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Intellectual ability in young men separated temporarily from their parents in childhood ☆

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ABSTRACT

We examined the effects of early life stress (ELS) on intellectual ability in 2,725 20-year-old male participants, of whom 321 were separated temporarily (mean 1.7 years) from both their parents during World War II, at an average age of 4.3 years. Intellectual ability was tested when entering compulsory military service. The separated men had −0.28 (95% CI −0.39, −0.16), −0.13 (95% CI −0.25, −0.01), −0.18 (95% CI −0.29, −0.06), and −0.19 (95% CI −0.30, −0.07) SD units lower verbal, visuospatial, arithmetic, and composite score of intellectual ability, respectively, compared to non-separated. Participants who were separated for more than a year and between two and four years had the lowest ability scores. ELS showed most consistent associations with verbal ability, but were not limited to it. Children beyond infancy and before their school-age may be the most vulnerable to the adverse effects of the ELS.

An experience of stress engages brain regions associated with learning and memory (the hippocampus), decision making (the prefrontal cortex), and emotion (the amygdala and the prefrontal cortex) (de Kloet, Joels, and Holsboer, 2005; Joëls and Baram, 2009; Joëls, Karst, Krugers, and Lucassen, 2007; McEwen, 2007; McGaugh, 2004). A prolonged stress experience early in life is particularly powerful, and may provoke sustained and/or prolonged changes in gene expression, neuronal structure and firing throughout the brain. These effects have been studied by numerous animal studies on early life stress (ELS), typically defined by temporary disruption of maternal care (Darnaudery and Maccari, 2008; McEwen, 2008). Permanent imprinting effects have been reported, for instance, in structure and function of the brain (Brunson et al., 2005; Rice, Sandman, Lenjavi, and Baram, 2008), in the function of the body's physiological feedback systems, such as the hypothalamic-pituitary-adrenal (HPA) axis system (Fish et al., 2004; Weaver et al., 2004), and in the dopaminergic system (Pryce, Dettling, Spengler, Spaete, and Feldon, 2004), all vital to cognitive function.

The extent to which these findings on ELS translate to long-term outcomes in human cognitive function is not entirely known. Retrospective evidence shows that childhood abuse is associated with changes in hippocampal structure and function (Bremner, 1999), and impairments in short-term memory in adulthood (Bremner et al., 1995). In contrast to experimental animal studies, the major challenge in studies on ELS in humans is to find an objectively defined stressor which influence could be measured prospectively. Studies on adopted children provide one such design. A randomized experiment showed that institutionalized children, in comparison to their siblings or peers who were adopted from these institutions, obtained lower scores on tests of intellectual ability at an average age of 54 months (Nelson et al., 2007). In a meta-analysis of non-experimental studies, inter-country adoptees as children did not differ from their peers or siblings in their new homeland in intelligence scores, but their school performance and language abilities lagged behind, and they had more learning problems (van

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Ijzendoorn, Juffer, and Poelhuis, 2005). As young military conscripts, adopted individuals scored lower on tests of intellectual ability, such that later adoption associated with worse test scores (Odenstad et al., 2008). Further, a recent study demonstrated that elderly Holocaust survivors had a greater age-related decline in explicit memory compared to their non-exposed peers (Yehuda et al., 2006).

Our study provides further prospective evidence on the long-term intellectual outcomes of ELS. The first objective of this study was to test if young adult men separated temporarily from their parents in childhood differ in their intellectual abilities from men who were not separated. The childhood separations took place during World War II, when the Finnish government organized a massive effort to protect the Finnish children from the strains of war, and carried out evacuations of over 70,000 children unaccompanied by their parents to temporary foster families, mainly in Sweden and Denmark. We have retrieved the evacuation data from the Finnish National Archives. Data on verbal, arithmetic and visuospatial intellectual abilities in young adulthood have been retrieved from the archives of the Finnish Defence Forces: since 1950's, every Finnish man has undergone this test in conjunction with their compulsory military service. As some developmental phases may be more sensitive to the influences of ELS, the second objective of our study was to test if age at separation and its duration mattered for the young adult intellectual outcomes.

