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Socioeconomic and cognitive roots of trait anxiety in young adults

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Abstract

In 54 participants (41% women) from the Czech arm of the European Longitudinal Study of Pregnancy and Childhood, a national birth cohort with prospectively collected data from their birth until young adulthood, we aimed to study the association between early-life socioeconomic deprivation (ELSD), cognitive ability in adolescence, trait anxiety and resting state functional connectivity of the lateral prefrontal cortex (LPFC) in young adulthood. We found that ELSD was associated with lower cognitive ability in adolescence (at age 13) as well as higher trait anxiety in young adulthood (at age 23/24). Higher cognitive ability in adolescence predicted lower trait anxiety in young adulthood. Resting state functional connectivity between the right LPFC and a cluster of voxels including left precentral gyrus, left postcentral gyrus and superior frontal gyrus mediated the relationship between lower cognitive ability in adolescence and higher trait anxiety in young adulthood. These findings indicate that lower cognitive ability and higher trait anxiety may be both consequences of socioeconomic deprivation in early life. The recruitment of the right LPFC may be the underlying mechanism, through which higher cognitive ability may ameliorate trait anxiety.

Key words: trait anxiety; cognition; epidemiology; birth cohort

Introduction

Trait anxiety predisposes people to the development of anxiety and affective disorders (Chambers *et al.*, 2004; Sandi and Richter-Levin, 2009), the most common mental disorders in the population.

It is a personality feature characterized by a tendency to respond with troubles, concerns and worries to various situations (Spielberger and Gorsuch, 1983). Trait anxiety is associated with a range of changes in cognitive functioning; studies show that individuals high in trait anxiety have deficient cognitive control (Bishop, 2009) and apply cognitive biases in the processing of threat-related stimuli (Eysenck, 2000). There is also evidence that higher trait anxiety impairs efficient functioning of the attentional system (Eysenck *et al.*, 2007) and is linked to lower academic achievements (Alfonso and Lonigan, 2021) and lower general cognitive ability (Moutafi *et al.*, 2006; Bartels *et al.*, 2012). Even though the association to cognitive ability may be explained by trait anxiety leading to nervousness, which affects performance in cognitive tests (Humphreys and Revelle, 1984), it is also plausible that high cognitive ability may help ameliorate anxiety by enabling reasoning over causes of distress, coping with concerns and promoting the ability to adjust in pursuing emotional needs.

Previously, we have demonstrated that young adults who grew up in poorer households had a higher trait anxiety (Čermaková *et al.*, 2020). A particularly strong risk factor is growing up in a household that cannot secure the family with basic things, such as food, clothes, heating, rent and necessities for the child (Čermaková *et al.*, 2020). As such early-life socioeconomic deprivation (ELSD) of a household is tied with lower cognitive ability of the children, in particular in combination with lower education of parents (Tong *et al.*, 2007), the association of ELSD with trait anxiety may be due to the fact that low socioeconomic resources do not allow children to cognitively develop towards their full potential, which deprives them from efficiently pursuing their mental health.

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There is a large body of literature on neural correlates of human cognitive ability (Rypma *et al.*, 2006), with a growing number of studies concerning disruptions of functional connectivity. It has been proposed that cognitive ability is the result of large-scale brain networks in frontal, parietal, temporal and cingulate cortices (Jung and Haier, 2007; Bressler and Menon, 2010; Brancucci, 2012). In particular, the lateral prefrontal cortex (LPFC) has been found to be a key brain region involved in cognitive ability (Gray and Thompson, 2004; Song *et al.*, 2008). Neuroimaging studies revealed a co-occurrence of cognitive distortions, ineffective emotion regulation and alterations in the function of LPFC related to anxiety (Goldin *et al.*, 2009), possibly reflecting functional impairment of the central executive network in the cognitive control of anxiety (Qiu *et al.*, 2011).

By using event-related functional magnetic resonance imaging (fMRI) and a behavioural measure of attention to angry faces, Monk *et al.* demonstrated that patients with generalized anxiety disorder manifested greater activation of the right ventral LPFC to trials containing angry faces (Monk *et al.*, 2006). Moreover, several previous studies, using both event-related fMRI (Monk *et al.*, 2006; Telzer *et al.*, 2008) and near-infrared spectroscopy scanning while performing a verbal fluency task (Yokoyama *et al.*, 2015), proposed that LPFC may play a role in the pathogenesis of trait anxiety (Telzer *et al.*, 2008), generalized anxiety disorder (Monk *et al.*, 2006) and social anxiety disorder (Yokoyama *et al.*, 2015).

