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## **The associations of childhood psychosocial factors with cognitive function in midlife – The Young Finns Study**

Amanda Nurmi, BM<sup>1</sup>, Laura Pulkki-Råback, PhD<sup>2</sup>, Pia Salo, MD, PhD<sup>1</sup>, Katja Pahkala, PhD<sup>1,3</sup>, Markus Juonala, MD, PhD<sup>4</sup>, Nina Hutri-Kähönen, MD, PhD<sup>5</sup>, Mika Kähönen, MD, PhD<sup>6</sup>, Terho Lehtimäki, MD, PhD<sup>7</sup>, Eero Jokinen, MD, PhD<sup>8</sup>, Liisa Keltikangas-Järvinen, PhD<sup>2</sup>, Tomi P. Laitinen, MD, PhD<sup>9</sup>, Päivi Tossavainen, MD, PhD<sup>10</sup>, Leena Taittonen, MD, PhD<sup>11</sup>, Jorma S.A. Viikari, MD, PhD<sup>4</sup>, Olli T. Raitakari, MD, PhD<sup>1,12</sup>, Suvi P. Rovio, PhD<sup>1</sup>.

**Affiliations:** <sup>1</sup>Research Centre of Applied and Preventive Cardiovascular Medicine, University of Turku, Turku, Finland; Centre for Population Health Research, University of Turku and Turku University Hospital, Finland; <sup>2</sup>Department of Psychology and Logopedics, Faculty of Medicine, University of Helsinki, Finland; <sup>3</sup>Paavo Nurmi Centre, Sports & Exercise Medicine Unit, Department of Physical Activity and Health, University of Turku, Turku, Finland; <sup>4</sup>Department of Medicine, University of Turku and Division of Medicine, Turku University Hospital, Turku, Finland; <sup>5</sup>Tampere Centre for Skills Training and Simulation, Tampere University, Tampere, Finland; <sup>6</sup>Department of Clinical Physiology, Tampere University Hospital and Faculty of Medicine and Health Technology, Tampere University, Tampere, Finland; <sup>7</sup>Department of Clinical Chemistry, Fimlab Laboratories and Finnish Cardiovascular Research Center-Tampere, Faculty of Medicine and Health Technology, Tampere University, Tampere, Finland; <sup>8</sup>Department of Pediatric Cardiology, Hospital for Children and Adolescents, University of Helsinki, Helsinki, Finland; <sup>9</sup>Department of Clinical Physiology, University of Eastern Finland and Kuopio University Hospital, Kuopio, Finland; <sup>10</sup>Department of Pediatrics, PEDEGO Research Unit, Medical Research Center, University of Oulu and Oulu University Hospital, Oulu, Finland; <sup>11</sup> Department of Pediatrics, Tampere University Hospital, Tampere, Finland; <sup>12</sup>Department of Clinical Physiology and Nuclear Medicine, Turku University Hospital, Turku, Finland

**Short title:** Childhood psychosocial factors and midlife cognition

**Address for correspondence:** Amanda Nurmi, Research Centre of Applied and Preventive Cardiovascular Medicine, University of Turku, Kiinanmyllynkatu 8-10, 20520 Turku, Finland. Email: [amanda.s.nurmi@utu.fi](mailto:amanda.s.nurmi@utu.fi), Telephone: +358 44 0949420

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## **ABSTRACT**

**Objective:** An adverse psychosocial environment in childhood may harm cognitive development, but the associations for adulthood cognitive function remain obscure. We tested the hypothesis that adverse childhood psychosocial factors associate with poor cognitive function in midlife by leveraging the prospective data from the Young Finns Study.

**Method:** At the age of 3-18 years, the participants' psychosocial factors (socioeconomic and emotional environment, parental health behaviors, stressful events, child's self-regulatory behavior and social adjustment) were collected. In addition to the separate psychosocial factors, a score indicating their clustering was created. Cognitive function was measured at the age of 34-49 years with a computerized test addressing learning and memory (N=1011), working memory (N=1091), sustained attention and information processing (N=1071) and reaction and movement time (N=999).

**Results:** We observed an inverse association between the accumulation of unfavorable childhood psychosocial factors and poorer learning and memory in midlife (age, sex, education, adulthood smoking, alcohol drinking and physical activity adjusted  $\beta=-0.032$ ,  $SE=0.01$ ,  $p=0.009$ ). This association corresponded approximately to the effect of 7 months aging. Specifically, poor self-regulatory behavior ( $\beta=-0.074$ ,  $SE=0.03$ ,  $p=0.032$ ) and social adjustment in childhood ( $\beta=-0.111$ ,  $SE=0.03$ ,  $p=0.001$ ) associated with poorer learning ability and memory 30 years later. No associations were found for other cognitive domains.

**Conclusions:** The findings suggest an association of childhood psychosocial factors with midlife learning ability and memory. If these links are causal, the results highlight the importance of a child's self-regulation and social adjustment as plausible determinants for adulthood cognitive health.

## **KEY POINTS**

**Question:** We examined whether the psychosocial environment in childhood is associated with cognitive function in midlife.

**Findings:** This study shows that unfavorable psychosocial factors in childhood may associate with poorer learning ability and memory in midlife.

**Importance:** These results highlight that a favorable psychosocial environment in childhood could promote cognitive and public health.

**Next steps:** Future studies should focus on the associations between childhood psychosocial factors and the life course trajectories of cognitive function.

## INTRODUCTION

*Psychosocial factors* is an overarching term for multiple aspects of childhood exposures, including emotional (e.g., responsiveness to child's needs), socioeconomic (e.g., family's financial resources), behavioral (e.g., health-promoting behaviors), and environmental factors (e.g., predictability of the environment) (Alvarez et al., 2018; Repetti et al., 2002; Shonkoff et al., 2012). There are theoretical models suggesting that early psychosocial factors affect a child's development and pediatric health outcomes over their lifespan (Alvarez et al., 2018; Oh et al., 2018; Repetti et al., 2002; Shonkoff et al., 2012). Furthermore, it has been suggested that the accumulation of multiple risk factors in childhood impacts health and development more profoundly than single factors (Evans et al., 2013; Hughes et al., 2017). Therefore, in addition to focusing on multiple psychosocial factors also the accumulation of childhood exposures should be emphasized when trying to understand the development of lifelong health.

Adverse childhood experiences may have long-lasting effects on the development of the brain's neural systems and neuroplasticity and thereby, on cognitive function (Guinosso et al., 2015; Mackes et al., 2020; Pakulak et al., 2018). Previous studies have suggested inverse associations between poor parenting, stress and adverse experiences in childhood, such as: early institutional care, poor material home conditions, single parenthood, low family income, maternal depression, marital conflicts or maltreatment on cognitive function in childhood (Bos et al., 2009; Cabrera et al., 2020; Cowell et al., 2015; Hanson et al., 2012; Kiernan & Huerta, 2008; Lund et al., 2020; Richards & Wadsworth, 2004; Wade et al., 2018). Associations have been observed between long-lasting poverty and stress in childhood with poor working memory (Evans et al., 2009; Hanson et al., 2012), and of parental divorce experienced in childhood with low cognitive function (Richards & Wadsworth, 2004) in adolescence. Prior retrospective studies on low childhood socioeconomic status (SES), family conflicts, absent

parenting, neglect and/or adoption have suggested links between the childhood psychosocial factors and cognitive function in old age (Aartsen et al., 2019; Anderson et al., 2017b; Fors et al., 2009b; Zhang et al., 2008). Noticeably, there is only one previous study that has coupled longitudinal prospective data on childhood psychosocial factors with adulthood cognitive function; the study was conducted on over 1300 British subjects (Richards & Wadsworth, 2004). This study suggested that poor material home conditions at the age of 4 years, such as crowding, uncleanliness or the poor condition of the child's clothes, was linked to low verbal memory and visual search speed at the age of 53 years. To conclude, even though the evidence comes mainly from either short-term or retrospective long-term studies focusing on single psychosocial factor or adversity, the previous findings indicate that childhood psychosocial factors may have long-term effects on later cognitive health. Concomitantly, there is a lack of evidence from prospective longitudinal cohorts with a broad outlook on both childhood psychosocial factors and adulthood cognitive function.

Although, the importance of multiple childhood experiences and of their accumulation on a child's development has been acknowledged, and the worsening of health outcomes has been suggested to occur with an increasing number of adversities (Evans et al., 2013; Guinasso et al., 2015), evidence is needed to elucidate whether exposure to adverse childhood psychosocial factors is linked to adulthood cognitive outcomes. We aimed to close the existing knowledge gap on the links between different childhood psychosocial factors as well as their accumulation with adulthood cognitive function by studying the associations between a wide array of childhood psychosocial factors and midlife performance in several cognitive domains. We hypothesized that childhood adverse psychosocial factors link with worse cognitive performance in adulthood, and tested this hypothesis by leveraging population-based data from the Cardiovascular Risk in Young Finns Study (YFS).

## **METHODS**

### **Participants**

This study is a part of the YFS, which is an ongoing longitudinal population-based study on cardiovascular risk factors from childhood to adulthood (Raitakari et al., 2008). The baseline study conducted in 1980 recruited 3,596 randomly selected children and adolescents (boys and girls; ages 3, 6, 9, 12, 15, and 18 years). The cohort has been followed regularly in 1983, 1986, 1989, 2001, 2007, and 2011. Figure 1 presents the formation of the analytical sample of this study including all participants with the exposure and outcome variables as well as data on all covariates.

### **Cognitive function**

Cognitive testing was introduced into the study protocol in the year 2011 follow-up study, and this cognitive data was used in the present study. Cognitive testing was conducted on 2,026 YFS participants using a computerized cognitive testing battery (CANTAB, Cambridge Cognition, Cambridge, United Kingdom). The test battery included tests measuring: 1) visual and episodic memory and visuospatial associative learning, hereafter learning and memory (Paired associates learning test; PAL); 2) short-term and spatial working memory (Spatial working memory test, SWM); 3) visual processing, recognition, and sustained attention (Rapid visual information processing test; RVP); and 4) reaction and movement speed (Reaction time test; RTI). Principal component analyses were conducted separately for data from each subtest of the CANTAB test battery in order to identify domain specific components accounting for the majority of the variation within the dataset (Rovio et al., 2016). The first components obtained from the test specific analyses were normalized using a rank order normalization procedure resulting in four outcome variables, each with a mean 0 and standard deviation (SD) 1. More detailed information on the cognitive testing and the principal component analyses is

presented in the Supplementary material (Supplementary Table 1 and Supplementary Figure 1). Validation of the YFS cognitive data has been published previously (Rovio et al., 2016).

