

1 **Sex-Specific Trajectories of Adolescent Brain Development and Behavioural Health in**

2 **Relation to Family Environments**

3 **Running title:** family environment and internalizing/externalizing symptoms

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Ethics Approval and Consent to Participants

In the ABCD study, all procedures were approved by a central Institutional Review Board
(IRB) at the University of California, San Diego, and in some cases by individual site IRBs
(e.g., Washington University in St. Louis)
(<https://www.sciencedirect.com/science/article/pii/S1878929317300622>). Parents or
guardians provided written informed consent after the procedures had been fully explained
and children assented before participation in the study.

Conflict of interest

No financial or non-financial benefits have been received or will be received from any party
related directly or indirectly to the subject of this article.

Funding

Data used in the preparation of this article were obtained from the ABCD study (<https://abcdstudy.org>), held in the NIMH Data Archive. This is a multisite, longitudinal study designed to recruit more than 10 000 children aged 9-10 years and follow them over 10 years into early adulthood. The ABCD study is supported by the National Institutes of Health and additional federal partners under award numbers U01DA041048, U01DA050989, U01DA051016, U01DA041022, U01DA051018, U01DA051037, U01DA050987, U01DA041174, U01DA041106, U01DA041117, U01DA041028, U01DA041134, U01DA050988, U01DA051039, U01DA041156, U01DA041025, U01DA041120, U01DA051038, U01DA041148, U01DA041093, U01DA041089. A full list of supporters is available at <https://abcdstudy.org/federal-partners.html>. A listing of participating sites and a complete listing of the study investigators can be found at <https://abcdstudy.org/scientists/workgroups/>. ABCD consortium investigators designed and implemented the study and/or provided data but did not necessarily participate in analysis or writing of this report. This manuscript reflects the views of the authors and may not reflect the opinions or views of the NIH or ABCD consortium investigators.

This study was supported by grants from the National Natural Science Foundation of China (82125032, 81930095, 81761128035, 82001771 and 82204048), the Science and Technology Commission of Shanghai Municipality (23Y21900500, 19410713500, and 2018SHZDZX01), the Shanghai Municipal Commission of Health and Family Planning (GWV-11.1-34, 2020CXJQ01, 2018YJRC03, 20214Y0125, and GWVI-11.2-YQ30), the Shanghai Clinical Key Subject Construction Project (shslczdzk02902), Innovative research team of high-level

84 local universities in Shanghai (SHSMU-ZDCX20211100), and the Guangdong Key Project
85 (2018B030335001).

86

87 **Author Contributions**

88 Y.L., M.W., F.L., T.R. and F.L. designed the study. M.W. and T.R. conducted data analysis.

89 Y.L., F.L., and T.R. drafted the manuscript. Y.L., M.W., F.L., L.Z., Q.Z., W.Z., W.D., Q.L.,

90 T.R., and F.L. contributed to the interpretation of the data and critically revised the

91 manuscript. F.L., T.R., and Q.L. contributed equally to the work as senior investigators. They

92 designed the study, supervised the data analyses, and supervised the drafting and revising of

93 the manuscript. The corresponding author attests that all the listed authors meet authorship

94 criteria and that no others meeting the criteria have been omitted.

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97 **Abstract**

98 **Background:** The impact of family environment on adolescent behavioral health is well
99 established, yet insights into how these influences are moderated by sex, particularly through
100 changes in brain structure, are limited.

101 **Methods:** This cohort study included over 9,000 children aged 9-12 from the Adolescent Brain
102 and Cognitive Development (ABCD) study. We used structural equation modeling to create a
103 composite measure of family environment, incorporating factors such as family conflict,
104 acceptance, parental monitoring, parental psychopathology, and socioeconomic status, as
105 reported by both children and parents. We conducted stratified analyses by sex to examine the
106 longitudinal associations between family environment and internalizing/externalizing
107 symptoms using generalized additive mixed models. Additionally, we explored the mediating
108 role of brain cortical alterations, measured by structural MRI, in these associations.

109 **Results:** Lower family environment scores in childhood were consistently linked to higher
110 internalizing and externalizing symptoms in follow-ups. The trajectories varied by sex, with
111 females showing greater vulnerability to internalizing symptoms when exposed to worse family
112 environment. These findings were consistent across both low-income and high-income families.
113 In a subset of children with no initial symptoms, lower family environment scores still predicted
114 more symptoms at a 3-year follow-up for both sexes. Sex-specific patterns emerged in brain
115 regions mediating the relationship between family environment and externalizing symptoms.
116 Males exhibited cortical alterations primarily in the left hemisphere and temporal lobe, while
117 females in the right hemisphere and parietal and temporal lobes.

118 **Conclusions:** These findings highlight the critical role of sex in considering the effects of
119 family environment on adolescent brain development and mental health.

120

121 **Keywords:** Adolescent, Family Environment, Brain, Internalizing and externalizing Symptoms,
122 Sex Differences

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Introduction

The influence of the family environment on adolescent behavioural outcomes and brain development is profound, particularly when considering sex-specific differences [REF]. During adolescence, a critical period of neural vulnerability, brain structures are highly sensitive to external factors such as family dynamics^{1, 2}. Previous research has highlighted how aspects of the family environment, including parental monitoring, acceptance, and conflict, are strongly associated with diverse developmental outcomes [3-6]. However, despite these insights, the differential impacts of these environmental factors on the developing brains of male and female adolescents are not fully understood.