There is also literature on alterations in the function of LPFC related to anxiety using resting-state fMRI techniques. Qiu *et al.* showed that individuals with social anxiety disorders have decreased coherence in spontaneous neural fluctuations in the blood oxygen level dependent (BOLD) signals of the right dorsal LPFC and inferior parietal gyrus, possibly reflecting the deficit of cognitive control of anxiety (Qiu *et al.*, 2011). Moreover, increased perfusion at rest was found in the ventral LPFC, right anterior frontal and right lateral frontal cortex and right cerebellum in individuals with social anxiety disorder (Warwick *et al.*, 2008). Liao *et al.* found that higher score on the Liebowitz Social Anxiety Scale was associated with greater functional connectivity of ventral LPFC with the rest of the dorsal attention network, possibly contributing to the higher state of vigilance and worse emotional regulation, which are characteristic for patients with social anxiety disorder (Liao *et al.*, 2010). Given that LPFC may play a role in cognitive control of emotional regulation of anxiety, this raises a question whether the functional connectivity between the LPFC and other regions of the brain underlie the association of cognitive ability with trait anxiety.

The aim of this study was to investigate cognitive mechanisms and biomarkers related to functional connectivity underlying the association of ELSD with trait anxiety in young adulthood. We tested the following hypotheses: (1) Worse ELSD is associated with lower cognitive ability in adolescence, but higher education of parents may reduce the negative impact of ELSD on cognitive ability of their children. (2) Higher cognitive ability in adolescence is associated with lower trait anxiety in young adulthood and this association depends on the level of ELSD. (3) The functional connectivity between LPFC and other regions of the brain underlies the association of cognitive ability with trait anxiety.

Methods

Participants

We studied participants of the Czech arm of the European Longitudinal Study of Pregnancy and Childhood (ELSPAC-CZ) (Piler *et al.*, 2017). ELSPAC-CZ is a prenatal cohort ($n = 5151$) whose members were born in 1991/1992. Their mothers were enrolled into the study between the ultrasound examination at 20th week of pregnancy and the birth of the child. They filled in several sets of questionnaires concerning their socioeconomic circumstances, such as experience of ELSD, their education and other markers of socioeconomic position (SEP). Sub-samples of the ELSPAC-CZ cohort were examined within different sub-studies.

At the age of 13, 617 individuals participated in a psychological sub-study, during which their cognitive ability was assessed. Details about the psychological sub-study are provided elsewhere (Ježek *et al.*, 2008). At the age of 23/24 years, 131 members of the ELSPAC-CZ took part in a neuroimaging sub-study 'Biomarkers and Underlying Mechanisms of Vulnerability to Depression' (VULDE) (Mareckova *et al.*, 2018, 2019a,b, 2020b), during which fMRI and assessment of trait anxiety were conducted. All participants provided written informed consent and ethical approval was obtained from ELSPAC Ethics Committee. All methods were performed in accordance with Declaration of Helsinki. Data from this study are available to researchers upon request, after approval from the scientific committee. Code can be shared to researchers by the corresponding author of this study upon request.

Measures

ELSD

The main exposure was ELSD, which is a subjective assessment of one's SEP and has been shown to best predict trait anxiety in young adulthood out of a number of early-life SEP including indicators of objective SEP (Čermaková *et al.*, 2020). ELSD was assessed by questionnaires administered to mothers at 6 and 18 months of the offspring. They had a four-point Likert scale to answer how difficult it is to secure the family with the following five things: food, clothes, heating, rent/other fees and things necessary for the child. The four possible answers ranged from 'very difficult' (coded as 3) to 'not difficult at all' (coded as 0). Scores on these five items were summed-up, creating an ELSD score reaching from 0 to 15, with higher values indicating more severe deprivation. The score showed a good internal consistency (Cronbach's alpha 0.81 at 6 months and 0.82 at 18 months). To reduce measurement error, the final ELSD score was calculated as the mean of the scores for 6 and 18 months.

Covariates

We used information on mother's and father's education as we hypothesized that education of parents can modify the association of ELSD with cognitive ability in adolescence. Education was coded in the following eight categories: (i) primary, (ii) vocational without high school graduation, (iii) vocational with high school graduation, (iv) specialized high school with graduation, (v) general high school with graduation, (vi) post-high school graduation study, (vii) university education and (viii) postgraduate education. We re-coded both measures so that higher values correspond to lower education.

