

The Role of ACEs, BMI, and Sex in Brain Development During Adolescence: Insights from the ABCD Study

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Adverse Childhood Experiences (ACEs) have long been recognized as significant risk factors for a range of physical and mental health outcomes. While prior research has identified sex differences in both exposure to ACEs and their long-term consequences in adults, few studies have thoroughly examined how ACEs impact brain structure and function in adolescents—an especially critical period for brain development. Similarly, although studies show that women experience more weight stigma, emotional eating, and depression associated with high BMI, and that BMI is linked to brain changes, few studies have explored sex differences in this relationship within adolescent populations. This gap in the literature, particularly regarding how ACEs and BMI jointly affect brain development in a sex-specific manner, is the focus of the current study.

This project aims to investigate how ACEs, BMI, and sex interact to influence brain development, using data from the Adolescent Brain Cognitive Development (ABCD) Study. The ABCD Study is a large-scale, prospective longitudinal study that began with participants aged 9-10, tracking them for 10 years. It includes a diverse sample of nearly 12,000 youth enrolled at 21 research sites across the United States. The study measures various aspects of brain development (including structural, task-based, and resting-state functional imaging), as well as social, emotional, and cognitive development, mental health, substance use, gender identity, sexual health, and biospecimens. In addition, the ABCD Study incorporates data from various external databases that provide insights into local environmental factors such as poverty, pollution, school conditions, and policy.

Aims of the Study:

1. Investigate how ACEs impact specific brain structures and functions during adolescence, and whether these effects vary by sex or puberty stage.
2. Explore the influence of BMI on brain development, particularly in reward-related regions such as the ventral striatum and prefrontal cortex, and whether these effects differ by sex or puberty stage.
3. Examine the combined effects of ACEs and BMI on brain biomarkers, with a focus on potential sex differences in how these factors interact and influence brain development.

To address the first aim, we explored the effects of sex and the experience of 12 subtypes of ACEs (e.g., sexual abuse, household mental illness) on specific brain structures (e.g., hippocampal volume, amygdala volume) and resting-state functional connectivity (e.g., Default Mode Network (DMN) within connectivity, Salience Network-Fronto-Parietal Network (FPN) between connectivity). Using mixed-effects models with False Discovery Rate (FDR) correction, we identified statistically significant interactions between specific ACE subtypes and sex. Preliminary findings indicate that, after FDR correction, the interaction between the ACE

subtype of sexual abuse and sex remained statistically significant for hippocampal volume, a region involved in memory formation, learning, and spatial navigation. Similarly, the interaction between the ACE subtype of household mental illness and sex remained significant for amygdala volume, a region associated with emotion processing, particularly fear, and social behavior. Specifically, boys who experience sexual abuse are more likely to exhibit a reduction in hippocampal volume compared to girls who experience sexual abuse. Similarly, boys exposed to household mental illness are more likely to show a reduction in amygdala volume than girls with the same experience. The study will also consider incorporating additional behavioral data, such as internalizing and externalizing symptoms from the Child Behavior Checklist (CBCL), as well as clinical data like BMI, to address more complex research questions.

By addressing the lack of sex-specific differences in the ABCD dataset, this study will provide novel insights into how early-life adversity and BMI influence brain development throughout adolescence, with a focus on sex-specific patterns. Understanding these mechanisms is crucial for developing tailored interventions for adolescents exposed to various types of ACEs or those with high BMI, potentially leading to more effective strategies for mitigating their impact on both mental and physical health.