Considerable evidence underscores the critical role of the family environment in either mitigating or exacerbating adolescent mental health issues^{1, 9-11}. Supportive family interactions have been associated with fewer behavioural problems, while negative family dynamics have been linked with increased prevalence of internalizing and externalizing symptoms [REF]. Sex differences are particularly pronounced, with females often more affected by adverse family environments, exhibiting heightened internalizing symptoms under stress [REF]. However, the specific brain regions affected and the processes involved in these gender-differentiated responses remain underexplored.

This study employs a comprehensive methodology, utilizing a large and diverse dataset from the Adolescent Brain and Cognitive Development (ABCD) study, which includes children aged 9-12 years across the United States. Our analysis focuses on how family environments influence brain morphology and behavioral outcomes, with particular attention to gender-specific effects over time. Family environment scores were calculated at baseline

147 using an integrated model of child-reported, parent-reported, and demographic data. We then
148 examined the sex-specific longitudinal associations between these family environment scores
149 and internalizing and externalizing symptoms, as measured by the Child Behavior Checklist
150 (CBCL). Additionally, this research investigates the mediating role of cortical areas,
151 determined through structural magnetic resonance imaging (MRI), in the relationship between
152 family environment and behavioral outcomes. Cortical areas of interest were identified in
153 both cross-sectional (baseline data) and longitudinal analyses (structural MRI data from the
154 second follow-up and behavioral outcomes at the third follow-up). By combining detailed
155 imaging studies with extensive behavioural assessments, this study seeks to elucidate the
156 intricate interactions between family dynamics and adolescent neurodevelopment,
157 highlighting the critical need to consider sex-specific pathways in understanding these
158 relationships.

Methods

Study population

This research utilized the dataset from the Annual Curated Data Release 5.1 of the ABCD study, which recruited over 10,000 children aged 9 to 12 years of age from 21 centers across the United States, representing the national adolescent diversity. The study protocols are detailed on the ABCD website (<https://abcdstudy.org/scientists/protocols/>). From the initial sample of 11,868 participants, we selected children with complete CBCL internalizing and externalizing symptoms data at baseline, the first, second, and third follow-ups (N=9710).

Family environment

We measured family environment using a set of indicators about family relationships, demographics, and parent information from questionnaires reported by children and parents, as reported in Thijssen et al¹⁰.

Three child-reported questionnaires were involved, including the abbreviated version of the maternal acceptance scale of the Child Report of Parent Behavior Inventory¹³, the conflict scale from the Family Environment Scale¹⁴ and the child-reported Parental Monitoring Survey¹⁵. The parent-reported information included the conflict scale from the Family Environment Scale, and one background question from the Kiddie Schedule for Affective Disorders and Schizophrenia about parent-child conflict¹⁶. Demographic and parent information included family yearly income, parental education, parental psychopathology^{17, 18}, parental relationship status, and the whether the pregnancy was planned.

Family environment scores were established using structural equation modeling with a structure reported in Thijssen et al¹⁰. After imputing the missing items and loading the items as latent variables, we combined the latent variables from the questionnaire scales into three categories: child-reported, parent-reported, and demographics. These three latent variables were then combined to yield an overall family environment latent variable and the model had reasonable fit (see the details of questionnaires and structural equation modeling in Supplementary Methods 1 and Figure S1). Low scores on the family environment variable indicate a more stressful/less supportive family environment.

Externalizing and internalizing symptoms

Externalizing and internalizing symptoms were assessed with the CBCL scale. CBCL contains 113 caregiver-reported items that measure a broad scope of emotional and behavioral problems, yielding two composite scores: externalizing and internalizing symptoms¹⁸. The CBCL scale has shown good validity in various studies¹⁹.

Mediators

Potential mediators included the cortical area of 68 cortical regions based on the ABCD summary of standard FreeSurfer v5.3.0 data from the Desikan atlas regions of interest. The details on MRI acquisition and standardized preprocessing in the ABCD Study has been described in Casey et al. (2018)²⁰ and Hagler et al. (2018)²¹. In this study, we followed the recommendations from the ABCD consortium's data analytic core and excluded images with poor-quality or with incidental findings after visual inspection, labeled by the ABCD teams. Children with incomplete MRI data were excluded (N=874) in analyses involving MRI data.

Covariates

Potential confounders included race/ethnicity (white, black, Hispanic, or other), sex, and age at assessment. We also involved signal-noise ratio as a confounder in the mediation analysis for MRI data. Missing values of race were imputed by chained equations with package mice (version 3.16.0).

Statistical analyses

All analyses were performed in R version 4.3.2. Family environment scores were calculated using structural equation modeling by the package lavaan (version 0.6-16)²². Missing items were imputed by chained equations with package mice (version 3.16.0). We described the demographics by categorizing the study population by the 25 and 75 percentiles of family environment score. All analyses were stratified by sex to account for sex differences in the development of internalizing and externalizing problems during adolescence^{5, 23}. We confirmed the sex-difference by testing the significance of the interaction term between family environment score and sex $\times$ age.