As ELSD is a subjective assessment of one's SEP, we also controlled for a measure of objective early-life SEP composed of five indicators: father's occupation, household income, number of basic utilities, number of household items and crowding ratio, as previously described in detail (Čermaková *et al.*, 2020). There were no signs of deviation from normal distribution, therefore, we created a composite score on objective early-life SEP, as follows: First, we recoded each of the five indicators of early-life SEP so that higher values indicate a more adverse SEP. Second, we created z-scores from each of the five indicators. Third, we averaged the five z-scores, which results in the composite 'objective early-life SEP', with higher values indicating a worse SEP. As the covariates correlate with ELSD, we tested for collinearity in our models, using variance inflation factor (VIF). The VIF reached below 4 in all analyses.

Cognitive ability in adolescence

Cognitive ability was measured within the psychological sub-study in adolescence at the age of 13 years with the Wiener Matrizen-Test (WMT) (Formann and Piswanger, 1979). The WMT is a timed one-dimension intelligence test measuring the ability to logically reason over abstract symbols, which is regarded as a non-verbal estimate of fluid intelligence. It is derived from the Raven's Progressive Matrices that is designed to measure the eductive component of general intelligence (Raven, 2000). The construct of general intelligence reflects the fact that one's performance on one type of cognitive task tends to be comparable to that person's performance on other cognitive tasks (Spearman, 1961). In WMT, there are 24 multiple choice items, listed in order of difficulty. The total score is the number of correctly answered items, which is a measure used in this study. It will be further referred to as 'cognitive ability in adolescence'.

Trait anxiety in young adulthood

Trait anxiety was assessed as part of VULDE in young adulthood at the age of 23/24 years with the Spielberger State-Trait Anxiety Inventory (STAI-T) (Spielberger and Gorsuch, 1983) by 20 questions rated on a four-point Likert scale, with higher scores indicating greater anxiety.

Functional connectivity of the brain

The participants of VULDE underwent a 7 min closed-eyes resting state fMRI exam, with the following acquisition parameters: voxel size 3 × 3 × 3 mm, repetition time (TR) 2080 ms, echo time (TE) 30 ms, flip angles 90°, 39 slices, matrix 64 × 64, 200 measurements. Functional connectivity analysis was performed using CONN Functional Connectivity Toolbox version 18.b. and its default pre-processing pipeline (Whitfield-Gabrieli and Nieto-Castanon, 2012). First, functional images were realigned, un-warped and slice-timing corrected. Next, the images were co-registered with structural data and spatially normalized to the Montreal Neurological Institute (MNI) space. Acquisitions with framewise displacement above 0.9 mm or global BOLD signal changes above 5 standard deviations (SDs) were flagged as potential outliers. No participant exceeded this threshold. Finally, the images were smoothed using a Gaussian kernel of 8 mm full width at half maximum and de-noised. Confounding effects of subjects' movement were addressed using CompCor method, which is implemented within CONN (Behzadi et al., 2007). White matter, cerebral spinal fluid and realignment parameters were entered as confounds in the first-level analysis (Behzadi et al., 2007), and the data were band-pass filtered to 0.008–0.09 Hz. Details about how head motion was addressed and quality assurance steps are described in detail in the Supplement.

Statistical analysis

Derivation of the analytical sample is shown in Figure 1. From 131 participants in the VULDE study, 2 did not undergo resting state fMRI assessment and 7 had missing data on ELSD. From the remaining 122 individuals, 54 had available data on cognitive ability in adolescence, which is the analytical sample used in this study (41% women). When compared to the original ELSPAC-CZ cohort, the analytical sample had a greater proportion of individuals with university educated mothers and a smaller proportion of those whose mothers were younger than 20 at birth. The analytical sample had lower trait anxiety relative to the whole VULDE cohort (Supplementary Table S1).

