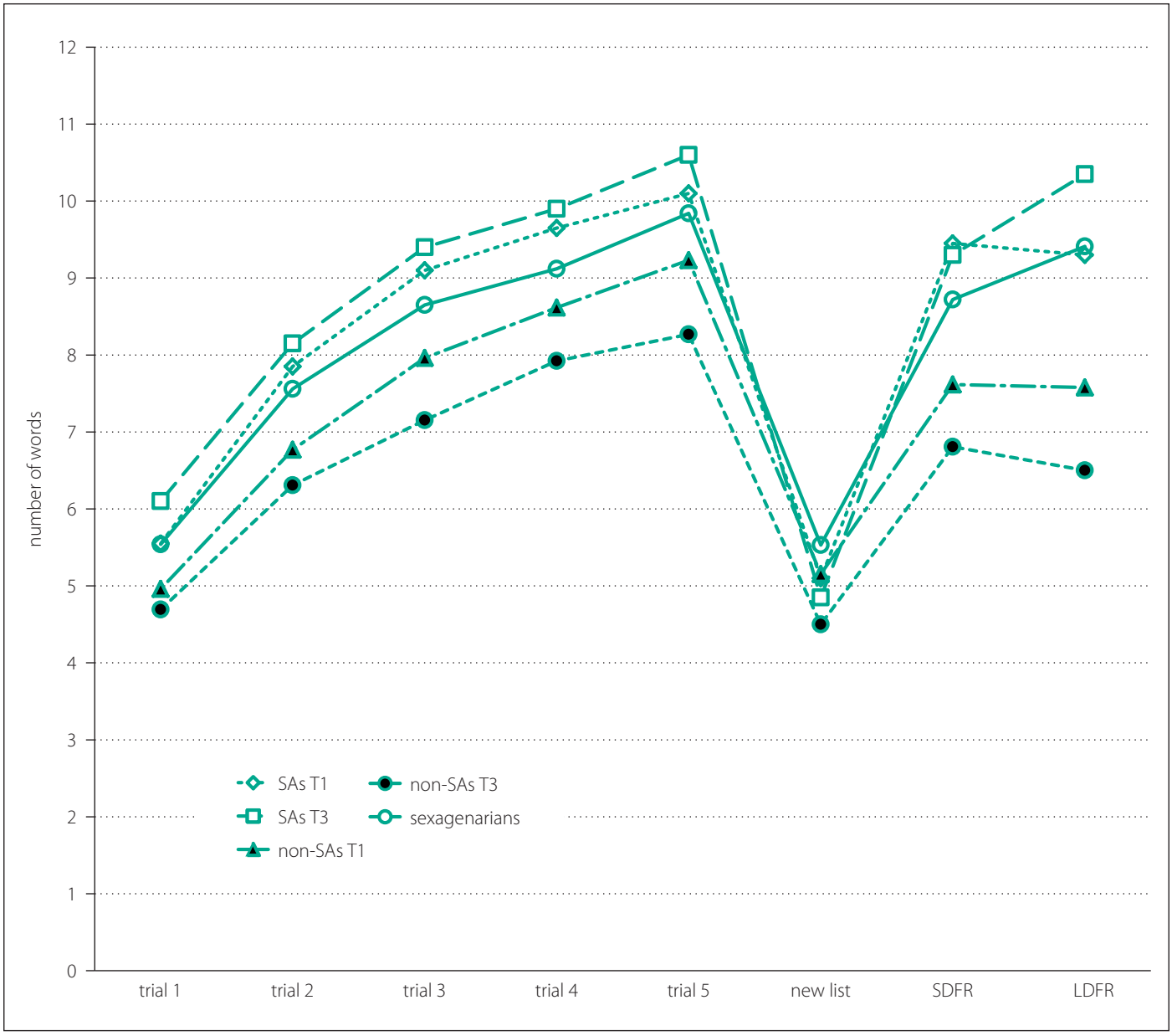


Fig. 1. The curve of learning and memory in sexagenarians, SuperAgers and non-SuperAgers at T1 and T3.

non-SAs T1 – non-SuperAgers performance in 2012; non-SAs T3 – non-SuperAgers performance in 2018; LDFR – Philadelphia Verbal Learning Test – Long Delayed Free Recall; SAs T1 – SuperAgers performance in 2012; SAs T3 – SuperAgers performance in 2018; SDFR – Philadelphia Verbal Learning Test – Short Delayed Free Recall; sexagenarians – average memory performance of healthy 60-years-old persons

Obr. 1. Křivka učení a paměti u šedesátníků, superúspěšně stárnoucích osmdesátníků a osmdesátníků v T1 a T3.