The scanty information on the effects of early life stress (ELS) on subsequent life in humans is mainly based on natural experimental designs. There remains the possibility of confounding, such that the effects of ELS are subordinate to other, unknown life circumstances that may have inducted the ELS itself. While this possibility can be ruled out only by applying randomized control trials, ethical reasons restrict their use in human ELS studies, with the exception of intervention studies. These are few and can only assess the effect of an intervention rather than the ELS itself (Marshall, Reeb, Fox, Nelson, and Zeanah, 2008; Nelson et al., 2007; Zeanah et al., 2009). Therefore, to increase the validity of this study, we have carefully tested whether there were any systematic biases in the selection of children (Alastalo et al., 2009; Pesonen et al., 2007a; Pesonen et al., 2007c; Pesonen et al., 2010; Räikkönen et al., 2011), and controlled for birth order, year of birth, childhood socioeconomic status, birth weight, and for age and height at the time of intellectual testing, factors commonly associated with intellectual ability (Belmont and Marolla, 1973; Räikkönen et al., 2009; Turkheimer, Haley, Waldron, D'Onofrio, and Gottesman, 2003).

1. Methods

1.1. Participants

The participants came from the Helsinki Birth Cohort Study (HBCS), comprised of 4630 men born at the Helsinki University Central Hospital during 1934–44, and described in detail elsewhere (Barker, Osmond, Forsen, Kajantie, and Eriksson, 2005). From this cohort, we identified 2768 (60%) men who served in the Finnish Defence Forces between 1952 and 1972 and who underwent tests on their intellectual abilities in young adulthood (Mean (M) = 20.0, Standard Deviation (SD) = 1.4 years). As previously reported (Kajantie et al., 2010) these men were more likely to be born later than those with no test data available.

We used records stored in the Finnish National Archives to identify 321 of the 2768 men (11.5%) who had been separated unaccompanied by their parent(s) to Sweden or Denmark during the World War II. Of the 2768 men, a small sample of 522 participants had participated in a clinical examination in 2004 in which we asked questions about evacuation. On the basis of this questionnaire, we found that 43 of these men had been separated from their parents within Finland (Pesonen et al., 2007a). Such separations were not organised by the Finnish Government and were thus not stored in the national archives. Since the information on unofficial evacuations within Finland was not available in the entire cohort of 2768, we excluded these 43 ‘false negatives’ from the group of non-separated. Thus, in our analyses we compare 321 separated men with 2404 non-separated men. Of the separated participants, 287 (89%) had data available on their age at separation and 279 (87%) on the duration of evacuation. On average the children were 4.3 years old at time of separation (SD = 2.2, range = 0.4 to 10.3), and the average separation lasted for 1.7 (SD = 1.0, range = 0.1 to 6.5) years.

1.2. Intellectual ability at conscription

The intellectual ability test scores were obtained from the Finnish Defence Forces Basic Ability Test, developed by the Finnish Defence Forces Education Development Center. The obligatory test is given to all new recruits during the first two weeks of their military service and is used when the conscripts are selected for leadership training. The test battery and its psychometric properties are described in detail elsewhere (Kajantie et al., 2010; Räikkönen et al., 2009; Tiihonen et al., 2005). It is designed to measure general ability and logical thinking, is composed of verbal, visuospatial, and arithmetic reasoning subtests. Each subtest is timed and consists of 40 multiple-choice questions that are ordered by difficulty. Correct answers are summed to yield a test score. Verbal and arithmetic subtests comprise four types of questions. In the verbal reasoning test the subject has to choose synonyms or antonyms of a given word, a word belonging to the same category as a given word pair, which word of a word list does not belong in the group, and similar relationships between two word pairs. The visuospatial reasoning subtest comprises a set of matrices containing a pattern problem with one removed part. Analogous to Raven's Progressive Matrices (Raven, Raven, and Court, 2000) the subject is asked to decide which of the given single figures completes the matrix. The subject must conceptualize spatial relationships ranging from the very obvious to the very abstract. In the arithmetic reasoning test the subject has to complete a series of numbers that have been arranged to follow a certain rule, to solve verbally expressed short problems, to compute simple arithmetic operations, and to choose similar relationships between two pairs of numbers. We also used a composite score of intellectual ability, analyzed as the mean of the three individual subtests.

1.3. Background variables

Subject's date of birth, birth weight and order were extracted from birth records. Social class in childhood, based on father's occupation (manual worker, junior clerical, senior clerical) was extracted from school, child welfare clinic and birth records. Height was measured at conscription. There is a Swedish speaking minority in Finland: participant's first language was defined according to the available register-based information on mother's first language (Finnish/Swedish).