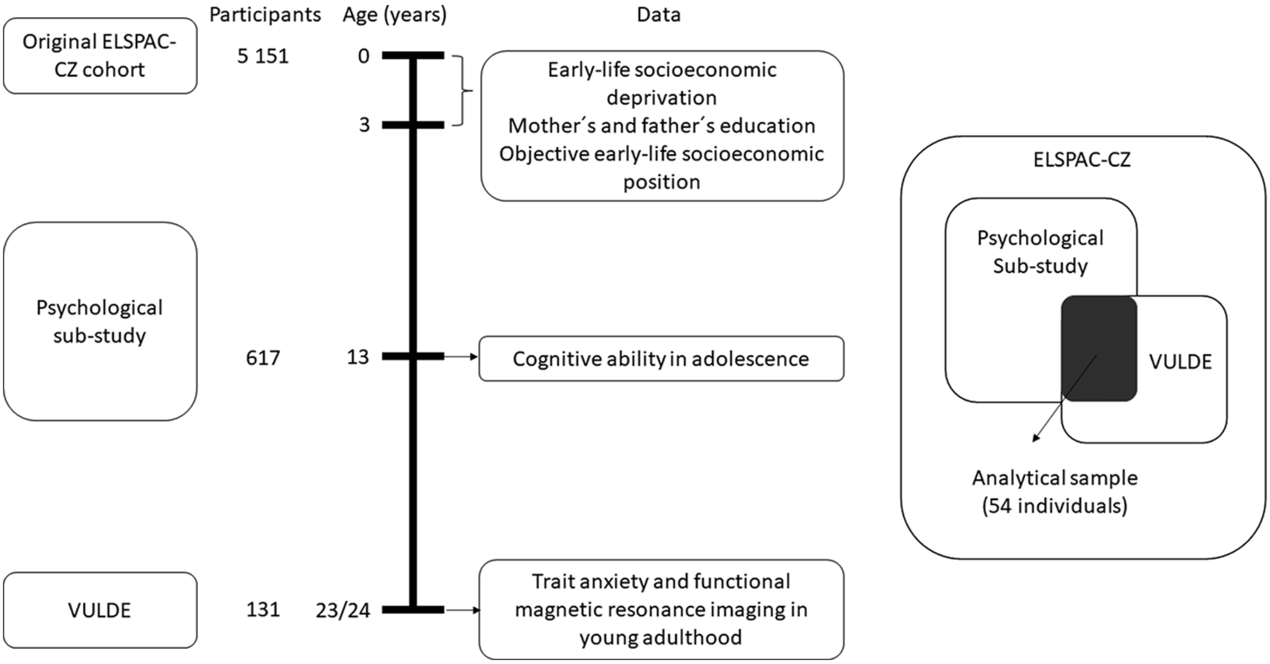

Fig. 1. Derivation of the study sample.

We conducted the analysis in three steps: (i) association of ELSD with cognitive ability in adolescence; (ii) association of cognitive ability in adolescence with trait anxiety in young adulthood and (iii) biomarkers related to functional connectivity underlying the association of cognitive ability in adolescence with trait anxiety in young adulthood. Descriptive data are presented as means ± SD, median and interquartile range (IQR) or frequency (*n*, %), where appropriate. We first assessed the relationships between the main measures with correlations and significant associations were further studied with linear regression. Next, we tested for effect modification of the associations. Effect modification describes the situation where the magnitude of the effect of an exposure variable on an outcome differs depending on the level of a third variable. To assess effect modification, we tested statistical interaction by including a two-way interaction term between the tested exposure and the potential effect modifier.

In all analyses, we tested for sex as a potential effect modifier. Next, we tested whether mother's education and father's education are effect modifiers in the association of ELSD with cognitive ability in adolescence. Finally, we tested whether ELSD is an effect modifier in the association of cognitive ability in adolescence with trait anxiety in young adulthood. For the ease of interpretability, if the interaction was significant, we re-coded the continuous measures into binary variables corresponding to high *vs* low level and conducted stratified analyses, adjusting for sex and the remaining covariates. In case of mother's and father's education, the binary variable was university and higher education *vs* no university education; in case of ELSD, the binary variable was higher than median *vs* lower than median ELSD. Data on cognitive ability in adolescence was normally distributed and was used in the analyses in its original form. Data on trait anxiety was skewed and was therefore log-transformed.

To study the underlying biomarkers related to functional connectivity, we conducted a seed-to-voxel analysis to evaluate correlations between the two seeds of our a priori interest (left LPFC and right LPFC) and all other voxels in the brain. These seeds were defined as 10 mm spheres centered at coordinates (MNI): left LPFC −43, 33, 28; and right LPFC: 41, 38, 30. They were defined from Fox *et al.* (2005). Functional connectivity maps were produced by averaging the BOLD time series in the seed and then computing the Pearson's correlation coefficient between the seed average time series and those from each voxel in the brain. The resulting correlations were transformed to normal distribution using Fisher's z transformation. This yielded a map representing the strength of the functional connectivity to the seed region in terms of the z values for each subject. Next, correlations between cognitive ability in adolescence and the strength of the functional connectivity between the left/right LPFC and other voxels were calculated. Seed-to-voxel results are reported when significant at a voxel-wise threshold of level of $P < 0.05$ uncorrected and a cluster-level threshold of $P < 0.05$ corrected for false discovery rate (FDR).