non-SAs T1 – výsledky osmdesátníků v roce 2012; non-SAs T3 – výsledky osmdesátníků v roce 2018; LDFR – Filadelfský test verbálního učení – oddálené spontánní vybavení; SAs T1 – výsledky superúspěšných osmdesátníků v roce 2012; SAs T3 – výsledky superúspěšných osmdesátníků v roce 2018; SDFR – Filadelfský test verbálního učení – bezprostřední spontánní vybavení po distraktoru ; sexagenarians – průměrný výkon v paměti šedesátníků

in 2012 (T1), 2015 (T2) and 2018 (T3). Our results showed that SAs had a higher memory reserve in verbal learning than non-SAs, i.e., their performance in the verbal learning was significantly higher 6 years before they attained the SuperAger status. We did not find the higher memory reserve in logical memory. It seems that main advantage of SAs over non-SAs is better verbal learning (Fig. 1).

We did not find a significant memory decline (logical and verbal learning) over the course of the three years, which indicates similar memory maintenance in either group. Nevertheless, we found a significant memory decline in verbal learning in non-SAs and no significant change in verbal learning in SAs after 6 years. These findings support our hypothesis about memory maintenance in SAs. The effect size between SAs and non-SAs in verbal learning at T3 was higher (Cohen's d 1.68) than at T2 (Cohen's d 0.89) and T1 (Cohen's d 0.79), which implies that differences at T3 were influenced not only by memory reserve at T1 but also by better memory maintenance in SAs than in nonSAs. We are not able to decide if the maintenance is specific for verbal learning

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or logical memory because we did not assessed logical memory at T3.

Our results revealed that both memory reserve and memory maintenance play a role in SuperAging SAs (Tab. 2 and 3).

Years of education, which is a common proxy variable for general cognitive reserve, did not turn out to play a significant role in this study as there was no significant difference in education between the SA and non-SA group. We can speculate that it may be due to the communist era in the Czech Republic (1948–1989), when persons from "wrong" political background, i.e., usually from middle or higher social classes and academia, had limited possibilities to study at universities regardless their intellectual potential.

We observed an effect of sex on SuperAging, which is in line with previously reported results [10,37]. Across their lifespan, women outperform males on verbal memory tests [38–40] and this female advantage may reflect a sex-specific form of cognitive reserve [41].

The present study has several limitations:

1) Although our exclusion criteria were carefully formulated to minimize the possibility of including individuals with pathological aging, our research sample did not undergo a thorough medical/neurological evaluation, including structural brain imaging, to exclude individuals with incipient or pronounced brain atrophy. On the other hand, we used standard psychometric criteria based on the 2018 assessment to exclude participants with probable mild cognitive impairment (MCI).
2) SuperAging was defined using PVLT-LDFR, but PVLT sum trials 1–5 were included in the memory tests, which could be interpreted as using dependent tests with PVLT-LDFR – and thus a tautology. This applies also to the evaluation of the crossover between groups at T3, where we defined the two groups. On the other hand, our hypotheses were primary based on differences at T1 and on longitudinal assessments. In theory, a change in memory performance over time within a group can take place in any direction. It can happen that even participants with superior baseline memory will experience a memory decline over a period of 6 years – but this was not the case in our study.
3) All participants in our study were Caucasian with a shared Central European history, which is why generalizability of the results to other ethnic and cultural groups must not be taken for granted.
4) We used a retrospective design (looking back at the cognitive evolution of SAs vs. non-SAs). This approach can substantially influence the results. It eliminates patients who converted to MCI or died, and it overestimates the differences in evolution between a SAs and a non-SAs (as those who declined during the follow-up had a much higher chance to be classified as non-SAs than SAs). The future design of study should be prospective.
5) Our study lacks neuroimaging and other biomarkers data. Such data would substantially increase the overall neuroscientific generalizability of our findings, and would also enable us to broaden the aims and conclusions to the "brain maintenance". The relationship between brain reserve, cognitive reserve, maintenance, and compensation and their contribution to resilience is the focus of a lively debate within the research community and the concept and definitions are still evolving [16,42].
6) The retrospective design and a small sample size do not allow us to test if the memory maintenance an inherent part of memory reserve. A larger sample size and prospective design may help to disentangle the role of both mechanisms.

Conclusions

Our study confirms that both memory reserve and memory maintenance play a role in the phenomenon of SuperAging. We replicate the finding that females are more likely to be SAs than males. It seems that the main advantage of SAs over non-SAs is better verbal learning.

Ethical principles

The entire study was conducted in accordance with the Helsinki Declaration of 1975 (as revised in 2004 and 2008). The study protocol was approved by the Institutional Ethical Review Board of the Czech National Institute of Mental Health (reference number: 115/17, date of approval: March 22, 2017) and written informed consent has been obtained from all participants.

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Conflict of interest

The authors declare they have no potential conflicts of interest concerning drugs, products, or services used in the study.

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