The generalized linear mixed-effect model was utilized to explore the associations of family environment with internalization and externalization symptoms. The mixed models were specified as family nested within site to accommodate the data structure of the ABCD study. For analyses involving MRI data, the mixed effect was specified as family nested within each MRI device. Poisson regression was applied to fit internalization and externalization due to their right-skewed distribution after confirming the overdispersion test. Potential confounders were adjusted as described in the covariates section. Firstly, we performed wave-by-wave

analyses by assessing the associations between baseline family environment with outcomes at each timepoints separately. To further understand the longitudinal association, we additionally adjusted for the externalizing and internalizing symptom score at baseline to account for the difference at baseline and focus on the changes in the symptoms.

Also, we identified a subsample of children who had no externalizing or internalizing problems at baseline (CBCL t score < 65) and investigating whether a more stressful family environment was associated with more externalizing and internalizing symptoms at follow-ups²⁴. Secondly, we performed longitudinal analysis by fitting age at assessment with restricted cubic splines. For interpretability of the model, we quartered the study population by the 25, 50, and 75 percentiles of the family environment score, where children in the lowest quartile had the worst level of family environment. We modeled and visualized the developmental patterns of externalizing and internalizing problems in relation to sex and age across four groups of family environment. As family income might moderate the association [ref], we examined the influence of family income levels on internalizing and externalizing problems by categorizing the cohort into low-income and high-income group and conducting analyses separately within the lower and upper income tertiles (Supplementary Methods 2).

Mediation analysis was performed using structural equation model to investigate the mediating role of cortical areas in the association of baseline family environment with internalizing and externalizing symptoms in males and females, respectively. Confounders were regressed out in the mediation model. We identified a set of brain regions that were significantly related to both exposure (family environment) and outcome (externalizing or internalizing symptom) variables (Bonferroni corrected $P < 0.05$ for both) by performing a

cortical intersection analysis. We then normalized and aggregated these regions to form a mediator variable. We first performed mediation analysis on family environment, cortical areas, and behavioral problems, all collected at baseline. Then we performed mediation analysis on family environment, cortical areas at the second follow-up, and behavioral problems at the third follow-up. For each outcome, if the two mediation analyses (at two timepoints) both showed significant indirect effect of altered cortical areas, we then identified brain regions that were overlapped in the two analyses. These regions were of specific interest because they consistently mediated the association between family environment and outcomes at multiple timepoints.

Results

The ages of the children in the study were comparable at both the initial and the follow-up assessments, regardless of their family environment score (mean age [SD] at baseline, the first, second, and third follow-up, 9.9 [0.6], 11.0 [0.6], 12.0 [0.7], 12.9 [0.6], respectively; range, 9 to 15; hereinafter referred to as baseline, 1-, 2-, and 3-year follow-ups; Table 1). In both sexes, children with lower family environment scores were more likely to be from racial and ethnic minority and had parents with lower levels of education and income (Table 1).

Family environment at childhood and behavioral problems at early adolescence

In the period from ages 9 to 15, the average internalizing symptom score exhibited an upward trajectory in females, whereas it remained constant in males (Figure 1A, 1B). Meanwhile, the average externalizing symptom score maintained a steady trend, with males consistently exhibiting higher average scores than females (Figure 1C, 1D). We observed sex differences in the longitudinal associations of baseline family environment with both internalizing and externalizing symptoms at follow-ups (P for interaction, <0.001 , for both outcomes). The following analyses were thus stratified by sex.

For children in the lowest quartile of family environment score that reflects a more stressful environment, the average internalizing score at baseline was 2.0 times higher for males (adjusted mean ratio, 2.01, 95% CI, 1.83-2.21; Table S2) and 2.0 times higher for females (adjusted mean ratio, 1.98, 95% CI, 1.79-2.18; Table S2) compared with those in the highest quartile, adjusting for age at assessment and race/ethnicity. In follow-ups, the average internalizing symptom scores tended to converge for females in the top three quartiles of family

environment score, whereas females in the lowest quartile experienced a worsening of internalizing symptoms over time, despite having higher levels of symptoms at baseline (Figure 1A). Meanwhile, the dose-response relationship between family environment score and internalizing symptom scores were persistent among males (Figure 1B).

For children in the lowest quartile of family environment score, the average externalizing score at baseline was 3.6 times higher for males (adjusted mean ratio, 3.60, 95% CI, 3.25-4.05; Table S2) and 4.4 times higher for females (adjusted mean ratio, 4.39, 95% CI, 3.87-4.99; Table S2) compared with those in the highest quartile. Notably, the higher risk estimates among female could reflect a relative scale, given a lower average externalizing symptom score in the reference group of females (Figure 1C). In follow-ups, the average externalizing symptom scores decreased among males in the lowest quartile who exhibited a high average externalizing score (mean score, 7.06, SD, 7.7, Figure 1D) from 9 to 15 years. The dose-response relationship between family environment score and externalizing symptom scores were stable in other groups (Figure 1D).

Despite different family income level, we observed that family environment score was associated with both internalizing and externalizing symptoms at baseline and follow-ups. Children in the lower income level generally showed higher average internalizing and externalizing symptom scores over time. Distinctive patterns emerged among females from the higher income group, whose internalizing symptom scores exceeded or got close to those of their lower-income counterparts from ages 9 to 15 (Figure S2). Treating the family environment score as a continuous variable, we consistently observed that both female and male children

with a more stressful family environment at baseline had more internalizing and externalizing symptoms at baseline and the subsequent three follow-ups (Figure S3).