We then extracted the correlation coefficients for clusters of voxels showing a significant association with cognitive ability in adolescence for each subject from CONN into STATA. Next, we evaluated whether they are associated with trait anxiety, correcting for FDR using Benjamini Hochberg method. In the end, we performed a mediation analysis. We hypothesized that connectivity between the right/left LPFC and the identified cluster of voxels mediates the association of cognitive ability in adolescence with trait anxiety in young adulthood. This mediation hypothesis was tested with a bootstrap procedure to determine the significance of the indirect effect (Preacher and Hayes, 2004). A total of 5000 bootstrap resamples were used to provide stable estimates of the direct, indirect, and total effects. We determined 95% confidence intervals (CIs) from the bootstrap resamples and any interval that did not include 0 was considered to be significantly different from 0. The correlation and regression analyses were performed using STATA version 15, mediation analyses were performed using SPSS version 27. $P < 0.05$ was considered as a threshold for statistical significance.

Table 1. Characteristics of participants

Characteristic	Value	*n*
Early-life socioeconomic deprivation	Mean 3.0 ± SD 2.2 Median 2.5 (IQR 3.5) Range 0–9.5	54
Cognitive ability in adolescence	Mean 13.6 ± SD 3.8 Median 13 (IQR 5) Range 3–22	54
Trait anxiety	Mean 26.4 ± SD 8.5 Median 24.5 (IQR 11) Range 14–51	54
Mother's education: university and higher, *n* (%)	20 (37)	43
Father's education: university and higher, *n* (%)	18 (33)	44
Objective early-life socioeconomic position		
Father's occupation: white-collar worker[a]	32 (59)	53
Household income in CZK, mean ± SD	8 090 ± 3 496	54
Number of basic utilities, mean ± SD	6.5 ± 1.4	54
Number of household items, mean ± SD	5.6 ± 1.5	42
Crowding ratio, mean ± SD	1.7 ± 0.7	54
Composite score, mean ± SD	0.02 ± 0.66	54

[a]White-collar worker defined as classes I, II and III according to Erikson, Goldthorpe and Portocareros (EGP) scheme (Erikson *et al.*, 1979).
SD, standard deviation; IQR, interquartile range.

Results

Characteristics of participants

We studied 54 individuals (41% women, Table 1), whose ELSD score was distributed around the mean of 3 (SD = 2). Cognitive ability in adolescence, as measured by the number of correctly answered items from WMT, reached the average of 14 (SD 4). Trait anxiety in young adulthood, as measured by STAI-T, reached the median of 25 (IQR 11). As in our previous study (Čermaková *et al.*, 2020), worse ELSD correlated with greater trait anxiety (Spearman's rho 0.275; $P = 0.044$).

Association of ELSD with cognitive ability in adolescence

Worse ELSD correlated with lower cognitive ability in adolescence (Spearman's rho −0.362, $P = 0.007$). There was no effect modification by sex (P for interaction = 0.232) or father's education (P for interaction = 0.842), but there was a borderline statistically significant interaction with mother's education (P for interaction = 0.058; see also Supplementary Figure S1). When stratified, worse ELSD was associated with lower cognitive ability in adolescence only in individuals, whose mothers had university or higher education ($B = -1.104$; 95% CI −1.675 to −0.533; $P = 0.001$; Table 2

Table 2. Relationships between the main variables, stratified by effect modifiers

	B (95% CI)	
	Mother's education	
Association of ELSD with cognitive ability in adolescence	**University or higher**	**No university education**
Unadjusted	−1.104 (−1.675; −0.533)**	0.164 (−0.530; 0.858)
Adjusted for sex	−1.169 (−1.742; −0.595)***	0.165 (−0.544; 0.875)
Adjusted for sex, father's education and objective socioeconomic position	−1.178 (−1.806; −0.549)**	−0.102 (−0.911; 0.707)
	ELSD	
Association of cognitive ability in adolescence with trait anxiety in young adulthood	**High**	**Low**
Unadjusted	−0.049 (−0.078; −0.020)**	0.002 (−0.028; 0.031)
Adjusted for sex	−0.044 (−0.072; −0.016)**	0.000 (−0.028; 0.028)
Adjusted for sex, father's education, mother's education and objective socioeconomic position	−0.063 (−0.105; −0.021)**	0.017 (−0.031; 0.065)

**$P<0.01$; ***$P<0.001$.
ELSD, early-life socioeconomic deprivation; CI, confidence interval.

and Supplementary Figure S2). This association persisted when adjusted for sex, father's education and objective early-life SEP ($B=-1.178$; 95% CI −1.806 to −0.549; $P=0.001$).

Association of cognitive ability in adolescence with trait anxiety in young adulthood

Higher cognitive ability in adolescence correlated with lower trait anxiety (Spearman's rho −0.293; $P=0.031$). There was no effect modification by sex (P for interaction = 0.925), but there was a significant interaction with ELSD (P for interaction = 0.033; see also Supplementary Figure S3). When stratified, the association of higher cognitive ability in adolescence with lower trait anxiety was present only in individuals with high ELSD ($B=-0.049$; 95% CI −0.078 to −0.020; $P=0.002$; Supplementary Figure S4). This association persisted when adjusted for sex, mother's education, father's education and objective early-life SEP (B −0.063; 95% CI −0.105 to −0.021; $P=0.005$).