### **Childhood psychosocial factors**

The participants' parents were asked about childhood psychosocial factors at baseline. The information was acquired from 40 individual questions, which are described in the Supplementary material Table 1. Similar to previously (Elovainio et al., 2018; Pulkki-Råback et al., 2015; Raitakari et al., 2008), the responses were used to create six psychosocial factors, and these are proposed as central components of the psychosocial environment in childhood (Adler & Stewart, 2010; Repetti et al., 2002; Slopen et al., 2013; Taylor et al., 2001): 1) socioeconomic environment, 2) emotional environment, 3) parental health behaviors, 4) stressful events, 5) self-regulatory behavior of the child, and 6) social adjustment of the child. The responses to the individual questions were first dichotomized (1=favorable, 0=less-than-favorable level) and then added together to form each psychosocial factor. Our previous analyses have confirmed that these 40 questions form a factor structure of six psychosocial factors (Elovainio et al., 2018; Pulkki-Råback et al., 2017), which verify the use of the particular factors applied in this study. In the statistical analyses all separate psychosocial factors were treated as continuous variables.

*Socioeconomic environment factor* consisted of four components: 1) upper white-collar occupation, 2) academic/college degree, 3) high family income as the highest quartile, and 4) occupational stability as the absence of unemployment spells/retirement/long-term sick leave. Thus, the values of this factor ranged from 0 to 4.

*Emotional environment factor* consisted of four components: 1) the absence of a diagnosed parental mental disorder, 2) high parental care-giving nurturance, 3) high parental life satisfaction, 4) reasonable alcohol use with either no intoxication or intoxication at most 3 times per year. The values for this factor also ranged between 0 and 4.

*Parental health behavior factor* consisted of three components: 1) body mass index (BMI;  $<30.0 \text{ kg/m}^2$  as a proxy of non-excessive energy intake), 2) nonsmoking, 3) regular physical activity. As the health behaviors of both parents were assessed, the values for this factor ranged between 0 and 6.

*Stressful events factor* included five events: 1) moving residence, 2) change of school, 3) parental divorce or separation, 4) death of a family member, 5) serious disease in the family. The absence of each event was considered, and thus, the values of the factor ranged between 0 and 5.

*Self-regulatory behavior factor* included both self-control and aggression control. It consisted of seven components: one indicating the child as being always or most of the time very controlled, and six indicating the child's poor aggression control. The values for this factor ranged between 0 and 7.

*Social adjustment factor* consisted of two components: 1) parental worry, and 2) parental evaluation of the child's adjustment, and thus, the values ranged between 0 and 2.

Before applying the separate psychosocial factors to form the psychosocial factors cumulative score, we analyzed the inter-correlation between the factors (Supplementary Table 2). The

correlation analyses indicated weak or at most moderate correlations between the factors as the highest correlation coefficient was  $r=0.34$ . This correlation was observed between the factors indicating the child's social adjustment and the child's self-regulation.

### **Psychosocial factors score (Cumulative score)**

The psychosocial factors were added together to form a psychosocial factors score similar to that described previously (Evans et al., 2013). We had no hypothesis to weight any one factor more than any other, and thus, each psychosocial factor was converted into a standard scale before final total. Due to the skewed distribution in some of the variables, the standardization was rerun with quantile-quantile normalization without effecting the score. Therefore, the same form of standardization was used for every psychosocial factor leading to an equal contribution of each factor to the score and a score that is on a standard deviation scale (i.e. one point increase corresponds to one standard deviation increase). Finally, the score was inverted so that a higher score indicates a more unfavorable psychosocial environment. In the statistical analyses the cumulative score was used as continuous. Additionally, the score was divided into quartiles for descriptive purposes. A detailed description of the score is presented in the Supplementary material (Supplementary Table 3).

### **Covariates**

Age was defined as full years at the time of cognitive testing. The maximum number of education years was assessed from data collected in all adulthood follow-up studies. Questions about daily smoking were asked at the baseline and in all follow-up studies from participants aged 12 years and older and used to dichotomize the participants into daily smokers and nonsmokers. Adolescents from the age of 12 years and older were asked about alcohol use. Participants reporting any drinking of alcohol at the baseline were considered alcohol users

while those reporting never drinking or were aged under 12 years were considered non-drinkers. Adulthood alcohol drinking was assessed as alcohol units per day. Questions about physical activity were asked at baseline and in all follow-up studies. As in previous studies, a physical activity index was calculated using information on frequency and intensity of physical activity, hours spent on vigorous physical activity, average duration of a physical activity session, and participation in organized physical activity (Telama et al., 2005).

Results from the YFS data have previously shown that an adverse family environment may be associated with cardiovascular risk factors and simultaneously, several favorable psychosocial factors have been associated with good cardiovascular health (Juonala et al., 2016; Pulkki-Råback et al., 2015, 2017). Furthermore, we have previously reported that cardiovascular risk factors from childhood may have independent negative associations with cognitive function in midlife (Rovio et al., 2017). Therefore, we conducted supplemental analyses adjusting for cardiovascular risk factors from childhood/adolescence and adulthood using data that was available for a restricted numbers of participants: childhood systolic blood pressure (N=1135), serum low-density lipoprotein (LDL) cholesterol (N=1130), BMI (N=1135) and school performance (N=1025) as well as adulthood systolic blood pressure (N=1103), LDL-cholesterol (N=1077) and BMI (N=1108). Standard methods were used for measuring systolic blood pressure, serum total cholesterol, high-density lipoprotein cholesterol, and triglycerides at baseline and all follow-up studies. LDL-cholesterol was calculated according to Friedewald's equation (Friedewald et al., 1972). In all phases, the participants' weight and height were measured and their BMI calculated ( $\text{kg}/\text{m}^2$ ). Finally, to overcome the lack of baseline cognitive measures, information was requested on childhood school performance expressed as grade point average (*i.e.* average of grades in all individual school subjects at baseline for those who were of school age or either of the two subsequent follow-ups for those

participants who were not of school age at baseline); these averages were used as a proxy for childhood cognitive ability in the supplementary analyses. Additionally, a polygenic score was calculated based on a GWAS on intelligence to indicate genetic propensity for poor cognitive function using standard methods (Browning & Browning, 2008; Savage et al., 2018; Teo et al., 2007; Vilhjálmsón et al., 2015) and used as a proxy for baseline level of cognitive function in the interaction analyses.

### **Statistical analyses**

Before creating the statistical models, the inter-correlations between all exposure variables, covariates and outcome variables were analyzed (Supplementary Table 4). Linear regression was used to study the associations between the childhood psychosocial factors score, separate psychosocial factors and cognitive function in midlife. Both the separate psychosocial factors and the cumulative psychosocial factors score were treated as continuous variables. Age, sex and education were used as primary covariates in all analyses (Model 1). Subsequently, the analyses were additionally adjusted for childhood/adolescence lifestyle factors such as smoking, alcohol drinking and physical activity (Model 2) or for corresponding adulthood factors (Model 3). The possible modification effect of sex, age and genetic propensity for intelligence was formally tested by adding multiplicative interaction terms (e.g. polygenic score\*psychosocial factors) in the age, sex and education adjusted models. Subsequently, for those variables suggesting a significant effect modification, stratified analyses were conducted.

In the supplemental analyses, the cardiovascular covariates from childhood were entered to the model including childhood lifestyle factors (Model 2B), while the corresponding adulthood variables were entered into the model including adulthood lifestyle factors (Model 3B). Finally, childhood school performance was entered as an additional covariate separately to the fully

adjusted childhood and adulthood models (to Models 2B and 3B). All statistical analyses were conducted using SAS 9.4. The level of statistical significance was set at  $p < 0.05$ .

### **Transparency and openness**

We report on how we determined our sample size, all data exclusions, and all measures in the study. Requests concerning the data, analysis code, and research materials may be directed to the steering committee of the YFS. The design of this study and its analysis were not pre-registered.

## **RESULTS**

### **Characteristics of the Study Population**

The characteristics of the study population and the numbers of participants in each cognitive test are presented in the Table 1. At the cognitive testing, the mean age of the participants was 41.2 years, 45.2% were men and the mean education was 15.7 years. Of those 2026 participants with cognitive function data, 1191 also had complete data on childhood psychosocial factors at the baseline. To examine the representativeness of the study population, we compared the baseline characteristics of the participants with cognitive data to those without (Supplementary Table 5). In brief, the participants with cognitive function data were somewhat older, more often women and alcohol users, and had a higher BMI as well as better performance at school in childhood. They also were prone to have a better psychosocial environment in childhood compared to the participants who did not participate in cognitive testing.

### **Childhood psychosocial factors score and cognitive function in midlife**

An inverse age, sex and education adjusted association was found for the childhood psychosocial factors score with learning and memory in midlife (PAL-test:  $\beta = -0.030$ ,  $SE = 0.01$ ,

$p=0.013$ ; Table 2, Model 1). This finding suggests that the accumulation of adverse childhood psychosocial factors associated with poorer learning and memory in midlife. The association remained essentially similar after additional adjustments for childhood/adolescence smoking, alcohol use and physical activity (Model 2:  $\beta=-0.030$ ,  $SE=0.01$ ,  $p=0.012$ ) or for corresponding adulthood factors (Model 3:  $\beta=-0.032$ ,  $SE=0.01$ ,  $p=0.009$ ). To illustrate this association, we calculated the mean values of memory and learning within the quartiles of the cumulative psychosocial factors score (Figure 2). A linear trend ( $p$ -value for trend= $0.004$ ) was observed over the quartiles: 1st quartile  $0.295SD$  ( $SE\ 0.06$ ), 2nd quartile  $0.096SD$  ( $SE\ 0.06$ ), 3rd quartile  $-0.012SD$  ( $SE\ 0.06$ ), 4th quartile  $-0.035SD$  ( $SE\ 0.06$ ). Furthermore, to increase the clinical interpretability of our findings, we transformed the associations of psychosocial factors score to correspond with ‘cognitive aging’ by comparing the  $\beta$  estimate of the score with the  $\beta$  estimate of age in the statistical model for learning and memory adjusted according to Model 2 (estimate for age: PAL-test  $\beta=-0.051SD$ ). Concluding, a one-point increase, i.e. one standard deviation increase, in the psychosocial factors score corresponded to the effect of 7 months aging on learning and memory. No associations were observed for other cognitive domains.

Subsequently, we conducted analyses reducing the childhood psychosocial factors cumulative score only to the psychosocial factors related to the child’s environment by excluding the factors related to child’s behavioral regulation (i.e. child’s social adjustment and self-regulation). The results adjusted for the similar covariate patterns as in the main analyses remained virtually unchanged. However, when the associations were further adjusted for the variables indicating child’s behavioral regulation the associations reduced (Supplementary table 6).