By additionally adjusting for the externalizing and internalizing symptom score at baseline, one at a time, we observed that the family environment score was still associated more specific behavioral symptoms, respectively, at the 3-year follow-up for both males and females (Table 2). Specifically, family environment score had a stronger association with changes in externalizing symptoms for males (adjusted mean ratio, 0.51, 95% CI, 0.40- 0.64) and females (adjusted mean ratio, 0.32, 95% CI, 0.25-0.43). In a subsample of children reported no internalizing and externalizing symptoms at baseline, we still observed associations of family environmental score at baseline with both internalizing and externalizing symptoms at 3-year follow-up (Table 2). Consistently, family environment score had a stronger association with externalizing symptoms for both males (adjusted mean ratio, 0.14, 95% CI, 0.10-0.20) and females (adjusted mean ratio, 0.10, 95% CI, 0.07-0.15).

Family environment, brain structure, and behavioral problems

By investigating cortical areas that were both associated with family environment and behavioral problems, we observed that the altered cortical areas at baseline significantly mediated the associations of baseline family environment with both baseline internalizing and externalizing symptoms for male (Figure 2 A-D; indirect effect, $P = 0.006$ and 0.003 , respectively), and with baseline externalizing symptoms for female (Figure 2 E-F, indirect effect, $P = 0.018$). Similarly, we investigated the mediating role of cortical areas at the 2-year follow-up that were both associated with family environment and behavioral problems at the 3-year follow-up. Altered cortical areas at the 2-year follow-up significantly mediated the

association with externalizing problems at the 3-year follow-up in both male and female (Figure 3A-D; indirect effect, $P = 0.004$ and 0.006 , respectively). We did not observe cortical areas at follow-up that mediated the association between family environment at baseline and internalizing symptoms at follow-up in both sexes (Table S3-5).

By intersecting the significant brain regions in the two mediation analyses, we observed cortical areas of the following regions that consistently mediated the association between family environment and externalizing problems in males at the two timepoints: posterior cingulate cortex, superior temporal gyrus and lingual gyrus in the left hemisphere, as well as middle temporal gyrus in the right hemisphere (Figure 3E). Among females we observed the following brain regions that consistently mediated the association between family environment and externalizing problems: anterior cingulate cortex, superior temporal gyrus, inferior parietal lobule, supramarginal gyrus in the right hemisphere, inferior temporal gyrus, and middle frontal cortex in the left hemisphere (Figure 3F). The results showed no overlaps between sexes.

Discussion

In this longitudinal study involving over 9,000 children aged 9 to 12 years, we investigated how early family environments influence the evolution of adolescent brain and behavioural development, with a particular focus on sex differences. Our findings reveal that both male and female children who were exposed to stressful family environments during childhood exhibited increased levels of internalizing and externalizing symptoms at subsequent follow-ups, including those who initially presented no behavioural issues. The patterns of these associations were distinctly influenced by sex. Additionally, our analysis identified sex-specific brain regions where alterations in cortical areas mediated the impact of family environment on behavioural symptoms observed both at baseline and during follow-ups.

Our study highlights a dose-response, longitudinal, and sex-specific association between family environment at childhood and behavioral problems in adolescence. Specifically, we observed that better family environment (supportive relationship^{25, 26}, etc.) was generally associated with less behavioral problems and worse family environment (poverty²⁷, high levels of conflict, and unstable family environments²⁸, etc.) was related to more severe behavioral problems. Previous evidence in longitudinal study also suggests that the effects of family environment on behavioral problems can persist over time²⁹. Children exposed to negative family environments may show escalating behavioral issues as they progress into adolescence, demonstrating a cumulative dose-response effect^{30, 31}. These findings suggested the importance of early and sustained positive family interactions. Interventions aimed at improving family dynamics could potentially mitigate the development and severity of behavioral issues in adolescents³². Additionally, our study showed that even among children who had no behavioral

problems at baseline, a more stressful family environment in childhood was also associated with more internalizing and externalizing symptoms at 3-year follow-up. This could potentially be attributed to the challenges children face in managing their emotions when raised in high-stress environments³³. Alternatively, the family environment might progressively deteriorate, leading to a continuous escalation of emotional and behavioral issues in children.

In line with previous studies, we observed sex-specific trajectories of behavioral problems and sex-specific association with family environment³⁴⁻³⁶. Our findings suggests that girls who experienced poor family environment in childhood had higher internalizing symptoms at baseline and showed even more increases in internalizing symptoms during adolescence. As internalizing problems were associated with higher risk of depression, self-harm, and even suicide³⁷, these girls may require family-centered interventions for prevention. In addition, the rise in internalizing behaviors observed in girls has been hypothesized to be related to increased vulnerability to stressors, an increased tendency to ruminate on events and emotions, and distinct socialization pressures based on sex³⁸⁻⁴⁰. Study focused on sex-specific interactions in brain maturation suggesting that higher levels of internalizing symptoms in female adolescents than in males relate to sex-differences in Hypothalamic-pituitary-adrenal (HPA)-axis function which represent critical factors for the development of brain networks of emotional regulation⁴¹. Future studies are needed to better understand the sex-specific association between family environment and the development of internalizing symptoms among females.