Biomarkers related to functional connectivity

We present results with the voxelwise threshold of $P<0.05$ corrected for multiple comparisons as we did not observe significant results at the level of <0.001, which is not consistent with the current standard of thresholding. Cognitive ability in adolescence was associated with functional connectivity between the seeds of interest and six clusters of voxels (Table 3). Specifically, it showed a negative relationship between the left LPFC and three clusters: First, a cluster including, among other regions, precuneus, cingulate gyrus and supramarginal gyrus (MNI coordinates +10, −26, +38; 4945 voxels, p-FDR < 0.001); second, a cluster including, among other regions, right frontal pole, cingulate gyrus and right paracingulate gyrus (MNI coordinates +28, +40, +18; 4699 voxels, p-FDR < 0.001); and third, a cluster including, among other regions, lateral occipital cortex, supramarginal gyrus and parietal operculum cortex (MNI coordinates −52, −28, +26; 2116 voxels, p-FDR = 0.04).

Furthermore, cognitive ability in adolescence showed a negative relationship between the right LPFC and one cluster of voxels including, among other regions, precuneus, cingulate gyrus and left middle frontal gyrus (MNI coordinates +18, −32, +26, 4772 voxels, p-FDR < 0.001). Finally, cognitive ability in adolescence showed a positive relationship between the right LPFC and two clusters: First, a cluster including several parts of cerebellum (MNI coordinates +18, −58, −24; 3148 voxels, p-FDR = 0.01; and second, a cluster including left precentral and postcentral gyrus and left superior frontal gyrus (MNI coordinates −62, −08, +18; 2360 voxels, p-FDR = 0.03).

Greater positive functional connectivity between the right LPFC and a cluster that included left precentral gyrus, left postcentral gyrus and superior frontal gyrus correlated with lower trait anxiety (Spearman's rho −0.407; $P=0.001$/p-FDR = 0.012). There was no interaction with sex (P for interaction = 0.670) and the association persisted when adjusted for sex ($B=-0.819$; 95% CI −1.501 to −0.137; $P=0.019$; Figure 2). While the total effect of cognitive ability in adolescence on trait anxiety in young adulthood reached borderline statistical significance ($R^2=0.07$, $B=-0.02$, $P=0.053$), a mediation analysis revealed that functional connectivity between the right LPFC and this cluster mediated the relationship between lower cognitive ability in adolescence and higher trait anxiety in young adulthood (ab = −0.012, SE= 0.005, 95% CI [−0.022; −0.002]; Figure 3). Functional connectivity between LPFC and any of the five remaining clusters did not correlate with trait anxiety (p-FDR > 0.05), therefore no further mediation analysis was performed.

Discussion

We aimed to study cognitive and neural mechanisms underlying the association of ELSD with trait anxiety in a cohort of young adults from the Czech Republic, who have been followed since their prenatal period. We found that worse ELSD was associated with lower cognitive ability in adolescence and that this association was strongest in individuals whose mothers reached university education. Further, higher cognitive ability in adolescence predicted lower trait anxiety in young adulthood, particularly among those who experienced high ELSD. The relationship between higher cognitive ability in adolescence and lower trait anxiety in young adulthood was mediated by functional connectivity between the right LPFC and a large cluster including left precentral, postcentral gyrus and superior frontal gyri.

Our results are in line with a number of studies suggesting that early-life stressors associated with lack of socioeconomic resources negatively influence cognitive functions (Hart et al., 2007; Von Stumm and Plomin, 2015; Alves et al., 2016; Cermakova et al., 2018; Flensborg-Madsen et al., 2020; Zhang et al., 2020). Previous studies also indicated that mother's education has a

Table 3. Clusters of voxels functionally connected with right and left lateral prefrontal cortex associated with cognitive ability in adolescence