1.4. Statistical analysis

The adult intellectual ability test scores were converted into z-scores, which represent the difference from the mean value for the whole cohort. The group differences are expressed in standard deviation (SD) units. We used multiple linear regression analyses to test the effect of separation on intellectual abilities. In addition to using duration of separation and age at separation as continuous variables, we split duration of separation (≤ 1 years, >1 and ≤2 years, >2 years) and age at separation (infancy ≤2 years; toddlerhood >2 and ≤4 years; early childhood >4 and ≤7 years; and school age >7 years) into categories that we have used in our previous studies (Pesonen et al., 2007b; Pesonen et al., 2010), dummy coded these and explored their associations with intellectual abilities in multiple linear regressions. We adjusted all the analyses for year of birth, childhood social class, birth weight, birth order, and for age and height at testing.

In principle, a conscript had the right to be tested in his own native language. However, in our sample the native Swedish speaking conscripts had 0.34, 0.16 and 0.21 SD units lower scores on verbal reasoning (95 percent confidence interval [95% CI] −0.44 to −0.24), arithmetic reasoning (95% CI −0.26 to −0.05), and on total score (95% CI −0.25 to −0.05), respectively, than the native Finnish speaking conscripts. The native Swedish and Finnish speaking conscripts did not differ from one another in visuospatial reasoning (−0.07, 95% CI −0.17 to 0.04), which might reflect that the Swedish speaking may not have been given the test in their own native language, but instead in Finnish. Therefore, we reran the analyses by excluding the native Swedish speaking participants (n = 422, of which 73 separated), leaving 2055 non-separated and 248 evacuated participants in the analyses.

2. Results

The mean raw scores, standard deviations and ranges for verbal, visuospatial, and arithmetic ability and composite scores in the entire analytic sample were 26.0 (SD = 8.3, range 1–40), 23.6 (SD = 6.0, range 3–36), 25.2 (SD = 9.9, range 1–40), and 25.0 (SD = 7.2, range 4–27), respectively. Fig. 1 shows the distributions of the composite scores in separated and non-separated participants and Table 1 shows descriptive statistics of the background variables according to the separation status. The birth order was higher among the group of separated than among the non-separated. There were no other significant differences between the groups. Participants who were older in age when the separation started had a shorter separation duration ($r = -0.13$, $p < 0.05$).

Table 2 shows the intellectual ability scores according to the separation status. The separated had −0.28 SD units lower verbal ability, −0.13 SD units lower visuosaptial ability, −0.18 SD units lower arithmetic ability and −0.19 SD units lower composite scores of intellectual ability as compared to

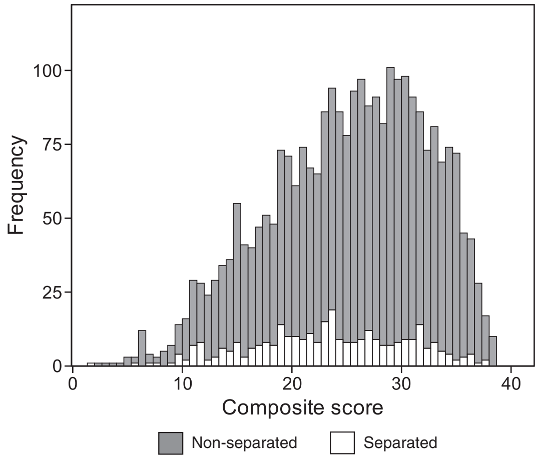

Fig. 1. Distributions of the composite raw scores in non-separated and separated participants.

the group of non-separated (all *P*-values ≤ 0.03). When we excluded Swedish speaking participants (n = 422, of which 73 separated), the results held essentially the same, except for visuospatial reasoning, in which the group difference became non-significant (*P* = 0.08).

2.1. Duration of separation

Fig. 2 shows the results from the multiple regression analyses exploring whether the duration of separation was associated with intellectual ability, the non-separated participants serving as the referent group. The results including and excluding the Swedish speaking participants were similar. Below we report the results when the Swedish speaking participants were excluded. A separation that lasted more than one and ≤2 years was associated with significantly lower scores in verbal (−0.39 SD units, 95% CI −0.57 to −0.22), visuospatial (−0.22 SD units, 95% CI −0.41 to −0.03), and composite ability (−0.22 SD units, 95% CI −0.40 to −0.03). A separation that lasted over two years was significantly associated with lower scores in verbal (−0.36 SD units, 95% CI −0.59 to-0.12),

Table 1
Descriptive statistics according to the separation status.