As expected, the association between childhood family environment and behavioral problems attenuated over time^{6, 29}. This attenuation may reflect Individual heterogeneity⁴² or changes in family environment that were not measured in our dataset, such as parents'

expectations^{43, 44}. Besides, we could not rule out other possible mechanism beyond the family environment underlying the observed pattern, such as the increased importance of social support and friendship in influencing behavioral problems during adolescence^{45, 46}. Interestingly, we also found a sex difference in the attenuation patterns: the risk estimates for both internalizing and externalizing symptoms declined over time among females, whereas they remained stable at 2-year and 3-year follow-ups among males. The results were consistent with studies that sex moderated the relationship between adverse childhood experiences and behavioral problems in adolescence⁴⁷. Also, parental attachment and monitoring were reported as protective factors for girls while serving as additional risk factors for boys for behavioral problems in conflictual families⁴⁸.

In this study, we found sex-specific cortical regions that mediated the association between family environment and externalizing symptoms, both at baseline and follow-up. Notably, we demonstrated that the cortical regions mediated the relationship between family environment and externalizing problems are mainly in the left hemisphere and temporal regions in males. This suggests that the male brain, which is more left-lateralized and may be highly sensitive to language environment⁴⁹. Previous research has indicated that the quality of marital relationships can influence the quality and frequency of mother-son conversations⁵⁰. Additionally, maternal anxiety may affect the expressive language of offspring⁵¹. This underscores the importance of good communication and support systems within the family environment for adolescent development. Worse family environment may inhibit language and communication skills and leading to an increase in externalizing behavior problems and face peer rejection⁵². In females, the right hemisphere is critical for emotional understanding and social interactions⁵³. Adverse

family environments, such as parental conflict, may impair the right hemisphere's function, causing emotional dysregulation and abnormal social behavior⁵⁴. Our findings emphasize the importance of a supportive family environment for healthy brain development and behavior in early adolescence. Addressing family dynamics and reducing stress can mitigate negative impacts, with specific attention to sex differences. We did not observe consistent structural alterations that mediated the association between family environment and internalizing problems. This could suggest a functional mechanism or varying cortical susceptibility across development. Future research is warranted to investigate the sex-specific neurobiological mechanism underlying the observed associations.

This study has several strengths. First, the large sample size of the ABCD study allowed sufficient statistical powered analysis for neuroimage investigation, and for even narrow subgroups, such as quartering the sex-stratified population. Second, this study used repeated measures (four per child) in a critical developmental period for externalizing and internalizing symptoms to estimate the trajectories related to family environment. Third, this study designed analyses considering the sex difference of the association and of the development of externalizing and internalizing symptoms, offering new insights on this topic. Fourth, we used longitudinal neuroimage and behavioral data to examine brain regions that overlapped between two mediation analyses, enhancing the validity of the identified brain regions. Fifth, we measured the family environment by various indicators from different sources, reducing the potential measurement error.

There were several limitations in our study. First, the follow-up period covered only early adolescence, limiting further investigation of late adolescence, another critical period for

behavioral problems. Second, we established a family environment score with a large number of indicators, some of which were known to be highly correlated with risk factors for neurodevelopmental outcomes, such as insufficient folic acid intake associated with unintended pregnancy, less period of breastfeeding associated with lower socioeconomic level, less parent-child interaction at early childhood associated with family conflict. Thus, the estimated risk reflected a composite of heterogeneous pathways between family environment and behavioral problem. Still, we highlighted a prominent and longitudinal association of the composite score of family environment, indicating a crucial and lasting role in the development of behavioral problems. Third, we did not assess the effect and the potential interactive role of peer relationship and social support in the development of behavioral problems in adolescence.

In conclusion, family environment at childhood was longitudinally associated with externalizing and internalizing symptoms in early adolescence with sex differences. Males and females showed different sets of brain regions with altered cortical areas that mediated the longitudinal associations. These findings contribute to our understanding of the complex interplay between family environmental and brain structure in the development of adolescent behavioral problems.

441 **Acknowledgement**

442 We thanked Dr. Mingyu Xu from Xinhua Hospital Affiliated to Shanghai Jiao Tong University
443 School of Medicine for their helpful comments and discussions.

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445 **Availability of Data and Materials**

446 The data that support the findings of this study are openly available in the ABCD Dataset Data
447 Release 5.0 at <https://nda.nih.gov/abcd>. DOI: 10.15154/xv6t-5462.