Seed	Correlation between seed and cluster	MNI coordinates (x, y, z)	Size of cluster	p-FDR	Brain regions included in the cluster
Left LPFC	Negative	+10 −26 +38	4945	0.0004	Precuneus; cingulate gyrus, posterior division; supramarginal gyrus, posterior division right; supramarginal gyrus, anterior division right; lateral occipital cortex, superior division right; angular gyrus right; parietal operculum cortex right; lateral occipital cortex, inferior division right; middle temporal gyrus, temporooccipital part right
Left LPFC	Negative	+28 +40 +18	4699	0.0004	Frontal pole right; cingulate gyrus, anterior division; paracingulate gyrus right; Superior frontal gyrus right; middle frontal gyrus right; right caudate
Left LPFC	Negative	−52 −28 +26	2116	0.0378	Lateral occipital cortex, superior division left; supramarginal gyrus, anterior division left; parietal operculum cortex left; middle temporal gyrus, temporooccipital part left; supramarginal gyrus, posterior division left
Right LPFC	Positive	+18 −58 −24	3148	0.0109	Cerebellum 4 5 6 7 8 left, cerebellum crus 1 2 left, cerebellum 4 5 6 right
Right LPFC	Positive	−62 −08 +18	2360	0.0269	Precentral gyrus left; postcentral gyrus left; superior frontal gyrus left
Right LPFC	Negative	+18 −32 +26	4772	0.0006	Precuneus; cingulate gyrus, posterior division; middle frontal gyrus left; lateral occipital cortex, superior division right; lateral occipital cortex, inferior division right; angular gyrus right)

LPFC, lateral prefrontal cortex; FDR, false-discovery rate; MNI, Montreal Neurological Institute.
Only regions included in the cluster that have min. 100 voxels are reported.

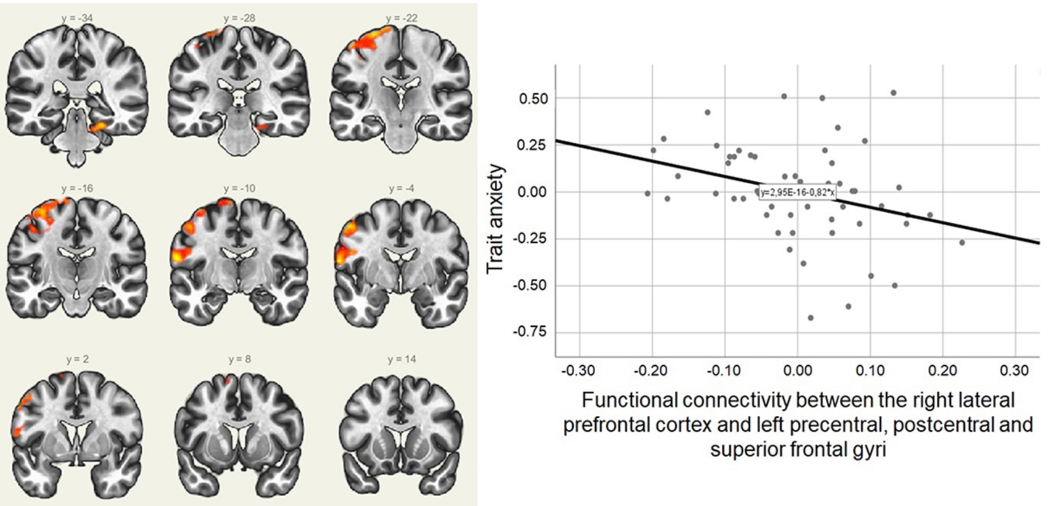

Fig. 2. Functional connectivity between the right lateral prefrontal cortex and a cluster including left precentral gyrus, left postcentral gyrus and left superior frontal gyrus. The left part of the figure shows a cluster of voxels functionally connected with the right lateral prefrontal cortex that is also associated with cognitive ability in adolescence. This cluster includes mainly left precentral gyrus, left postcentral gyrus and left superior frontal gyrus. Coordinates: −62 −08 +18; size of cluster: 2360. The right part of the figure shows an association of greater functional connectivity between this cluster and the right lateral prefrontal cortex with lower trait anxiety, adjusted for sex.

greater impact on brain health of the offspring than father's education (Cermakova *et al.*, 2020). Surprisingly, here we show that the combination of mother's high education and ELSD is the most detrimental to cognitive ability in adolescence. It has been described that a mis-match between the achieved level of education and corresponding socioeconomic status negatively affect one's mental health (Bracke *et al.*, 2013; Wolbers, 2013) and that poor mental health of mothers is linked to worse mental health and accelerated brain ageing of their offspring (Mareckova *et al.*, 2020a). Our study shows that this may hold for cognitive ability of the offspring as well. Possibly, the stress associated with ELSD may deprive the well-educated mothers from being available for cognitively stimulating activities with their children.

