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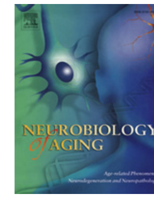

Cognitive ability and decline after early life stress exposure

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ABSTRACT

We examined the effects of early life stress on cognitive ability and decline among men of the Helsinki Birth Cohort Study, 10% of whom were separated temporarily (mean age at separation = 4.1 years) from their parent(s) during World War II. The men underwent the Finnish Defense Forces Basic Intellectual Ability Test twice, at 20 years and retest at 70 years. Compared with the men without childhood separation and matched for year of birth ($n = 186$), men separated from their parents ($n = 93$) scored lower by 5.5 (95% confidence interval [CI], −9.2 to −1.7), 4.2 (95% CI, −8.1 to −0.3), 3.1 (95% CI, −7.0 to 0.8), and 4.5 (95% CI, −10.5 to −1.4) standardized points (SD = 15) on verbal, visuospatial, arithmetic, and general cognitive ability, respectively, at 70 years. Longer duration of separation was associated with lower test scores. Though early life stress was also associated significantly with weaker cognitive performance at the ages 20 and 70 years, it was not associated with cognitive decline over the 50-year period within this sample.

1. Introduction

Animal models suggest that cognitive ability across the life span might be permanently affected by early life stress (ELS) (Pardon and Rattray, 2008). This might result from epigenetic programming of stress-related genes, which is likely to be associated with permanent impairments in hippocampal structure, neurogenesis (Korosi et al., 2011; McClelland et al., 2011), and synaptic plasticity (Aisa et al., 2009)—all important in cognition and emotions later in life. The effects of early environmental exposures might be causal, as an enriched early life experience has been shown to improve learning and memory (Fenoglio et al., 2005).

In accordance with the animal evidence, studies in humans have determined an association between retrospectively reported childhood traumas and stressful events, including physical/sexual abuse, neglect, family conflict, illness/death, and natural disasters, and smaller hippocampal volume in adulthood (Bremner et al., 1997; Gatt et al., 2009; Vythilingam et al., 2002) and lower cognitive ability among adolescents and middle-aged adults (Bremner, 2006; Gatt et al., 2009; Saigh et al., 2006; Yasik et al., 2007). Prospective evidence relying on objectively documented ELS in humans is, however, scarce, and whether ELS extends to long-term effects on human cognitive function across the life span remains unclear (Hedges and Woon 2010; Pechtel and Pizzagalli, 2011). Existing prospective evidence shows that, as children, intercountry adoptees did not differ from their peers or siblings in intelligence scores, but their language abilities and school performance lagged behind and they had more learning problems (van Ijzendoorn et al., 2005). In another study, the adoptees scored lower than their peers on intelligence tests as military conscripts (Odenstad et al., 2008). One study reported that elderly Holocaust survivors had a greater age-related decline over a 5-year follow-up period in explicit memory tasks than their nonexposed peers (Yehuda et al., 2006).

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We have previously shown that, compared with their non-exposed peers, men who as children were separated from their biological parents because of child evacuations to temporary foster care abroad during World War II scored lower on cognitive tests measuring verbal, arithmetic, and visuospatial abilities as conscripts at an average age of 20.1 years (Pesonen et al., 2011a). We also found a threshold effect of duration of separation; separation lasting for less than 1 year was not associated with later cognitive performance. Here, we extend these analyses to test whether the effects of ELS on cognitive ability (1) persist to old age among these men re-tested using the same cognitive test battery 50 years after the initial test, at an average age of 69.9 years; and (2) predict age-related changes in cognitive ability after the age of 20.1 years. We hypothesized that the effects of ELS on lower cognitive ability persist to old age and are associated with greater age-related cognitive decline.

2. Methods

2.1. Study population

The study cohort comprised men born at Helsinki University Central Hospital during 1934–1944. We identified 4630 men who had birth and child welfare clinic records and were still residents of Finland in 1971, when a unique personal identification number was allocated to each Finnish citizen. Most of them (77%) also went to school in Helsinki and had school health care records. The cohort has been described in detail elsewhere (Barker et al., 2005). Of the 4630 men, we identified 2786 (60% of the original cohort of men) who had served in the Finnish Defense Forces between 1952 and 1972, and who had undergone a compulsory test of cognitive ability within the first 2 weeks of their military service at an average age of 20.1 (SD, 1.4; range, 17.0–28.1) years. In 2009, in old age, 1750 of these men (63.2% of the subsample of 2786 men) were invited to a retest. Of the 1036 men who were not invited, 647 had died, 206 had previously declined further follow-up, and 183 either lived abroad, further than 200 km from the Helsinki area, or their addresses were not found. Of those invited, we obtained complete measurements of cognitive ability for 931 men (53.2%) at an average age of 67.9 (SD, 2.5; range, 64.5–75.7) years. The average time interval between the 2 tests was 47.7 (SD, 2.9; range, 38.9–54.7) years. The current study participants did not differ (1) from the cohort as a whole ($n = 4630$); (2) from the subsample for whom data on cognitive abilities at the age of 20 years were available ($n = 2786$); or (3) from the men who were invited to retest of cognitive ability in old age, but who did not participate ($n = 1750$) in birth anthropometry, length of gestation, parity, history of breastfeeding, or maternal characteristics ($p > 0.05$), but did more frequently have fathers with senior clerical occupations, and had themselves attained an upper tertiary education in adulthood, were older at the first test of cognitive ability, and had scored higher on cognitive ability at the first assessment ($p < 0.03$).