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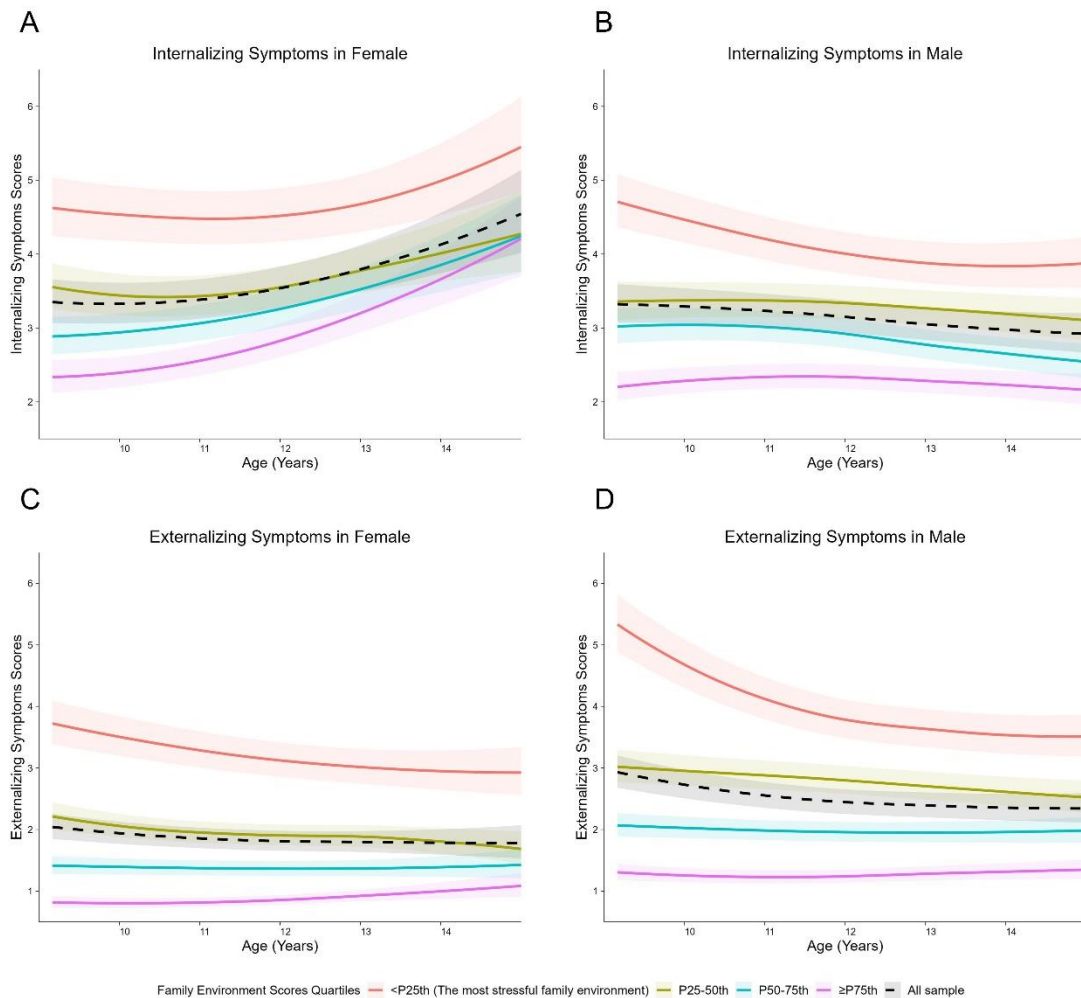


Figure 1 Developmental patterns of internalizing and externalizing symptoms, stratified by sex. A, B, developmental patterns of internalizing symptoms related to age across four groups quartered by family environment scores (solid lines) and group of all sample (dashed lines) for female and male respectively. **C, D,** developmental patterns of externalizing symptoms related to age across four groups quartered by family environment scores (solid lines) and group of all sample (dashed lines) for female and male respectively. Models were adjusted for race and age at assessment.