Furthermore, this study is in accord with evidence that low cognitive ability is associated with higher morbidity (Starr *et al.*, 2004; Deary *et al.*, 2009; Sorberg Wallin *et al.*, 2019). Previous

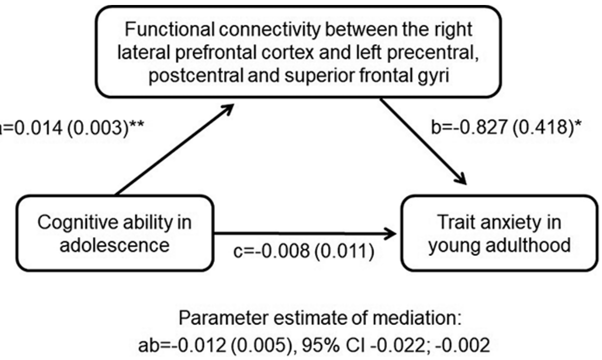

Fig. 3. Mediation analysis results are *B* (standard error); *$P < 0.05$, **$P < 0.001$ CI, confidence interval.

studies also indicated that the way adults use their cognitive ability in pursuing their mental health depends on the socioeconomic resources they had at their disposal when they were children (Huisman *et al.*, 2010). Here we show that the association of cognitive ability with trait anxiety is present particularly among those who experienced high ELSD. High cognitive ability may armour people with resilience. Possibly, these individuals could be more successful in finding solutions for stressful situations or learn more quickly how to avoid them. It is documented that children with a higher cognitive ability regain functioning in the face of adversity easier than children with lower cognitive ability (Garmezy, 1993). Higher cognitive ability may thus indicate a higher cognitive reserve in overcoming disadvantages caused by ELSD and buffer against the odds of developing trait anxiety.

We identified several brain regions, specifically left precentral and postcentral gyrus and superior frontal gyri, whose strength of the functional connectivity with the right LPFC underlies the association between higher cognitive ability in adolescence and lower trait anxiety in young adulthood. These results are in line with the growing evidence that altered somatic brain network, including precentral gyrus (somatic motor cortex) and postcentral gyrus (somatosensory cortex) plays a major role in trait anxiety (Li *et al.*, 2019). Another study of adolescents with anxiety disorders (generalized anxiety disorder, social phobia, separation anxiety disorder) demonstrated that the difference in grey-matter volume in these regions is an essential factor in the pathogenesis of trait anxiety (Strawn *et al.*, 2015). Our results are in accord with these findings, reveal the importance of somatic brain regions in trait anxiety and provide a new perspective on anxiety, which could be followed-up by further research. We speculate that higher cognitive ability and the associated increase in functional connectivity between both somatic and prefrontal brain regions during rest could inhibit the activity of right LPFC and protect against development of trait anxiety. Previous studies showed that anxious people require greater activity of the postcentral gyrus to cope with anxiety (Li *et al.*, 2019). We suggest that the synchronous activation of the LPFC and the somatic brain network may indicate the involvement of cognitive control, mitigating anxiety.

Superior frontal gyrus, part of the prefrontal cortex, is generally considered to be the vital brain region for the cognitive control system (Niendam *et al.*, 2012) and emotion-regulation processes (Frank *et al.*, 2014). Superior frontal gyrus is also involved in both acute psychosocial stress (Pruessner *et al.*, 2008) and chronic life stress (Li *et al.*, 2016). As cognitive control is a fundamental part of cognitive ability and psychosocial stress is undoubtedly linked to trait anxiety, these studies provide a solid basis for the interpretation of our findings. To the best of our knowledge, the present study is the first to suggest simultaneous involvement of both somatic and prefrontal brain regions in the association between cognitive ability and trait anxiety.

This study is limited by its low sample size and selective dropout. As expected in longitudinal studies with a long follow-up (Young *et al.*, 2006), the participants in the analytical sample are not representative towards the general population. In our case, the analytical sample had better socioeconomic conditions than the whole ELSPAC cohort at baseline and they also seemed to have better mental health as compared to the complete VULDE cohort. This biases our results due to selection. However, we repeated some analyses on a larger sample of participants from the whole ELSPAC cohort and found consistent associations (Supplementary Table S2). As in the smaller analytical sample, we found an association of worse ELSD with lower cognitive ability in adolescence and we also found no effect modification by sex and father's education, but significant effect modification by mother's education.

In addition, we found the association using a voxelwise threshold of $P < 0.05$, but not using the threshold of $P < 0.001$, which is the current standard. That may increase the chance of false positive results. Given this, the results need to be replicated in the future. Finally, we acknowledge that this study is observational in design and causality cannot be established as there may be residual confounding factors. We conclude that growing up in households that face socioeconomic difficulties may have long-term negative consequences on one's cognitive ability and mental health. Higher cognitive ability and the related increase in the recruitment of the right LPFC may, however, ameliorate the experience of anxiety.

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Conflict of interest

The authors declared that they had no conflict of interest with respect to their authorship or the publication of this article.

Supplementary data

Supplementary data is available at *SCAN* online.

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