### **Childhood psychosocial factors and learning and memory in midlife**

We analyzed separately the associations of the six factors forming the cumulative score with learning and memory in midlife (PAL-test) to study whether there are specific psychosocial factors that contribute to the found association. The analyses adjusted for age, sex and education suggested an association between a poor socioeconomic environment ( $\beta=-0.044$ ,  $SE=0.02$ ,  $p=0.050$ ), the self-regulatory behavior of the child ( $\beta=-0.068$ ,  $SE=0.03$ ,  $p=0.049$ ), and the social adjustment of the child ( $\beta=-0.108$ ,  $SE=0.03$ ,  $p=0.001$ ) with poorer learning ability and memory in midlife, while no associations were found for the other factors (Table 3, Model 1). The observed associations remained similar for the child's self-regulatory behavior ( $\beta=-0.072$ ,  $SE=0.03$ ,  $p=0.037$ ) and social adjustment ( $\beta=-0.107$ ,  $SE=0.03$ ,  $p=0.002$ ) after additional adjustments for childhood/adolescence smoking, physical activity, and alcohol use; however, the association of socioeconomic environment was reduced (Table 3, Model 2). Similarly, the adjustment for corresponding lifestyle factors from adulthood did not alter the association between the child's self-regulatory behavior ( $\beta=-0.074$ ,  $SE=0.03$ ,  $p=0.032$ ) and social adjustment ( $\beta=-0.111$ ,  $SE=0.03$ ,  $p=0.001$ ) (Table 3, Model 3). The analyses of the possible effect modification of sex, age and genetic propensity for intelligence were performed for the psychosocial factors cumulative score and for the separate psychosocial factors. The analyses for the cumulative score revealed a statistically significant interaction term for age ( $p$ -value for interaction term 0.01), while no significant interactions were observed for sex or genetic propensity. Finally, no significant interaction were found when the interaction analyses were conducted separately for the psychosocial factors.

As the interaction analyses suggested that the associations between the psychosocial factors and cognitive function might differ based on the age at which the psychosocial exposures were experienced, we conducted additional analyses where the participants were divided into three separate age groups: 1) baseline age 3-6 years, 2) 9-12 years, and 3) 15-18 years. In the analyses

conducted separately for the three age groups, the analyses adjusted for age, sex, education and childhood lifestyle factors revealed an association between a child's poor social adjustment and learning and memory in the group of 3-6 years old participants ( $\beta=-0.179$ ,  $SE=0.06$ ,  $p=0.003$ ) as well as in those aged 9-12 years at baseline ( $\beta=-0.140$ ,  $SE=0.06$ ,  $p=0.013$ ) (Table 4). Additionally, in the group of 9-12 years-old participants, the socioeconomic environment ( $\beta=-0.081$ ,  $SE=0.04$ ,  $p=0.046$ ) and the child's self-regulation ( $\beta=-0.150$ ,  $SE=0.06$ ,  $p=0.008$ ) were observed to associate with learning and memory. However, no associations were found with psychosocial factors and memory and learning in the group of participants aged 15-18 years.

### **Supplementary analyses**

The association of the child's social adjustment with learning and memory in midlife remained virtually unchanged after additional adjustments for childhood and adulthood cardiovascular risk factors. Furthermore, when childhood school performance was entered separately into the childhood and adulthood models, the associations were reduced but remained statistically significant. Detailed supplementary results are presented in the Supplementary Table 7.

A statistical model where all individual psychosocial factors were simultaneously entered into the same statistical model was also conducted. This analysis indicated that for the child's social adjustment the association remained almost the same while the association with the child's self-regulatory behavior was reduced when the other psychosocial factors were considered (Supplementary Table 8).

Finally, to take the possible inter-correlation of the predictors into account in the multivariable models, we produced variance inflation factors (VIF) for each variable in each statistical model.

In all analyses, the VIF-values remained low (VIF 1.07-1.97) for all variables in the fully adjusted model (adjusted for age, sex, adulthood education, childhood and adulthood lifestyle factors and childhood school performance). In the fully adjusted model, the highest VIFs were observed for age (1.97), childhood alcohol use (1.87), adulthood education (1.44) and childhood school performance (1.43).

## **DISCUSSION**

We demonstrated that unfavorable psychosocial factors in childhood may associate with poorer cognitive function in midlife. Specifically, two specific psychosocial factors such as a child's poor self-regulation and child's low social adjustment were observed to associate with poorer learning ability and memory in midlife even after adjusting for a wide array of covariates including education, lifestyle and cardiovascular risk factors. No associations were observed for other cognitive domains or for factors related to child's psychosocial environment, which suggests that psychosocial factors related to child's behavioral regulation are stronger predictors of adulthood cognitive function than the psychosocial environment.

This study is one of the first longitudinal studies focusing on the associations between multiple childhood psychosocial factors and adulthood cognitive function. The present results confirm our hypothesis that childhood adverse psychosocial factors might have carry over associations into adulthood cognitive function, and are in line with previous short-term and/or retrospective findings suggesting an association between early life adversities and low cognitive function (Aartsen et al., 2019; Anderson et al., 2017a; Evans et al., 2009; Fors et al., 2009a; Kaplan et al., 2001; Lyu & Burr, 2016; Richards & Wadsworth, 2004; Wilson et al., 2005). Additionally, our findings are supported by previous findings suggesting that increasing number of psychosocial risk factors (e.g. single parenthood, low income, maternal depression) may be

associated negatively with a child's cognitive function (Wade et al., 2018). Furthermore, there are two previous studies applying retrospectively collected data from childhood that have reported links between low childhood SES or conflicts in the family and low cognitive function in late adulthood (Aartsen et al., 2019; Fors et al., 2009a). One of these studies used a brief screening test for overall cognitive function (Fors et al., 2009b), while another has measured the specific cognitive domains of delayed recall and verbal fluency (Aartsen et al., 2019). Furthermore, a study conducted with British women participants found an association between the father's low occupation, overprotective or absent parenting, emotional neglect and adoption in childhood and low cognitive function in midlife (Anderson et al., 2017a). Simultaneously, a high childhood SES and early urban residence have been suggested to protect against cognitive impairment in a Chinese cohort with a mean age of 90 years (Zhang et al., 2008). Noticeably, even though being retrospective, these data support our findings which suggest longitudinal associations of childhood psychosocial factors with memory and learning in midlife.

Furthermore, our results extend the previous knowledge on the associations between childhood psychosocial factors and adulthood cognitive function by suggesting that rather than the actual psychosocial environment of the child, the psychosocial factors mostly contributing might be those related to child's behavioral regulation. As far as we know there are only few previous studies elucidating these associations (Brody et al., 1996; Brody & Flor, 1997; Evans et al., 2005; Evans & English, 2002; Evans & Rosenbaum, 2008). Childhood psychosocial factors are a complex and multifaceted set of factors that may, in addition to their associations with cognitive function, also correlate strongly with one another. This means, that for example adverse emotional environment in childhood might contribute to the level and development of the child's self-regulation and social adjustment, which in turn, might contribute to parenting attitudes and emotional environment within the family. We studied the correlations between

the separate psychosocial factors, and indeed learned, that there are modest but still statistically significant correlations between the factors representing child's behavioral regulation (child's social adjustment and self-regulation) and factors representing the environmental aspects (i.e. socioeconomic and emotional environment). Similar links have been observed in previous studies reporting associations between low socioeconomic status and poor self-regulation (Brody et al., 1996; Brody & Flor, 1997; Evans et al., 2005; Evans & English, 2002; Evans & Rosenbaum, 2008). Interestingly, one prior study suggests that economic deprivation might matter more for child's cognitive development while mother's mental health issues could contribute to child's behavioral adjustment. Maternal depression was also associated with harsh parenting and reports of child's behavioral problems (Kiernan & Huerta, 2008). Furthermore, it has been suggested that parenting habits may act as an important mediator for the link between poverty and child's development (McLoyd, 1998), and it has also been observed that unpredictable and less supportive environment may lead to low reflective self-regulation and high behavioral reactivity (Blair, 2010). Concluding, these prior observations suggest that adverse childhood psychosocial environment may provoke poorer behavioral regulation, and simultaneously depict the plausible multifaceted network between the psychosocial factors. Linking to this background, it may be that the shared information on these two psychosocial aspects (i.e. psychosocial environment and child's behavioral regulation) as well as the connections between them may partly contribute to our observations on the associations specifically for child's social adjustment and self-regulation and not for the childhood environmental factors.

The human brain and sensory-system development are partly induced by experiences in childhood (Greenough et al., 1987). Therefore, adverse childhood experiences may affect brain development, and thereby, alter cognitive function. The term "experience-expectant factors"

refers to environmental elements that have remained the same throughout the evolutionary history, such as visual and other cognitive or sensory stimulation, nutrition and access to parents, whereas “experience-dependent factors” are unique to the individual. Children in deprived circumstances, e.g. living in an institution, might grow up without these necessary “expectant” environmental factors, which might be harmful for the immature nervous system (Greenough et al., 1987). For example, The Bucharest Early Intervention Project suggests there is a sensitive period for adverse psychosocial factors, due to their observations that children placed from institutional care into family care before the age 2 years had a higher cognitive function compared to those who remained in the institution (Nelson et al., 2007). Importantly, at the age of 8 years, both groups with an institutional history had poorer memory and executive functions compared to children who grew up with their parents (Bos et al., 2009). Despite the differences in the exposures between this cohort with extreme adversity and our cohort of typically developing Finnish children, this observation supports our results showing links between childhood psychosocial factors and memory.

There are some plausible biological pathways explaining the found associations (Pakulak et al., 2018). Early continuous stress can lead to hypothalamus-pituitary-adrenal (HPA) -axis’ dysregulation, which can manifest as elevated cortisol levels, poor recovery from a stressful event or, in contrast, no glucocorticoid response to stress at all (McEwen & Seeman, 1999; Repetti et al., 2002). During the first years of life, nurturant and supportive parent-child relationships buffer the HPA stress system activity (Gunnar & Quevedo, 2007). Another plausible pathway may be the ‘allostatic load’, which refers to wear and tear of stress reactions, when physiological regulatory systems need to adapt constantly to environmental demands. Simultaneously, frequent stress responses and high levels of circulating glucocorticoids may have a pronounced effect on those specific neural structures that are developing at the time of

stressful events (McEwen & Seeman, 1999). In our study, the psychosocial factors were determined in early childhood and adolescence – i.e. during the age when the hippocampus and prefrontal cortex are developing, and therefore, may be specifically vulnerable (Lupien et al., 2009; McEwen, 2006). In line with this, we specifically observed associations between childhood psychosocial factors and learning and memory, i.e. brain functions that localize mainly in the medial temporal lobes, the hippocampus and the parahippocampal gyrus, and also involve the neural networks with the prefrontal cortex. Furthermore, neurotoxicity hypothesis suggests that long lasting stress, activity of the HPA-axis and exposure to glucocorticoids may cause the neurons ability to resist damage to deteriorate, cause hippocampal atrophy (Lupien et al., 2009) and lead to poorer memory function (Fillit et al., 2002; Lupien et al., 1998). As a biological link for our finding that specifically factors related to the child's behavioral regulation might contribute to adulthood cognitive function, prior animal studies have mainly suggested the effect of stress hormones on brain areas that are important for self-regulation and behavior such as e.g. amygdala, prefrontal cortex and hippocampus (Braun et al., 1999; Kinnunen et al., 2003; Lemaire et al., 2000; Liu et al., 2000; Naninck et al., 2015) - i.e. brain areas that are involved in emotions, executive function as well as learning and memory. It is plausible, that these links exists similarly also in humans, which further support our findings on the associations between factors related to child's behavioral regulation and learning and memory.