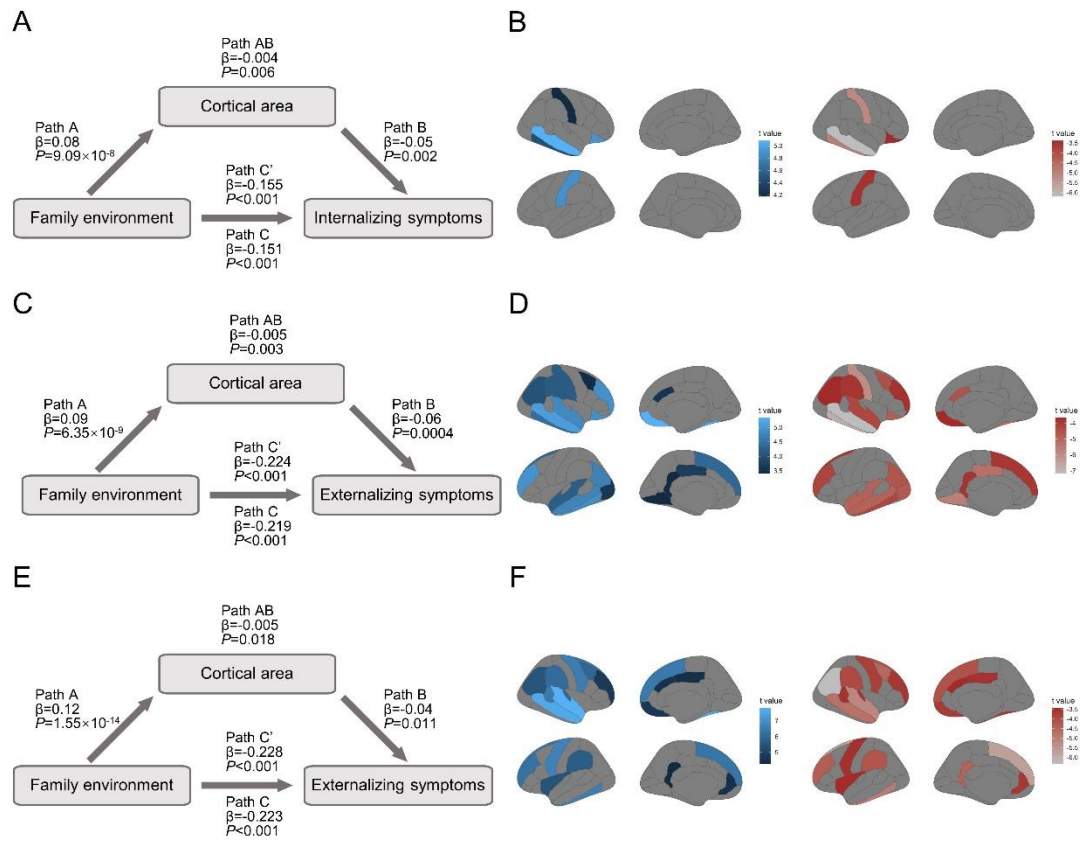


Figure 2 Mediation analysis and the brain regions with their cortical areas correlated with both family environment and behaviors at baseline. **A**, mediation analysis showed that the cortical areas significantly mediate the association between the family environment and internalizing symptoms at baseline for male. **C**, **E**, mediation analysis on family environment, cortical areas, and externalizing symptoms at baseline for male and female respectively. **B**, **D**, **F**, the brain regions with their cortical areas significantly (Bonferroni corrected $P < 0.05$) related to both family environment and behaviors. The blue color indicates that lower cortical areas were correlated with worse family environment. The red color indicates that lower cortical areas were correlated with severe behavioral problems.

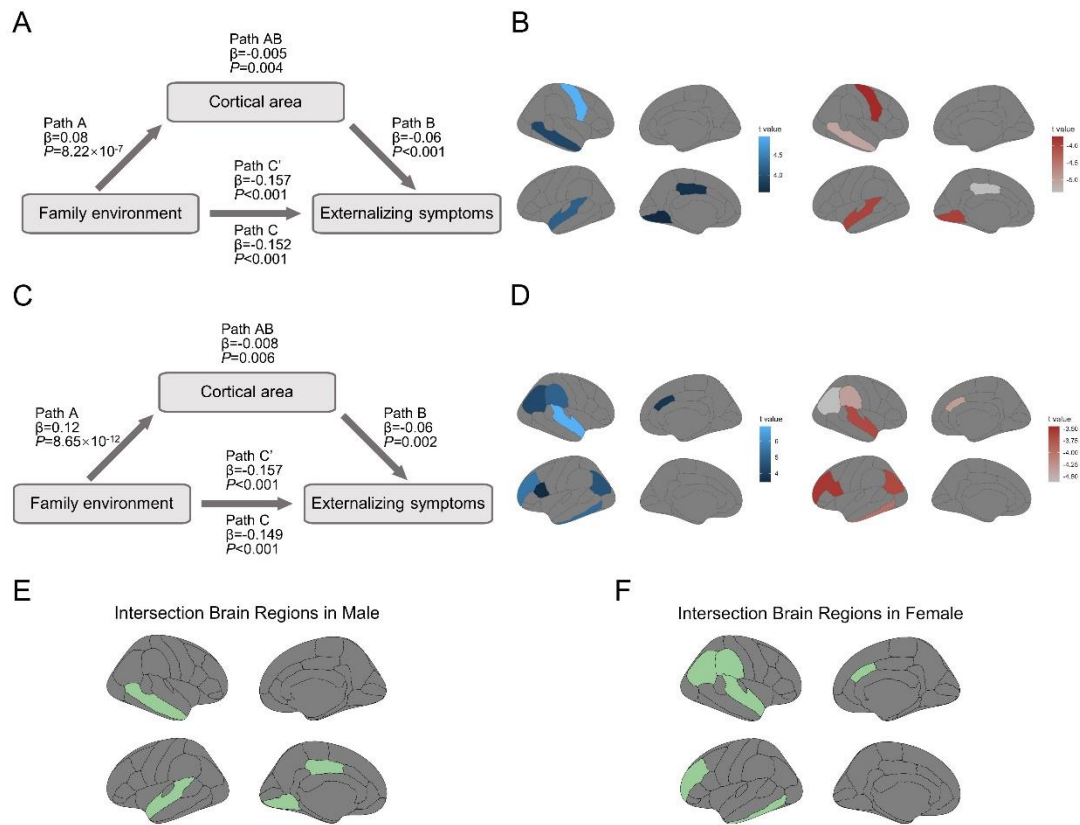


Figure 3 Mediation analysis and the brain regions with their cortical areas mediates family environment and behaviors at both baseline and follow-ups. A, C, mediation analysis showed that the cortical areas at 2-year follow-up significantly mediates the association between the family environment at baseline and externalizing symptoms at 3-year follow-up for male and female respectively. B, D, the brain regions with cortical areas significantly (Bonferroni corrected $P < 0.05$) related to both family environment and behaviors at follow-ups. The blue color indicates that lower cortical areas were correlated with worse family environment. The red color indicates that lower cortical areas were correlated with severe behavioral problems. E, F, the brain regions with their cortical areas mediates family environment and behaviors at both baseline and follow-ups for male and female, respectively.

Table 1 Baseline characteristics of the study children from the Adolescent Brain

Cognitive Development study.