	Non-separated N = 2404	Separated N = 321	*P*
	Mean (SD)/ N (%)	Mean (SD)/ N (%)	
Child			
Birth weight (g)	3462.3 (482.2)	3441.8 (536.8)	0.48
Length at birth (cm)	50.7 (2.0)	50.5 (2.1)	0.23
Head circumference at birth (cm)	35.4 (1.5)	35.4 (1.6)	0.46
Birth order	1.9 (1.3)	2.2 (1.6)	< 0.001
Father's occupation			0.12
Manual worker	1617 (67.3)	202 (62.9)	
Junior clerical	528 (21.1)	69 (26.2)	
Senior clerical	314 (11.6)	23 (10.9)	
Adult			
Age at cognitive test (years)	20.0 (1.4)	20.0 (1.1)	0.99
Height at conscript (cm)	176.5 (6.0)	176.0 (6.0)	0.11

Table 2
Change in standard deviation unit in intellectual ability scores according to separation experience.

	Model A			Model B		
	SD unit change	95% CI	*P*	SD unit change	95% CI	*P*
Non-separated vs. separated						
Verbal reasoning	−0.28	−0.39,-0.16	<0.001	−0.23	−0.36, −0.10	<0.001
Visuospatial reasoning	−0.13	−0.25, −0.01	0.03	−0.12	−0.25, 0.01	0.08
Arithmetic reasoning	−0.18	−0.29, −0.06	0.003	−0.14	−0.27, −0.01	0.04
Composite score	−0.19	−0.30, −0.07	0.002	−0.19	−0.32, −0.06	0.005

Note. Model A is conducted in the entire sample, in the Model B the Swedish speaking participants are excluded.
The analyses are adjusted for year of birth, childhood social class, birth weight, birth order, and for age and height at testing.
SD refers to Standard Deviation and 95% CI refers to 95 percent confidence interval.

arithmetic (−0.24 SD units, 95% CI −0.49 to −0.001) and composite ability (−0.25 SD units, 95% CI −0.49 to −0.03). If the participant was separated for ≤1 year, it was not associated with lower cognitive performance (*P*-values>0.46) in comparison to the non-separated. The duration of separation analyzed as a continuous variable within the separated participants was not associated with intellectual performance (*P*-values>0.09).

2.2. Age at separation

Fig. 3 shows the results from the multiple regression analyses exploring whether the age period at separation was associated with intellectual ability, the non-separated participants serving as the referent group. As the results including and excluding the Swedish speaking participants were similar, below we report the results when the Swedish speaking participants were excluded. Separation was associated with lower scores in verbal ability when it took place in infancy (−0.35 SD units, 95% CI −0.66 to −0.03), in toddlerhood (−0.39 SD units, 95% CI −0.59 to −0.20), and in early childhood (−0.26 SD units, 95% CI −0.48 to −0.04). In addition, separation in toddlerhood was associated with lower scores in visuospatial ability (−0.23 SD units, 95% CI −0.44 to −0.02), arithmetic ability (−0.29 SD units, 95% CI −0.49 to −0.09), and in composite ability (−0.31 SD units, 95% CI −0.51 to −0.11). Participants separated at school-age did not score significantly lower in any of the tests (*P*-values>0.25). The age at separation analyzed as a continuous variable within the separated participants was not associated with intellectual performance (*P*-values>0.28 for linear associations, *P*-values>0.06 for quadratic associations).

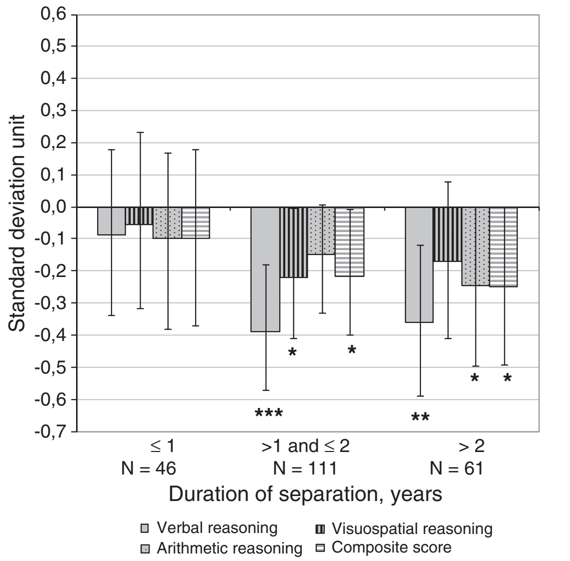

Fig. 2. Intellectual ability scores according to duration of separation. Bars represent Standard Deviation unit change with 95% percent Confidence Intervals in intellectual ability scores in the categories of duration of separation compared to non-separated. The model is adjusted for year of birth, childhood social class, birth weight, birth order, and for age and height at testing, and exclude Swedish speaking participants.***$P<0.001$,** $P<0.01$, * $P\leq0.05$ when contrasted against non-separated.