In addition to the hippocampus, prior evidence suggests that children exposed to early maltreatment have reduced cortical thickness in the anterior cingulate, superior frontal gyrus and orbitofrontal cortex, and may also have a reduced surface area and atypical local gyrification compared to a control group (Kelly et al., 2013). Furthermore, one study on brain structures of maltreated children found smaller right orbitofrontal cortex volume compared to

a control group (de Brito et al., 2013), while another study reported differences in the right temporal, right frontal and both parietal lobes (Hanson et al., 2010). In a recent meta-analysis, the frontal cortex was suggested as a shared neuronal substrate for self-regulation, cognitive emotion and action regulation that are all related e.g. to executive function (Langner et al., 2018). Additionally, children who have experienced early neglect have been observed to have reduced total white matter volumes compared to the control group (Hanson et al., 2013). Specifically, the organization of the white matter (i.e. fractional anisotropy) has been found to be poor in the prefrontal cortex and in the tracts connecting prefrontal cortex and temporal lobe. Importantly, the decreased fractional anisotropy was linked to a lower score in the CANTAB PAL-test reflecting the results from our present study (Hanson et al., 2013).

Some limitations need to be acknowledged. First, the psychosocial factors were subjectively measured, which means that no specific measurement was available e.g. to exactly quantify the amount of stress. Furthermore, in cases where parents provided the data on their child, the parents' attitudes may affect their responses. Second, the questionnaire used is not a standardized instrument, which limits the generalizability of our findings. However, the construct validity and factor structure of the questionnaire have been previously shown to be good (Elovainio et al., 2018; Pulkki-Råback et al., 2015). Third, it should be noted that the health behaviors were requested from both parents, while the items included in the other factors were requested only from the primary caregiver, which usually was the mother. This might have affected our results due to e.g. that the parents may differ in the way they engage with the child. Fourth, the age range of the children was rather wide at the time of the psychosocial factor assessment, with the children's age varying from 3 to 18 years. We were not able to assess exact timing for the childhood psychosocial experiences (i.e. the child's exact age when the psychosocial factors were present), which limits our findings. There may be specific

sensitive periods in childhood for brain development and future studies will need to address this topic. Fifth, we took childhood school performance into account in the analyses as a proxy for childhood cognitive performance. Unfortunately, as we only had data on that specific covariate from a single time point for each participant and as the age at which the school performance was reported varied between 9 and 18 years we did not have the possibility to take it into account more centrally in building the analytical models. Sixth, as with all observational studies, also our study suffered from a loss-to-follow-up. Even though the differences between the participants who remained within the study until the cognitive testing and those who did not were relatively small, we cannot exclude the possibility of selection bias; due to the fact that it is usually participants with more risk factors, poor health and low SES who are often the ones who do not remain in such studies. In our study, the participants without cognitive data had poorer school performance in childhood compared to participants with cognitive data. For our results, the plausible selection bias may thus cause underestimation rather than overestimation of the true associations between the childhood psychosocial factors and cognitive function. Seventh, the generalization of our results is compromised e.g. due to the homogenous SES within the YFS cohort. Our cohort does not include families with an extremely low income level because the income is secured through the social support system in Finland. Additionally, the well-baby clinics and school health care provided for all children give psychosocial support to families. Eighth, cognitive function was assessed once in midlife, and we have no data on baseline cognitive performance. To overcome this, we have used the participants' school performance and data on genetic propensity for poor cognitive function as proxies for childhood cognitive function. Finally, as all observational studies, we cannot make assumptions on causal relationships. The obvious strengths of our study are the longitudinal study design from childhood to midlife with prospectively collected data on childhood psychosocial factors and the large random sampled cohort including both males and females.

In conclusion, our findings indicate that unfavorable psychosocial factors in childhood may be linked to poorer learning ability and memory in midlife. These results can be leveraged to develop targeted interventions directed towards those families with adverse psychosocial factors. This is especially important as accumulation of psychosocial adversity in childhood has been associated with poor parenting habits in later decades (Schwabe et al., 2012). This means that interventions towards promoting a better psychosocial environment in childhood might have carry over associations on cognitive function and thus be reflected in future generations. A reasonable approach to tackle this issue would be to promote parental mental health, general life satisfaction and children's social adjustment. If the associations found were causal, interventions targeted at ameliorating children's psychosocial environment could have wide beneficial ramifications on cognitive and public health.

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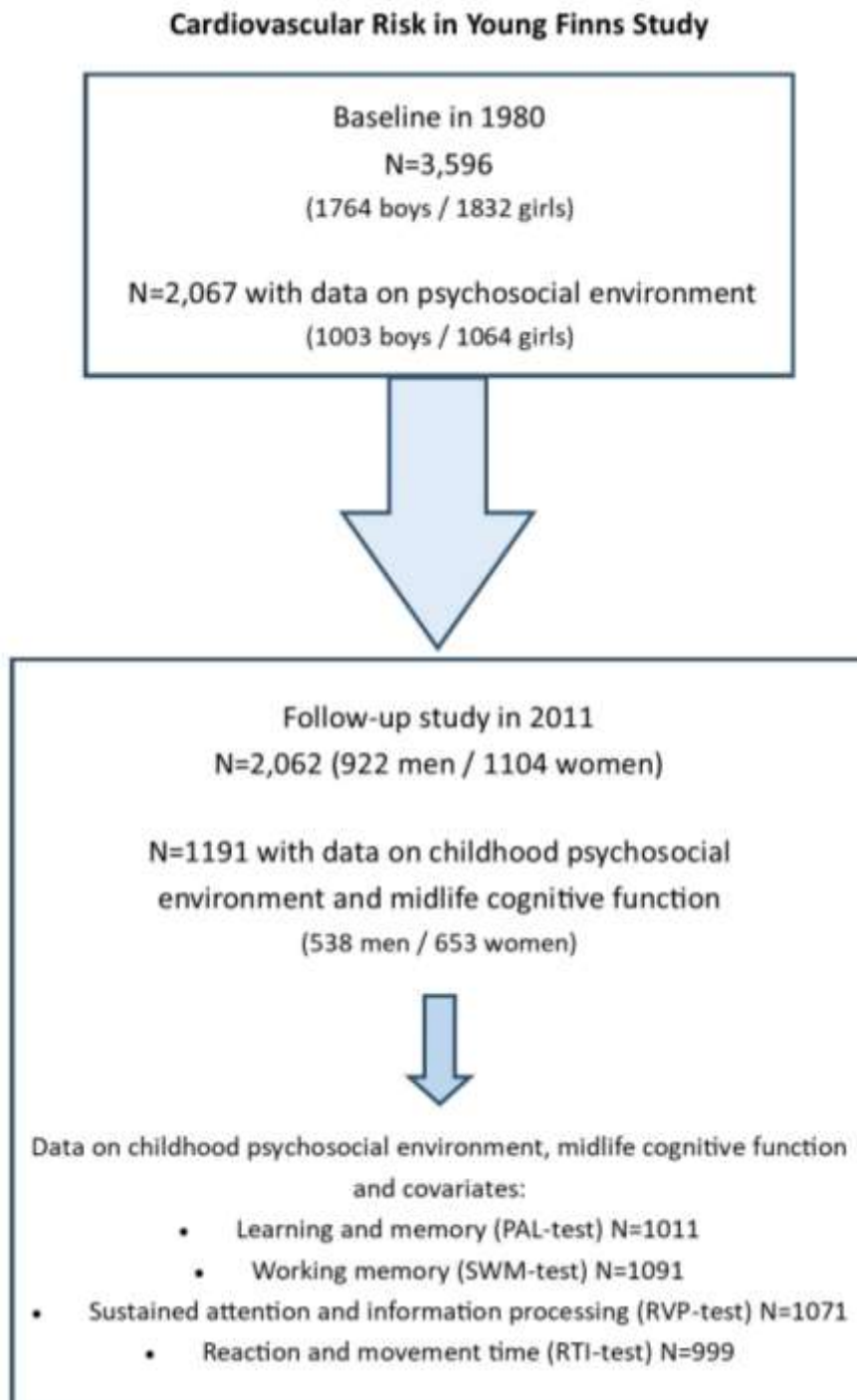
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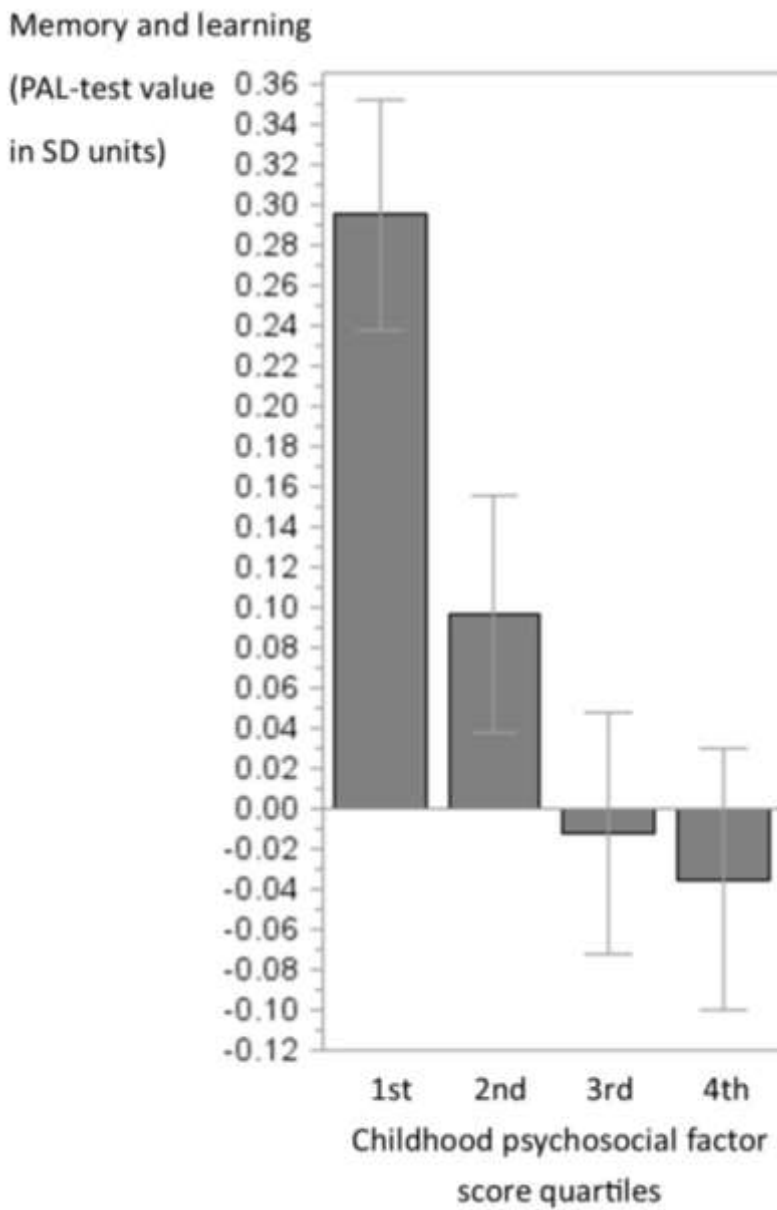
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Zhang, Z., Gu, D., & Hayward, M. D. (2008). Early Life Influences on Cognitive Impairment Among Oldest Old Chinese. *The Journals of Gerontology: Series B*, 63(1), S25–S33.