Variable	Female			Male		
	Family environment score*			Family environment score*		
	≤p25 th (N=1155)	p25-75 th (N=2308)	p75-100 th (N=1155)	≤p25 th (N=1273)	p25-75 th (N=2546)	p75-100 th (N=1273)
Age at baseline, years, mean (SD)	9.8 (0.6)	9.9 (0.6)	10.0 (0.6)	9.9 (0.6)	9.9 (0.6)	10.0 (0.6)
Age at the first follow-up, years, mean (SD)	10.8 (0.6)	10.9 (0.6)	11.0 (0.6)	10.9 (0.6)	10.9 (0.6)	11.0 (0.6)
Age at the second follow-up, years, mean (SD)	11.9 (0.7)	12.0 (0.7)	12.1 (0.7)	12.0 (0.7)	12.0 (0.7)	12.1 (0.7)
Age at the third follow-up, years, mean (SD)	12.8 (0.7)	12.9 (0.6)	13.0 (0.6)	12.9 (0.6)	12.9 (0.6)	13.0 (0.6)
Race/Ethnicity, N (%)						
White	452 (18.1)	1216 (48.6)	831 (33.3)	533 (18.6)	1420 (49.6)	910 (31.8)
Black	274 (43.8)	292 (46.6)	60 (9.6)	267 (43.5)	292 (47.6)	55 (9.0)
Hispanic	281 (31.5)	491 (55.1)	119 (13.4)	309 (31.2)	525 (53.0)	157 (15.8)
Other	140 (23.8)	305 (51.9)	143 (24.3)	159 (26.4)	297 (49.3)	146 (24.3)
Parental average education, years, mean (SD)	15.5 (3.0)	16.8 (2.6)	18.2 (1.6)	15.7 (3.0)	16.9 (2.5)	18.0 (1.8)
Income, N (%)						
Low income, <\$50,000	446 (58.2)	319 (41.7)	1 (0.1)	497 (59.0)	334 (39.7)	11 (1.3)
Middle income, \$50,000-\$100,000	277 (22.0)	742 (58.9)	240 (19.1)	287 (20.9)	794 (57.8)	292 (21.3)
High income, >\$100,000	199 (10.5)	868 (45.5)	839 (44.0)	238 (11.3)	992 (47.2)	870 (41.4)
Family environment						
Child-reported						
Parental monitoring, mean (SD)	4.2 (0.6)	4.5 (0.4)	4.7 (0.3)	3.9 (0.6)	4.3 (0.4)	4.6 (0.3)
Parental acceptance, mean (SD)	2.6 (0.4)	2.8 (0.2)	3.0 (0.1)	2.5 (0.4)	2.8 (0.2)	2.9 (0.1)

Family conflict, mean (SD)	3.4 (2.1)	1.7 (1.6)	0.6 (0.9)	3.7 (2.1)	2.0 (1.7)	0.8 (1.0)
Parent-reported						
Family conflict, parent, mean (SD)	3.9 (2.1)	2.3 (1.6)	1.1 (1.0)	4.1 (2.1)	2.6 (1.7)	1.2 (1.1)
Getting along, mean (SD)	1.3 (0.5)	1.2 (0.4)	1.1 (0.3)	1.3 (0.5)	1.2 (0.4)	1.1 (0.3)
Parental psychopathology, mean (SD)	29.3 (22.3)	19.3 (15.1)	13.5 (10.7)	29.0 (21.2)	20.6 (16.1)	13.8 (11.6)
Parental divorce/separation, N (%)	490 (43.8)	533 (47.7)	95 (8.5)	530 (43.7)	571 (47.0)	113 (9.3)
Planned pregnancy, N (%)	519 (18.5)	1383 (49.4)	899 (32.1)	595 (18.5)	1593 (49.6)	1021 (31.8)

699 Monitoring score range, 1 to 5. Parental acceptance range, 1 to 3. Family conflict score range,
700 0 to 9. Getting along score range, 1 to 3. Psychopathology score range, 0 to 154. The
701 proportion of missing value was detailed in Table S1. The highest proportion of missing value
702 was 7.9% in parental income level.

703 *The family environment score was calculated using all described child- and parent-reported
704 variables.

705

706

Table 2 Association between family environment score at baseline and behavioral problems at 3-year follow-up.

Analysis/ Outcome	N	CBCL at baseline, mean (SD)	CBCL at 3-year follow-up, mean (SD)	Crude mean ratio (95% CI)	Adjusted mean ratio (95% CI)
Additionally adjusting for baseline behavioral problems					
Internalizing problems					
Male	5092	5.0 (5.4)	4.7 (5.5)	0.81 (0.75, 0.88)	0.66 (0.54, 0.81)*
Female	4618	4.9 (5.4)	5.6 (6.3)	0.91 (0.83, 0.10)	0.70 (0.56, 0.90)*
Externalizing problems					
Male	5092	4.9 (6.1)	4.4 (5.9)	0.66 (0.60, 0.72)	0.51 (0.40, 0.64)†
Female	4618	3.6 (5.0)	3.4 (4.9)	0.36 (0.32, 0.40)	0.32 (0.25, 0.43)†
Population: children with no behavioral problems at baseline assessment					
Internalizing problems					
Male	4007	2.7 (2.4)	3.3 (3.9)	0.59 (0.52, 0.67)	0.44 (0.32, 0.60)‡
Female	4034	3.2 (2.8)	4.5 (5.1)	0.68 (0.61, 0.77)	0.53 (0.39, 0.71)‡
Externalizing problems					
Male	4007	2.7 (2.9)	3.0 (4.1)	0.21 (0.19, 0.24)	0.14 (0.10, 0.20)‡
Female	4034	2.2 (2.7)	2.5 (3.7)	0.11 (0.10, 0.13)	0.10 (0.07, 0.15)‡

CBCL, Child Behavioral Checklist; SD, standard deviation; CI, confidence interval.

* Adjusted for age at assessment, race, and internalizing problems at baseline.

† Adjusted for age at assessment, race, and externalizing problems at baseline.

‡ Adjusted for age at assessment and race.