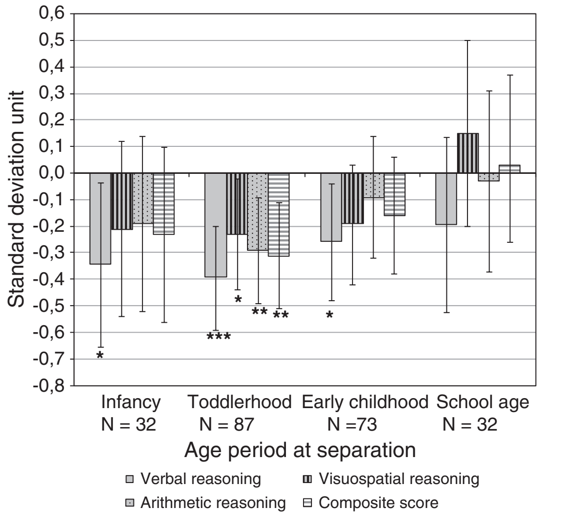

Fig. 3. Intellectual ability scores according to age period at separation. Bars represent Standard Deviation unit change with 95% percent confidence intervals in intellectual ability scores in the categories of age at separation compared to non-separated. The model is adjusted for year of birth, childhood social class, birth weight, birth order, and for age and height at testing, and exclude Swedish speaking participants. ***$P<0.001$,** $P<0.01$, * $P\leq0.05$ when contrasted against the non-separated .

3. Discussion

ELS due to a separation experience from both or the only parent(s) was associated with considerably lower intellectual ability test scores in young adulthood, at the age of 20 years, compared to non-separated participants. Consistent with previous evidence, we found the strongest relationship between ELS and lower scores on verbal reasoning (Bremner, 2006; Saigh, Yasik, Oberfield, Halamandaris, and Bremner, 2006; Yasik, Saigh, Oberfield, and Halamandaris, 2007). The associations were not confounded by childhood social class, birth order, birth weight or by age or height at time of intellectual assessment, factors that previous research has found as predictors of intellectual achievement (Belmont and Marolla, 1973; Räikkönen et al., 2009; Turkheimer et al., 2003).

Our study is among the few longitudinal studies with a relatively long follow-up, extending into adulthood. The current findings thus add to the previous literature mostly based on adoption (Odenstad et al., 2008) in several ways. In addition to showing considerable main effects of ELS, we were able to show a threshold effect between duration of stress exposure and impairment of intellectual ability, such that a separation lasting one year or less was not associated with worse intellectual performance. Secondly, we were able to specify an age period when the child is probably most vulnerable to ELS. The most widely affected children were aged from two to four years, whereas separation in infancy (≤2 years), in early childhood (>4 and ≤7 years) or at school-age (>7 years) had fewer effects on the test scores, except for the verbal ability score, which was lower for all participants separated before their school-age. Our findings showing that infancy may be a period of lesser vulnerability parallels findings showing that adoption during infancy may buffer the potentially adverse developmental consequences of institutionalization (Gunnar and van Dulmen, 2007; Nelson et al., 2007). However, the analogy may be misleading. Whereas earlier adoption is likely to reduce the potential time of social deprivation, we do not know whether the separated children were actually deprived in their foster families. In addition, not all adoption studies have reported significant age-related effects on cognitive abilities (van Ijzendoorn et al., 2005), or different categorizations of age have been used, making the comparison difficult (Odenstad et al., 2008).