**Figure 1. Flow-chart of the study population.**



**Figure 2.** Memory and learning in childhood psychosocial environment cumulative score quartiles. The mean PAL-test values for the quartiles: 1st quartile: 0.295SD (SE 0.06), 2nd quartile: 0.096SD (SE 0.06), 3rd quartile: -0.012SD (SE 0.06), 4th quartile: -0.035SD (SE 0.06). Mean values are presented in a standard deviation scale and error bars represent standard deviation. Higher value on the psychosocial environment cumulative scale indicates worse childhood psychosocial environment. Age, sex and education adjusted p-value for trend=0.004.



**Table 1. Characteristics of the study population**

<b>Age, years</b>	<b>N</b>	
<b>At baseline</b>	1191	10.2 (4.9)
<b>At cognitive testing</b>	1191	41.2 (4.9)
<b>Sex, (males)</b>	1191	45.2 %
<b>Education at cognitive testing, years</b>	1122	15.7 (3.6)
<b>Daily smoking</b>		
<b>At baseline</b>	1178	24.2 %
<b>At cognitive testing</b>	1130	12.4 %
<b>Body mass index, kg/m<sup>2</sup></b>		
<b>At baseline</b>	1185	17.7 (3.0)
<b>At cognitive testing</b>	1186	26.4 (5.0)
<b>Physical activity</b>		
<b>At baseline</b>	755	9.2 (1.8)
<b>At cognitive testing</b>	1090	9.1 (1.9)
<b>Alcohol use</b>		
<b>At baseline</b>	1191	24.3 %
<b>At cognitive testing (2011)</b>	1117	0.79 (1.1)
<b>Cognitive function</b>		
<b>Memory and learning (PAL-test)</b>	1094	<i>Cognitive function variables were standardized; mean=0, SD=1</i>
<b>Spatial working memory (SWM-test)</b>	1182	
<b>Visual information processing (RVP-test)</b>	1161	
<b>Reaction time (RTI-test)</b>	1081	

Values are means, standard deviations (SD) for continuous variables and percentages for categorical variables. The study population is restricted to participants with no missing information on cognitive

function and childhood psychosocial environment. Physical activity was defined using physical activity index created from the data collected on frequency, duration, intensity and participation in organized physical activity (range 5-15 points). For baseline alcohol use the participants were divided into non-drinkers and drinkers according to any reported use of beer, wine and/or spirit. All participants aged  $\leq 12$  years were non-drinkers. Adulthood alcohol use was defined as drinks per day. PAL-test=Paired Associates Learning test, SWM-test=Spatial Working Memory test, RVP-test=Rapid Visual Information Processing test, RTI-test=Reaction Time test. Principal component analyses was used to calculate components indicating episodic memory and associative learning (PAL-test), short term working memory (SWM-test), visual processing, recognition and sustained attention (RVP-test), and reaction and movement speed and attention (RTI-test) based on CANTAB<sup>®</sup> (Cambridge Cognition, Cambridge, UK) cognitive test battery. The principal components were standardized into a standard deviation scale (mean=0, SD=1.00 for all cognitive function components).

**Table 2. The association between childhood psychosocial factors score and cognitive function in midlife**

	Model 1			Model 2			Model 3		
	$\beta$ (SE)	p- value	95 % CI	$\beta$ (SE)	p- value	95 % CI	$\beta$ (SE)	p- value	95 % CI
<b>Episodic memory and associative learning (<i>PAL-test</i>) (n=1011)</b>	<b>-0.030</b> <b>(0.01)</b>	<b>0.013</b>	<b>-0.053,</b> <b>-0.006</b>	<b>-0.030</b> <b>(0.01)</b>	<b>0.012</b>	<b>-0.054,</b> <b>-0.007</b>	<b>-0.032</b> <b>(0.01)</b>	<b>0.009</b>	<b>-0.055,</b> <b>-0.008</b>
<b>Spatial working memory (<i>SWM-test</i>) (n=1091)</b>	0.017 (0.01)	0.126	-0.005, 0.040	0.017 (0.01)	0.149	-0.006, 0.039	0.017 (0.01)	0.128	-0.005, 0.040
<b>Visual information processing (<i>RVP-test</i>) (n=1071)</b>	-0.002 (0.01)	0.843	-0.025, 0.020	-0.002 (0.01)	0.845	-0.025, 0.020	-0.002 (0.01)	0.852	-0.025, 0.020
<b>Reaction and movement time (<i>RTI-test</i>) (n=999)</b>	0.006 (0.01)	0.632	-0.018, 0.030	0.009 (0.01)	0.490	-0.016, 0.032	0.010 (0.01)	0.438	-0.015, 0.034

Values are  $\beta$  estimates (standard errors), p-values and 95% confidence intervals from linear models for continuous psychosocial factors score. A higher value in the score indicates poorer environment. Analyses were adjusted for age, sex and adulthood education (Model 1) and additionally for childhood/adolescence smoking, physical activity and alcohol use (Model 2) or adulthood smoking, physical activity and alcohol use (Model 3). Cognitive function was measured using four tests from the CANTAB cognitive test battery; PAL-test=Paired Associates Learning test, SWM-test=Spatial Working Memory test, RVP-test=Rapid Visual Information Processing test, RTI-test=Reaction Time test. Principal component analyses was conducted to form components representing the performance in each test. The cognitive function components were standardized (mean=0, SD=1) for the analyses for childhood psychosocial factors. The childhood psychosocial factors score is in a standard deviation scale. Statistically significant results are indicated with bold font.

**Table 3. Association of childhood psychosocial factors with learning and memory in midlife**

	Model 1			Model 2			β
	β (SE)	P-value	95 % CI	β (SE)	P-value	95 % CI	
<b>Socioeconomic environment (n=1432)</b>	<b>-0.044</b> (0.02)	<b>0.050</b>	<b>-0.089, -</b> <b>0.000</b>	-0.044 (0.02)	0.052	-0.089, 0.000	-
<b>Emotional environment (n=1272)</b>	-0.041 (0.03)	0.149	-0.097, 0.015	-0.044 (0.03)	0.130	-0.100, 0.013	-
<b>Health behaviors of parents (n=1354)</b>	-0.025 (0.02)	0.264	-0.069, 0.019	-0.023 (0.02)	0.300	-0.068, 0.021	-
<b>Stressful events (n=1613)</b>	-0.012 (0.04)	0.740	-0.083, 0.059	-0.011 (0.04)	0.771	-0.082, 0.061	-
<b>Self-regulatory behavior of the child (n=1451)</b>	<b>-0.068</b> (0.03)	<b>0.049</b>	<b>-0.135, -</b> <b>0.000</b>	<b>-0.072</b> (0.03)	<b>0.037</b>	<b>-0.140, -</b> <b>0.004</b>	-
<b>Social adjustment of the child (n=1603)</b>	<b>-0.108</b> (0.03)	<b>0.001</b>	<b>-0.174, -</b> <b>0.042</b>	<b>-0.107</b> (0.03)	<b>0.002</b>	<b>-0.173, -</b> <b>0.041</b>	-

Values are β estimates (standard errors) and p-values from linear models for continuous psychosocial factors, in which a higher value indicates poorer psychosocial factors. Analyses were adjusted for age, sex and education (Model 1) and additionally for childhood/adolescence smoking, physical activity and alcohol use (Model 2) or adulthood smoking physical activity and alcohol use (Model 3). Memory and learning is assessed using Paired Associates Learning (PAL) test from the CANTAB cognitive test battery. Principal component analyses was conducted to form a component representing the performance in the PAL-test. The cognitive function component was standardized (mean=0, SD=1) for the analyses for childhood psychosocial factors. Statistically significant results are indicated with bold font.

**Table 4. Association of childhood psychosocial factors with learning and memory in midlife in three age groups**

	3-6 years				9-12 years			
	N	$\beta$ (SE)	p-value	95 % CI	N	$\beta$ (SE)	p-value	95 % CI
<b>Socioeconomic environment</b>	472	0.020 (0.04)	0.609	-0.057, 0.096	508	<b>-0.081 (0.04)</b>	<b>0.046</b>	<b>-0.160, -0.001</b>
<b>Emotional environment</b>	432	-0.045 (0.05)	0.381	-0.146, 0.056	455	-0.055 (0.05)	0.262	-0.152, 0.041
<b>Health behaviors of parents</b>	449	-0.018 (0.04)	0.645	-0.095, 0.059	471	-0.025 (0.04)	0.540	-0.105, 0.055
<b>Stressful events</b>	509	0.071 (0.11)	0.535	-0.154, 0.297	557	-0.042 (0.06)	0.503	-0.165, 0.081
<b>Self-regulatory behavior of the child</b>	478	-0.036 (0.06)	0.528	-0.149, 0.076	518	<b>-0.150 (0.06)</b>	<b>0.008</b>	<b>-0.261, -0.039</b>
<b>Social adjustment of the child</b>	503	<b>-0.179 (0.06)</b>	<b>0.003</b>	<b>-0.295, 0.062</b>	555	<b>-0.140 (0.06)</b>	<b>0.013</b>	<b>-0.250, -0.030</b>

Values are beta estimates (standard errors), p-values and 95% confidence intervals from linear models for continuous psychosocial factors, in which a higher value indicates poorer environment. The analyses were adjusted for age, sex, education, childhood/adolescence smoking, physical activity, alcohol use. Memory and learning is assessed using Paired Associates Learning (PAL) test from the CANTAB cognitive test battery. Principal component analyses was conducted to form a component representing the performance in the PAL-test. The cognitive function component was standardized (mean=0, SD=1) for the analyses for childhood psychosocial factors. Statistically significant results are indicated with bold font.

## **Supplementary Material**

### **The associations of childhood psychosocial factors with cognitive function in midlife – The Young Finns Study**

by Nurmi A et al, 2022

#### **SUPPLEMENTARY METHODS**

##### **Cognitive function measurement**

During the latest follow-up examination in 2011, the Cambridge Neuropsychological Test Automated Battery (CANTAB) was used to assess cognitive function among the participants. The CANTAB is a computerized, predominantly nonlinguistic, and culturally neutral test focusing on a wide range of cognitive domains. The test is performed using a validated touchscreen computer system. The full test battery includes 24 individual tests from which a suitable test battery for each particular study may be selected. In the YFS, the test battery was selected so that it could be accomplished in 20–30 min and included tests that are sensitive to aging (De Luca et al., 2003; Robbins et al., 1994). The tests measured several cognitive domains: (a) short-term memory, (b) spatial working memory, (c) problem solving, (d) reaction time, (e) attention, (f) rapid visual processing, (g) visual memory, (h) episodic memory, and (i) visuospatial learning.