As described in our previous studies (Alastalo et al., 2012; Pesonen et al., 2010, 2011a, 2011b; Räikkönen et al., 2011), we used records stored in the Finnish National Archives to identify men who had been separated unaccompanied by their parent(s) to Sweden or Denmark during World War II. We excluded 29 men whose separation status was unclear (Pesonen et al., 2011a). In total, we identified 93 (10% of the sample) men who had been separated from their parents, leaving 812 nonseparated men. Of the separated participants, 84 (90.3%) had data available on their age at separation (mean, 4.1 years; SD, 2.0; range, 0.4–9.3), and 83 (89.2%) on the duration of separation (mean, 1.8 years; SD, 1.1; range, 0.2–6.5).

The separated participants were 2.3 years older during the second cognitive testing than the nonseparated participants (Table 1). To control for differences in age, we matched by birth year 2 nonseparated participants for each separated participant (n for nonseparated 186; n for separated 93). Table 1 shows that the separated and age-matched nonseparated participants did not differ from each other in age at the initial cognitive test and age at the cognitive retest, nor were differences present between these groups in any of the background variables assessed. For simplicity, we use 20 and 70 years in the text as the ages at cognitive tests.

We also tested whether the matched subsample (N = 186) of nonseparated participants differed from the remaining sample of nonseparated participants ($n = 623$), but found no differences between the groups ($p > 0.10$) other than the expected difference in old age (−2.9 years; $p < 0.001$). The Helsinki Birth Cohort Study has been approved by the Coordinating Ethics Committee of the Helsinki and Uusimaa Hospital District. Military service data were linked with the permission from the Finnish Defense Command. All study participants signed a written informed consent.

2.2. Cognitive ability at age 20 and in old age

The ability test scores were obtained from the Finnish Defense Forces basic ability test. The group-administered ability test battery is composed of verbal, arithmetic, and visuospatial reasoning subtests, each consisting of 40 timed multiple-choice questions. In

Table 1
Descriptive statistics according to separation status

	Nonseparated (all $n = 809$), mean (SD) or n (%)	Nonseparated matched sample ($n = 186$[a]), mean (SD) or n (%)	Separated ($n = 93$), mean (SD) or n (%)	$p/p2$[b]
Child				
Birth weight (g)	3479.7 (465.6)	3430.1 (487.2)	3488.1 (547.9)	0.87/0.37
Length at birth (cm)	50.7 (2.0)	50.6 (2.0)	50.6 (2.2)	0.66/0.99
Head circumference at birth (cm)	35.5 (1.5)	35.3 (1.4)	35.5 (1.7)	0.65/0.21
Birth order	2.0 (1.3)	2.0 (1.2)	2.0 (1.2)	0.61/0.87
Father's occupation				0.44/0.26
Manual worker	510 (63.0)	114 (61.3)	55 (59.1)	
Junior clerical	175 (21.6)	38 (20.4)	26 (28.0)	
Senior clerical	124 (15.3)	34 (18.3)	12 (12.9)	
Adult				
Age at first cognitive test (y)	20.2 (1.6)	20.2 (1.5)	20.1 (1.3)	0.82/0.89
Height at conscript (cm)	176.5 (6.0)	177.0 (6.2)	176.0 (6.0)	0.99/0.99
Age at second cognitive test (y)	67.6 (2.4)	69.9 (2.4)	69.9 (2.4)	<0.001/0.92
Height at second cognitive test (cm)	175.0 (6.0)	175.0 (6.2)	174.7 (5.3)	0.64/0.81
Cardiovascular disease	71 (8.8)	17 (9.1)	12 (12.9)	0.19/0.41
Time difference between tests (y)	47.4 (2.8)	49.7 (2.7)	49.8 (2.3)	<0.001/0.86

[a] For each separated case, 2 nonseparated participants matched for year of birth were randomly selected.
[b] p refers to the significance of the difference between all nonseparated ($n = 809$) and separated ($n = 93$) participants. $p2$ refers to the significance of the difference between the matched subsample of the nonseparated ($n = 186$) and separated ($n = 93$) participants.