In natural experiments on ELS such as this, the selection of the children was not random. We found higher birth order among the separated than non-separated children, and adjusted for this in all analyses. However, as shown among 250,000 military conscripts (Kristensen and Bjerkedal, 2007), birth order did not have an effect on adult IQ when social order was taken into account, i.e. the death of previous child(ren). They argued that the relationship between birth order and IQ score is dependent on the social rank in the family and not birth order as such. We do not know how evacuation (or war) changed the social rank of the separated children in our cohort. We know from historical sources that in many cases the foster families were childless couples, making the social rank of the evacuees potentially higher in the foster family than in their biological family. Change in social rank may have occurred among those non-separated whose sibling(s) were evacuated. Second, in our previous studies, we have also tested the possibility of selection bias, but not found evidence for systematic selection (Alastalo et al., 2009; Pesonen et al., 2010, 2007a, 2007b, 2007c; Räikkönen et al., 2011). Given the possibility that parents may have sent away their most emotionally labile child, we have also tested whether there were differences in the Big Five personality traits between separated and non-separated adults, but did not find any such differences (unpublished data). The differences between the groups, however, were clear in the function of the HPA axis (Pesonen et al., 2010) and in psychiatric disorders (Räikkönen et al., 2011). The separated had 1.3 to 1.6-fold higher risks of any psychiatric disorder, and of substance use and personality disorders (Räikkönen et al., 2011), severe enough to warrant or contribute to hospitalization or being the underlying, intermediate or contributing cause of death.

The internal validity of our findings is increased by the fact that a longer duration of separation, representing more prolonged stress, was associated with lower adult intellectual abilities. Second, the highest odds for worse intellectual performance in adulthood were observed among children separated from their parents beyond infancy. This observation corresponds to adoption studies, showing poorer outcomes for children adopted after infancy (Gunnar and van Dulmen, 2007; Nelson et al., 2007), and to our previous study reporting highest salivary cortisol reactivity to stress among those separated in toddlerhood and early childhood (Pesonen et al., 2010), i.e., among children having the poorest test results in the present study.

Indeed, animal models have enlightened the potential biological mechanism that could mediate the associations between ELS and cognitive impairment. In terms of physiology, ELS is known to reprogram the set point of the HPA axis, leading to persistently altered CRH and mRNA expression (Rice et al., 2008), and enhanced reactivity to subsequent stress (Brunson, Avishai-Eliner, Hatalski, and Baram, 2001). In addition, prolonged ELS is known to have long-lasting effects on hippocampal structure and function, associated with learning and memory (Fenoglio, Brunson, and Baram, 2006). Both retrospective (Bremner, 1999, 2006; Bremner et al., 1995) and prospective (Eluvathingal et al., 2006; Marshall et al., 2008) human studies have also provided converging, although less specific evidence. In addition, a number of human ELS studies have shown that cognitive deficits and neurological alterations are characteristic of individuals with post traumatic stress disorder (PTSD) (Bremner, 2006; Gale et al., 2008; Vasterling, Brailey, Constans, and Borges, 1997). Since PTSD was not measured in our study, hypotheses on the neurological mechanisms remain elusive.

A number of limitations are apparent. First, when compared to the non-separated, the birth order of the separated was higher, and there was a trend, although not significant, towards a lower socioeconomic background among the separated. Although we adjusted for childhood SES and birth order in all our analyses, it remains possible that their influence on intellectual performance is more complex than statistically modelled in the present study. Second, the age and duration categories applied in the present study included uneven number of subjects, and thus the power to detect significant age and duration effects varied between the categories. Third, we do not have data on the quality of foster care, or of the care given at the biological home, both of which are likely to modulate the effect of ELS on intellectual ability; we also acknowledge that for some children the separation might have been a positive experience. Similarly, the available nutrition in foster families may have been better than in Finland which experienced food shortages during the war. However, these factors are likely only to reduce rather than increase our ability to detect significant associations. Fourth, we do not know whether there was overrepresentation of former evacuees among those who were disqualified from service in the Finnish Defence Forces due to poor health. Yet, a bias towards inclusion of healthier participants might again diminish rather than increase the power of our study. Similarly, we acknowledge that among the non-separated there might be individuals who are misclassified because their evacuation may have been organized by unofficial routes. The actual difference between the groups may then be greater than reported here. Finally, the results were obtained among men only, and may not generalize to women.

In summary, this study is among the few longitudinal epidemiological cohort studies on the relation of ELS and intellectual ability in adulthood. The challenge in all ELS studies is to define ELS such that it would not be confounded by other environmental and/or genetic factors such as parental psychopathology, prenatal complications, poor nutrition, crowding, or poverty, all factors which may contribute to cognitive development of the child (Cicchetti and Lynch, 1993). The strength of this study is in the natural experimental setting, in which a rather equal distribution of these confounders was presumed, although could not be tested. In line with previous clinical studies, ELS seemed to most adversely affect verbal performance, but was not limited to it. The study provided the first evidence that longer duration of ELS is associated with worse intellectual outcome, and showed that children beyond infancy and before their school age may be the most vulnerable to the adverse effects of the ELS.

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