Cognitive testing was performed during clinical examination. Due to the blood sampling included in the study protocol, the subjects came to the examinations after fasting at least 12 hr. They were instructed to avoid smoking and heavy physical activity as well as to avoid drinking alcohol and coffee during the previous evening and the morning before the examinations. Before the cognitive

testing, the subjects were provided with a light snack, including a whole grain oat-based snack biscuit, a small portion of fruit or berry oatmeal, and weak fruit or berry juice.

During cognitive testing, the participants first conducted a motor screening test (MOT) measuring psychomotor speed and accuracy. In this study, the MOT was considered a training procedure where the participants were introduced to the equipment used in the testing and a screening tool to point out any difficulties in vision, movement, comprehension, or ability to follow simple instructions. During the MOT, a series of red crosses were shown in different locations on the screen, and the participants were advised to touch, as quickly as possible, the center of the cross every time it appeared. The PAL test was used to assess visual and episodic memory as well as visuospatial associative learning, containing aspects of both a delayed-response procedure and conditional learning. During the PAL test, one, two, three, six, or eight patterns were displayed sequentially in boxes placed on the screen. After that, the patterns were presented in the center of the screen, and the participants were supposed to point to the box in which the particular pattern was previously seen. The test moves on to the next stage if all the patterns are placed to the right boxes. In the case of an incorrect response, all the patterns are redisplayed in their original locations and another recall phase is followed. The test terminated if the patterns were still incorrectly placed after 10 presentation and recall phases. The SWM test was used to measure ability to retain spatial information and to manipulate items stored in the working memory, problem solving, and the ability to conduct a self-organized search strategy. During this test, the participants were presented with randomly distributed colored boxes ranging in number from four to eight. After that, the participants were supposed to search for tokens hidden in the boxes. When a token was found, it was supposed to be moved to fill an empty panel on the right-hand side of the screen. Once the token had been moved from the box, the participant had to recall that the computer would never hide a new token in a box that previously contained one; therefore, the participants were not supposed to revisit the same boxes again. The reaction time (RTI) test assessed speed of response and movement on tasks where the stimulus was either predictable (simple location

task) or unpredictable (five-choice location task). In the first part of this test, a large circle was presented in the center of the screen. The participant was supposed to press a button on a press pad until a small yellow spot appeared in the large circle. When the yellow spot appeared, the participant was supposed to touch the spot as soon as possible with the same hand that was pressing the button on the press pad. In the second part of the test, the same task was performed, except that in this part, five large circles were presented on the screen, and the small yellow spot could appear in any of the five circles. Again, the participant was supposed to touch, as soon as possible, the yellow spot with the hand pressing the button on the press pad. The rapid visual information (RVP) test was used to assess visual processing, recognition, and sustained attention. In this test, the participant was presented with a number sequence (e.g., 3, 5, 7) next to a large box where numbers appeared in a random order. Whenever the particular sequence was presented, the participant was supposed to press a button on a press pad. At the beginning, the participant was given visual cues (i.e., colored or underlined numbers) to help the participant recognize the particular sequence. When the test proceeded, the cues were removed.

### **Principal component–based classification of cognition**

Each of the CANTAB tests produced several variables. Principal component analysis was conducted to reduce the number of variables and to identify components accounting for the majority of the variation within the cognition data set. Principal component analysis was selected since it allows the identification of the main sources of variation in multidimensional data without losing important information and without introducing inherent bias due to subjectivity. First, principal component analyses were performed separately for all individual subtests of the CANTAB test battery. The first components resulting from these analyses were considered to represent cognitive performance related to the particular subtest/domain. After creating the testwise principal components, their distributions were analyzed. The component for the motor screening test was excluded from further analyses

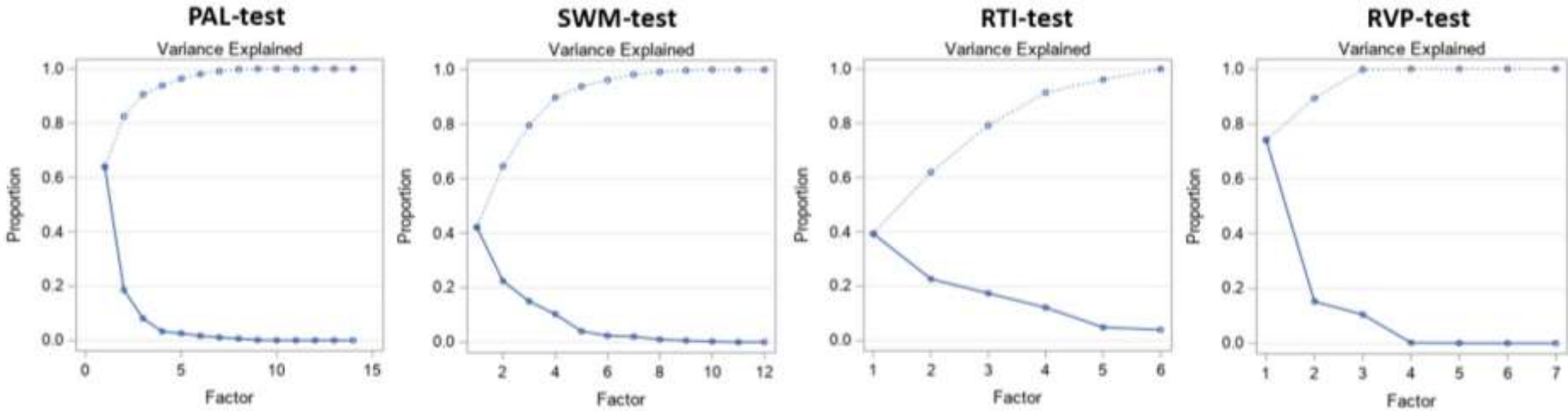
because it did not discriminate the subjects, indicating a ceiling effect. All other components were normalized based on the rank order normalization procedure, resulting in five separate variables, each with a mean value of 0 and a standard deviation of 1.

**Supplementary Table 1. The loadings of the variables on the test specific first principal components**

Paired associates learning test		Spatial working memory test		Rapid visual information processing test		Reaction time test	
Total trials adjusted for the stages completed	0.11576	Total errors	0.59128	A'	0.19115	Mean movement time / Five-choice stage	0.33031
Total errors adjusted for the stages completed	0.11459	Total errors at 4 boxes stage	0.31835	Total correct rejections	0.18888	Mean movement time / Simple choice stage	0.32413
Total errors at 8 pattern stage adjusted for the stages not completed	0.10804	Between errors	-0.24728	Probability of hit	0.18884	Mean reaction time / Five-choice stage	0.31913
Mean trials to succeed	0.10778	Double errors	0.20845	Total hits	0.18884	Mean reaction time / Simple choice stage	0.31537
Mean errors to succeed	0.10348	Double errors at 4 boxes stage	0.16792	Total misses	-0.18883	Accuracy score / Five-choice stage	0.07552
Total errors	0.09745	Mean time to last response	0.13033	Mean latency	-0.10048	Accuracy score / Simple choice stage	0.05693
Number of patterns succeeded on	-0.09431	Strategy	0.11025	Probability of false alarm	-0.05958		
Stages completed	-0.09417	Mean token-search preparation time	0.08324				
Total errors at 6 pattern stage adjusted for the stages not completed	0.09272	Mean time to first response	0.06275				
First trial memory score	-0.08934	Between errors at 4 boxes stage	0.03452				
Total trials	0.08903						
Stages completed on first trial	-0.06605						
Number of patterns reached	-0.06006						

The values are loadings of the variables on the test specific first components from unrotated principal component analyses. Only variables with loading differing from 0 are presented.

**Supplementary Figure 1.** The proportions of variance explained by the cognitive domain specific principal components. The components are calculated using SAS 9.4 version and applying 'Proc Factor' –procedure without rotation. Thus, the resulting components are orthogonal and uncorrelated with each other.



## **Psychosocial factors in childhood**

Information on socioeconomical and psychosocial factors were queried from the participants' parents in 1980 when the participants were 3, 6, 9, 12, 15 and 18 years old. Questions included information about income level of the family, parental mental health, parental evaluation of the child's temperament and behavior, and parenting styles.

We assessed 6 psychosocial factors that have been proposed as central components of childhood psychosocial environment in previous literature (Adler & Stewart, 2010; Repetti et al., 2002; Slopen et al., 2013; Taylor et al., 2001). The psychosocial factors were socioeconomic environment, emotional environment, parental health behaviors, stressful events, self-regulation of the child, and social adjustment of the child. These factors were assessed by parents who filled in hand-written questionnaires at the baseline examination in 1980.

Cumulative scores have recently become common in research on childhood psychosocial factors (Evans et al., 2013). Typically, such models define binary risk factors (risk versus no risk), which are then summed together to form a cumulative score. Such an approach has the advantage of being parsimonious, making no assumptions about the relative strengths of multiple risk factors or their collinearity, and enabling testing of additive effects over a range of exposures (Evans et al., 2013). We built the 6 psychosocial factors from binary variables in which 1 stands for favorable and 0 for less-than-favorable level. The cutoff points were based on previous evidence and theoretical knowledge, as described in the following:

1. Socioeconomic factors score consisted of 4 components: upper white-collar occupation (1 point), academic/college degree (1 point), family income in highest 25% (1 point), and occupational stability as indicated by the absence of unemployment spells/retirement/long-term sick leave (1 point). Thus, the score ranged from 0 points (less than favorable level in all components) to 4 points (favorable level in all components).

2. Emotional family environment score consisted of 4 components. The first was absence of previously diagnosed parental mental disorder (1 point), measured by asking both parents whether they had ever been diagnosed as having mental disorder. The second was high parental care-giving nurturance, measured with a 7-item scale ( $\alpha=0.70$ ) previously used in this data set. A reply of “very often” to all items (shown in Table II) gave 1 point. The third component was high parental life satisfaction, measured with a 3-item scale (Table II;  $\alpha=0.70$ ). A positive reply to all 3 items gave 1 point. Fourth, reasonable alcohol use was included because of evidence indicating that unhealthy parental drinking is harmful to offspring emotional development (Johnson & Leff, 1999). Parents reporting intoxication “never or at maximum 3 times per year” were classified as reasonable users (1 point). Altogether, the scale range was 0 to 4.

3. Health behaviors of the parents were asked separately from both parents. Because we had no data on parental diet, we used body mass index  $<30.0$  kg/m<sup>2</sup> as a proxy of excess energy intake (0=overweight, 1=not overweight). Other health behaviors were nonsmoking (1 point) and participating in regular physical activity (1 point for exercise at least once a week). Summing together maternal and paternal health behaviors resulted in a scale with a range of 0 to 6.

4. Stressful events included events that may threaten the child’s sense of stability and continuity (J., 1974; Rutter, 2002). Stressful events were moving residence, change of school, parental divorce or separation, death of a family member, and serious disease in the family. The absence of each event gave 1 point; thus, the scale range was 0 to 5.

5. Self-regulatory behavior of the participant consisted of 2 scales measuring high self-control and high aggression control. The predictive validity of both scales has been established previously (Keltikangas-Järvinen et al., 2006; Pulkki-Råback et al., 2005). The self-control scale consisted of 1 question in which children described as being very controlled “always or most of the time” received 1 point. Aggression control ( $\alpha=0.60$ ) was measured with 6 items, each giving 1 point. The total score was formed by combining scores from self-control and aggression control (range, 0–7).

6. Social adjustment consisted of a question about parental worry about the child’s adjustment (1 point) and parental evaluation of the child’s general level of adjustment (1 point). Our previous work has shown that these questions predict outcomes that are theoretically related to social adjustment (Katainen et al., 1997; Pulkki-Råback et al., 2015).

**Supplementary Table 2. Correlations between the individual psychosocial factors**

	<b>Socioeconomic environment</b>	<b>Emotional environment</b>	<b>Health behaviors of parents</b>	<b>Stressful events</b>	<b>Self-regulatory behavior of the child</b>	<b>Social adjustment of the child</b>
<b>Socioeconomic environment</b>						
<b>Emotional environment</b>	-0.012 0.558 N=2552					
<b>Health behaviors of parents</b>	<b>0.198</b> <b>&lt;0.0001</b> N=2721	<b>0.169</b> <b>&lt;0.0001</b> N=2453				
<b>Stressful events</b>	<b>-0.042</b> <b>0.025</b> N=2908	0.024 0.218 N=2594	0.0001 0.996 N=2762			
<b>Self-regulatory behavior of the child</b>	<b>0.073</b> <b>&lt;0.001</b> N=2608	<b>0.158</b> <b>&lt;0.0001</b> N=2385	<b>0.111</b> <b>&lt;0.0001</b> N=2477	0.001 0.959 N=2975		
<b>Social adjustment of the child</b>	<b>0.080</b> <b>&lt;0.0001</b> N=2872	<b>0.144</b> <b>&lt;0.0001</b> N=2576	0.034 0.075 N=2713	0.033 0.060 N=3286	<b>0.337</b> <b>&lt;0.0001</b> N=2995	

Values are correlation coefficients and p-values from Pearson’s correlation analyses.

*Psychosocial Factors Score (Cumulative Score)*

The 6 psychosocial factors were summed together to form a psychosocial factors score (cumulative score) following a procedure recommended previously (Evans et al., 2013). However, summing together psychosocial factors with different variances would lead to a score that gives greater weight to factors with greater variance. We had no hypothesis to weigh any factor more than the other; thus, each psychosocial factor score was converted into a standard score before summation. (Because some of the variables were skewed, the standardization was rerun with quantile-quantile normalization to a standard normal distribution, but that had no effect on the score; therefore, the same form of standardization was used for every psychosocial factor.) Such a procedure would treat each psychosocial factor as an equal contributor to the cumulative score. The formula for the score was as follows: socioeconomic environment (z score) + emotional environment (z score) + parental health behaviors (z score) + stressful events (z score) + self-regulation (z score) + social adjustment (z score) = favorable psychosocial factors score. Distribution was slightly skewed to the left (mean=0.00; SD=2.84; range, -11.58 to 6.09).

**Supplementary Table 3. Formation of the childhood psychosocial environment cumulative score.**

<b>Item</b>	<b>Scoring</b>	<b>Range</b>
<b>Variables of socioeconomic environment</b>		
Occupational status	1=manual, 2=lower manual, 3=higher nonmanual	1-3
Maternal education	Total number of years of education	3-22
Paternal education	Total number of years of education	2-28

Family income	Total annual income (Finnish marks), 7-point scale	0-7
Maternal employment	0=unemployed, retired or sick leave, 1=employed	0-1
Paternal employment	0=unemployed, retired or sick leave, 1=employed	0-1
<b>Variables of the emotional environment</b>		
Maternal mental health	0=diagnosis of mental disorder, 1=free of diagnosis	0-1
Paternal mental health	0=diagnosis of mental disorder, 1=free of diagnosis	0-1
Parental caregiving nurturance	7-item scale ( $\alpha=0.70$ ): “I lose nerve with my child. (reversed)” “My child is burdensome in difficult situations. (reversed)” “My child takes too much of my time. (reversed)” “My child is important to me.” “I am important to my child.” “I enjoy spending time with my child.” “I am able to self-actualize myself when being with my child.”	1-5* 1-5* 1-5* 1-5* 1-5* 1-5* 1-5*
Parental life satisfaction	3-item scale ( $\alpha=0.71$ ): “I am satisfied with myself as a mother/father.” “I am satisfied with myself as a spouse/life companion.” “I am satisfied with myself as an employee.”	1-5 1-5 1-5
Maternal alcohol use	Frequency of intoxication, 8-point scale	1-8
Paternal alcohol use	Frequency of intoxication, 8-point scale	1-8
<b>Variables indicating parental health behaviors</b>		

Maternal body-mass index	kg/m <sup>2</sup>	
Paternal body-mass index	kg/m <sup>2</sup>	
Maternal smoking	0=smoker, 1=non-smoker	0-1
Paternal smoking	0=smoker, 1=non-smoker	0-1
Maternal physical activity	1=no exercise, 2=some (irregular) exercise , 3=regular weekly	1-3
Paternal physical activity	1=no exercise , 2=some (irregular) exercise , 3=regular weekly	1-3
<b>Variables indicating stressful events</b>		
Change of residence	0=yes, 1=no	0-1
Change of school	0=yes, 1=no	0-1
Parental divorce/separation	0=yes, 1=no	0-1
Death of family member	0=yes, 1=no	0-1
Long-term hospitalization	0=yes, 1=no	0-1
<b>Variables indicating self-regulatory behavior of the child</b>		
Self-control scale	Please, choose the option that most accurately describes your child:  1=My child is always on the move, restless, and unable to control him(her)self  2=My child is more restless and less controlled than children of same age  3=My child is restless/poorly controlled only when tired or bored, but mostly within normal limits.	1-4
Aggression control scale		

	<p>4=My child is very controlled and stays calm even in situations where most children would become restless and out of control.</p> <p>6-item scale (<math>\alpha=0.60</math>):</p> <p>"Other children say that my child gets easily into fights."</p> <p>"My child hits/pushes other children "by accident."</p> <p>"My child needs a lot of discipline to control aggression."</p> <p>"My child uses swear words very often."</p> <p>"Other children complain often about my child's behavior."</p> <p>"Other parents have complained about my child's behavior."</p>	<p>1-2**</p> <p>1-2**</p> <p>1-2**</p> <p>1-2**</p> <p>1-2**</p> <p>1-2**</p>
<b>Variables indicating social adjustment of the child</b>		
<p>'I am not worried about the child'</p> <p>'My child is well adjusted'</p>	<p>Please, choose the option that most accurately describes your child:</p> <p>0=Not true</p> <p>1=True</p> <p>Please, choose the option that most accurately describes your child:</p> <p>0=Not true</p> <p>1=True</p>	<p>0-1</p> <p>0-1</p>

\* 1=extremely seldom, 2=seldom, 3=in between, 4=often, 5=very often

\*\* 1=true, 2=not true

**Supplementary Table 4. Correlations between the cognitive outcomes, exposure variables and covariates**

	<b>Memory and learning (PAL test)</b>	<b>Working memory (SWM test)</b>	<b>Information processing (RVP test)</b>	<b>Reaction and movement time (RTI test)</b>
<i>Exposure variables</i>				
<b>Socioeconomic environment</b>	<b>-0.11</b> <b>&lt;0.0001</b> N=1571	<b>-0.05</b> <b>0.036</b> N=1712	<b>-0.19</b> <b>&lt;0.0001</b> N=1681	<b>-0.07</b> <b>0.004</b> N=1548
<b>Emotional environment</b>	-0.02 0.403 N=1387	<b>0.06</b> <b>0.027</b> N=1499	<b>0.06</b> <b>0.028</b> N=1470	0.02 0.547 N=1365
<b>Health behaviors of parents</b>	<b>-0.06</b> <b>0.021</b> N=1481	<b>-0.06</b> <b>0.023</b> N=1605	<b>-0.09</b> <b>&lt;0.001</b> N=1574	-0.01 0.580 N=1458
<b>Stressful events</b>	<b>-0.07</b> <b>0.002</b> N=1771	-0.02 0.495 N=1930	0.01 0.602 N=1899	<b>-0.06</b> <b>0.019</b> N=1747
<b>Self-regulatory behavior of the child</b>	<b>-0.06</b> <b>0.010</b> N=1589	0.02 0.356 N=1725	<b>-0.07</b> <b>0.003</b> N=1693	0.02 0.439 N=1569
<b>Social adjustment of the child</b>	<b>-0.09</b> <b>&lt;0.0001</b> N=1755	-0.01 0.744 N=1910	-0.03 0.240 N=1879	0.02 0.488 N=1734
<i>Covariates</i>				
<b>Age</b>	<b>-0.26</b> <b>&lt;0.0001</b> N=1848	<b>-0.23</b> <b>&lt;0.0001</b> N=2011	<b>-0.12</b> <b>&lt;0.0001</b> N=1975	<b>-0.08</b> <b>&lt;0.001</b> N=1822
<b>Sex</b>	<b>-0.05</b> <b>0.022</b> N=1848	<b>0.18</b> <b>&lt;0.0001</b> N=2011	<b>0.07</b> <b>0.003</b> N=1975	<b>0.20</b> <b>&lt;0.0001</b> N=1822
<b>Education at cognitive testing</b>	<b>0.20</b> <b>&lt;0.0001</b> N=1756	<b>0.10</b> <b>&lt;0.0001</b> N=1914	<b>0.28</b> <b>&lt;0.0001</b> N=1879	<b>0.08</b> <b>&lt;0.001</b> N=1731
<b>Childhood school performance</b>	<b>0.22</b> <b>&lt;0.0001</b> N=1624	<b>0.09</b> <b>&lt;0.0001</b> N=1764	<b>0.27</b> <b>&lt;0.0001</b> N=1730	<b>0.06</b> <b>0.027</b> N=1601
<b>Daily smoking</b>				
<b>At baseline</b>	<b>-0.08</b> <b>&lt;0.001</b> N=1822	0.00 0.989 N=1981	<b>-0.06</b> <b>0.011</b> N=1945	-0.01 0.696 N=1796
<b>At cognitive testing</b>	0.00 0.932 N=1751	-0.03 0.180 N=1909	<b>-0.09</b> <b>&lt;0.001</b> N=1874	<b>-0.05</b> <b>0.024</b> N=1726

<b>Physical activity</b>				
<b>At baseline</b>	-0.02 0.383 N=1799	0.03 0.212 N=1960	-0.02 0.486 N=1925	<b>0.13</b> <b>&lt;0.0001</b> N=1774
<b>At cognitive testing</b>	<b>0.06</b> <b>0.022</b> N=1673	0.00 0.959 N=1826	<b>0.07</b> <b>0.005</b> N=1791	<b>0.12</b> <b>&lt;0.0001</b>
<b>Alcohol use</b>				
<b>At baseline</b>	<b>-0.17</b> <b>&lt;0.0001</b> N=1848	<b>-0.13</b> <b>&lt;0.0001</b> N=2011	-0.03 0.164 N=1975	<b>-0.08</b> <b>0.001</b> N=1822
<b>At cognitive testing</b>	-0.02 0.398 N=1724	<b>0.05</b> <b>0.018</b> N=1882	<b>05</b> <b>0.031</b> N=1849	0.04 0.148 N=1701

The values are correlation coefficients, p-values and numbers of participants from Pearson's correlation analyses.

**Supplementary Table 5. Comparison of the participants with and without cognitive function data**

	Cognitive function data		No cognitive function data		p-value
	N		N		
<b>Age at baseline, mean</b>	2026	10.8	1570	9.9	<b>&lt;0.001</b>
<b>Sex, male</b>	2026	45.5 %	1570	53.6 %	<b>&lt;0.001</b>
<b>Daily smoking at baseline</b>	2026	27.3 %	1570	27.1 %	0.900
<b>BMI at baseline, mean (SD)</b>	2011	18.0 (3.1)	1556	17.7 (3.1)	<b>0.010</b>
<b>Physical activity at baseline, mean (SD)</b>	1974	1.62 (1.1)	1531	1.62 (1.1)	0.952
<b>Alcohol use at baseline</b>	2026	28.2 %	1570	22.3 %	<b>&lt;0.001</b>
<b>Childhood school performance, mean (SD)</b>	1777	7.8 (0.02)	1293	7.6 (0.02)	<b>&lt;0.001</b>
<b>Psychosocial factors score</b>	1191	53.2 %	876	57.8 %	<b>0.041</b>
<b>Socioeconomic environment</b>	1727	63.3 %	1274	67.7 %	<b>0.013</b>
<b>Emotional environment</b>	1512	49.9 %	1142	53.4 %	0.076
<b>Health behaviors of parents</b>	1619	32.2 %	1220	35.8 %	<b>0.042</b>
<b>Stressful events</b>	1944	26.4 %	1497	28.5 %	0.177
<b>Self-regulatory behavior of the child</b>	1736	23.0 %	1329	30.2 %	<b>&lt;0.001</b>
<b>Social adjustment of the child</b>	1923	41.4 %	1485	44.8 %	<b>0.048</b>

Values are means (standard deviations) and p-values from Student's T-test for the continuous variables, and percentages and p-values from  $\chi^2$ -test for the categorical variables. Adulthood education years queried in the follow-up study prior to cognitive function testing (in 2007 follow-up study). For the childhood psychosocial factor variables, the percentages are for the participants with unfavorable childhood psychosocial factors. For attrition analysis psychosocial cumulative score was divided into two groups: 1) to participants whose score was less than 1 (unfavorable psychosocial environment group) and 2) those whose score was 1 or more (favorable psychosocial environment group). Socioeconomic environment factor was dichotomized using 2 points as a cutoff (0-1 points for unfavorable; 2-4 points for favorable). Emotional environment factor was dichotomized using 3 points as a cutoff for dichotomization (0-2 points for unfavorable; 3-4 points for favorable). In

parental health behavior factor 5 points was used as a cutoff for dichotomization (0-4 points for unfavorable; 5-6 points for favorable). Stressful events factor was dichotomized using 1 event as a cutoff (1-5 events for unfavorable; 0 events for favorable). Self-regulatory behavior factor was dichotomized using 7 points as a cutoff (0-6 points for unfavorable; 7 points for favorable). Social adjustment factor was dichotomized using 2 points as a cutoff (0-1 points for unfavorable; 2 points for favorable).

**Supplementary table 6. The association between reduced childhood psychosocial factors score and cognitive function in midlife**

		Model 1			Model 2			Model 3		
		$\beta$ (SE)	p-value	95 % CI	$\beta$ (SE)	p-value	95 % CI	$\beta$ (SE)	p-value	95 % CI
<b>Panel A</b>	<b>Episodic memory and associative learning (<i>PAL-test</i>) (n=1118)</b>	<b>-0.030 (0.01)</b>	<b>0.037</b>	<b>-0.058, -0.002</b>	<b>-0.030 (0.01)</b>	<b>0.039</b>	<b>-0.059, -0.002</b>	<b>-0.032 (0.01)</b>	<b>0.028</b>	<b>-0.061, -0.004</b>
	<b>Spatial working memory (<i>SWM-test</i>) (n=1210)</b>	0.023 (0.01)	0.096	-0.004, 0.051	0.023 (0.01)	0.098	-0.004, 0.051	0.023 (0.01)	0.104	-0.005, 0.051
	<b>Visual information processing (<i>RVP-test</i>) (n=1186)</b>	-0.008 (0.01)	0.580	-0.035, 0.020	-0.007 (0.01)	0.601	-0.035, 0.020	-0.007 (0.01)	0.594	-0.035, 0.020
	<b>Reaction and movement time (<i>RTI-test</i>) (n=1102)</b>	0.001 (0.01)	0.965	-0.029, 0.030	0.003 (0.01)	0.827	-0.026, 0.033	0.006 (0.01)	0.709	-0.024, 0.035
<b>Panel B</b>	<b>Episodic memory and associative learning (<i>PAL-test</i>) (n=1011)</b>	-0.021 (0.02)	0.171	-0.051, 0.009	-0.021 (0.02)	0.171	-0.052, 0.009	-0.022 (0.02)	0.148	-0.053, 0.008
	<b>Spatial working memory (<i>SWM-test</i>) (n=1091)</b>	0.024 (0.01)	0.103	-0.005, 0.053	0.024 (0.01)	0.102	-0.005, 0.054	0.024 (0.01)	0.107	-0.005, 0.053
	<b>Visual information processing (<i>RVP-test</i>) (n=1071)</b>	0.000 (0.01)	0.983	-0.029, 0.029	0.001 (0.01)	0.955	-0.028, 0.030	-0.000 (0.01)	1.000	-0.029, 0.029
	<b>Reaction and movement time (<i>RTI-test</i>) (n=999)</b>	-0.000 (0.02)	0.998	-0.031, 0.031	0.004 (0.02)	0.823	-0.027, 0.035	0.003 (0.02)	0.832	-0.028, 0.034

Values are  $\beta$  estimates (standard errors), p-values and 95% confidence intervals from linear models for continuous psychosocial factors score. A higher value in the score indicates poorer environment. In the Panel A the score is calculated including socioeconomic environment, emotional environment, parents' health habits, stressful events as well as child's social adjustment and self-regulation, while in the Panel B child's social adjustment and self-regulation were not included in the score. Analyses were adjusted for age, sex and adulthood education (Model 1) and additionally for childhood/adolescence smoking, physical activity and alcohol use (Model 2) or adulthood smoking, physical activity and alcohol use (Model 3). Cognitive function was measured using four tests from the CANTAB cognitive test battery; PAL-test=Paired Associates Learning test, SWM-test=Spatial Working Memory test, RVP-test=Rapid Visual Information Processing test, RTI-test=Reaction Time test. Principal component analyses was conducted to form components representing the performance in each test. The cognitive function components were standardized (mean=0, SD=1) for the analyses for childhood psychosocial factors. The childhood psychosocial factors score is in a standard deviation scale. Statistically significant results are indicated with bold font.

**Supplementary Table 7 Association of self-regulatory behavior and social adjustment of the child with learning and memory in midlife**

	Model 2B			Model 3B		
	$\beta$ (SE)	p-value	95 % CI	$\beta$ (SE)	p-value	95 % CI
<b>Self-regulatory behavior of the child (N=1372)</b>	<b>-0.080 (0.04)</b>	<b>0.027</b>	<b>-0.150, -0.009</b>	<b>-0.081 (0.04)</b>	<b>0.024</b>	<b>-0.151, -0.010</b>
<b>Social adjustment of the child (N=1510)</b>	<b>-0.109 (0.03)</b>	<b>0.002</b>	<b>-0.178, -0.040</b>	<b>-0.112 (0.03)</b>	<b>0.001</b>	<b>-0.181, -0.044</b>
<i>Models including childhood school performance as additional covariate</i>						
<b>Self-regulatory behavior of the child (N=1238)</b>	-0.068 (0.04)	0.075	-0.144, 0.007	-0.071 (0.04)	0.064	-0.147, 0.004
<b>Social adjustment of the child (N=1354)</b>	<b>-0.087 (0.04)</b>	<b>0.017</b>	<b>-0.161, -0.016</b>	<b>-0.094 (0.04)</b>	<b>0.012</b>	<b>-0.166, -0.022</b>

Values are  $\beta$  estimates (standard errors) and p-values from linear models. Model 2B was adjusted for age, sex, education, childhood/adolescence smoking, physical activity, alcohol use, systolic blood pressure, LDL-cholesterol and BMI. Model 3B was adjusted for age, sex, education, adulthood smoking physical activity, alcohol use, systolic blood pressure, LDL-cholesterol and BMI. The childhood psychosocial environment domains were treated as continuous variables. Memory and learning was assessed using Paired Associates Learning (PAL) test from the CANTAB cognitive test battery. Principal component analyses was conducted to form a component representing the performance in the PAL-test. The cognitive function component was standardized (mean=0, SD=1) for the analyses for childhood psychosocial environment domains.

**Supplementary Table 8. Association of childhood psychosocial factors with learning and memory in midlife**

N=1011	Model 1		Model 2		Model 3	
	$\beta$ (SE)	p-value	$\beta$ (SE)	p-value	$\beta$ (SE)	p-value
<b>Socioeconomic environment</b>	-0.046 (0.03)	0.084	-0.045 (0.03)	0.092	-0.046 (0.03)	0.089
<b>Emotional environment</b>	-0.008 (0.03)	0.801	-0.010 (0.03)	0.756	-0.007 (0.03)	0.822
<b>Health behaviors of parents</b>	-0.013 (0.03)	0.623	-0.012 (0.03)	0.652	-0.017 (0.03)	0.530
<b>Stressful events</b>	0.025 (0.07)	0.718	0.024 (0.07)	0.731	0.022 (0.07)	0.746
<b>Self-regulatory behavior of the child</b>	-0.027 (0.05)	0.556	-0.032 (0.05)	0.480	-0.032 (0.05)	0.485
<b>Social adjustment of the child</b>	<b>-0.093 (0.05)</b>	<b>0.043</b>	-0.090 (0.05)	0.051	<b>-0.094 (0.05)</b>	<b>0.040</b>

Values are  $\beta$  estimates (standard errors) and p-values from linear models where all psychosocial factors were entered simultaneously. Model 1 was adjusted for age, sex and education. Model 2 was additionally adjusted for childhood/adolescence smoking, physical activity and alcohol use, whereas Model 3 was adjusted for corresponding lifestyle factors in adulthood. The childhood psychosocial environment domains were treated as continuous variables. Memory and learning was assessed using Paired Associates Learning (PAL) test from the CANTAB cognitive test battery. Principal component analyses was conducted to form a component representing the performance in the PAL-test. The cognitive function component was standardized (mean=0, SD=1) for the analyses for childhood psychosocial environment domains.

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