Exploring Behavioral Patterns in Youth Predisposed to Bipolar Disorder and the Role of Interpersonal Trauma Using the Adolescent Brain Cognitive Development (ABCD) Dataset

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Abstract

Introduction: Bipolar Disorder (BD) is a severe, persistent disorder that causes functional impairment. Besides heritability, environmental factors, such as traumatic experience, impact the development of BD. Little is known about the early developmental signs of this disorder; therefore, this study aims to look at the impact of interpersonal trauma on the early developmental signs of BD. Specifically, differences in psychopathological behaviors were investigated between (1) at-risk children to controls and (2) at-risk children who experienced an interpersonal traumatic event to those who did not. **Methods**: Using the Adolescent Brain Cognitive Development (ABCD) dataset, participants with a first-degree relative with BD were identified ($N_{\text{at-risk}}$=625) and matched on sex and age to a control group (N_{control}=625). The Kiddie Schedule for Affective Disorders and Schizophrenia (KSADS) was used to assess interpersonal trauma and psychopathological symptoms. The trauma (N_{trauma}=198) and no trauma subgroups ($N_{\text{no trauma}}$=428) were built from the at-risk population. Group comparison was conducted on depressive, manic, and anxiety symptoms. **Results:** Compared to controls, at-risk children exhibited a significantly greater number of manic symptoms at baseline, and depression and anxiety symptoms at two-year follow-up. No significant differences were found between the trauma and no-trauma groups at either baseline or follow-up. **Discussion:** These results confirm the presence of early symptoms in at-risk children, in line with the staging model of BD. Extended longitudinal research is needed to further investigate the potential specific role of trauma on its early behavioral patterns.

Data availability statement and funding

Data used in the preparation of this article were obtained from the Adolescent Brain Cognitive Development[SM](ABCD) Study (https://abcdstudy.org), held in the NIMH Data Archive (NDA). This is a multisite, longitudinal study designed to recruit more than 10,000 children age 9-10 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, U24DA041123, U24DA041147. 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/consortium_members/. ABCD consortium investigators designed and implemented the study and/or provided data but did not necessarily participate in the 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.

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Methods : Using the Adolescent Brain Cognitive Development (ABCD) dataset, participants with a first-degree relative with BD were identified ($N_{at\text{-}risk}$=625) and matched on sex and age to a control group ($N_{control}$=625). The Kiddie Schedule for Affective Disorders and Schizophrenia (KSADS) was used to assess interpersonal trauma and psychopathological symptoms. The trauma (N_{trauma}=198) and no trauma subgroups ($N_{no\ trauma}$=428) were built from the at-risk population. Group comparison was conducted on depressive, manic, and anxiety symptoms.

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Discussion: These results confirm the presence of early symptoms in at-risk children, in line with the staging model of BD. Extended longitudinal research is needed to further investigate the potential specific role of trauma on its early behavioral patterns.

Keywords: adverse childhood experience, anxiety, bipolar disorder, children, depression, mania, mental disorders, risk factor

Bipolar disorders (BD) are severe, persistent mental disorders characterized by fluctuations in mood, energy, and activity levels (Nierenberg et al., 2023) and are marked by substantially reduced psychosocial functioning (Akers et al., 2019) and premature mortality (Kessing et al., 2015). The onset of BD typically occurs in adolescence and early adulthood (Faedda et al., 2019; McGrath et al., 2023). BD impairs people's lives, families, work, and general functioning (American Psychiatric Association, 2013). Its burden becomes substantially larger with unrecognized or misdiagnosed individuals (McIntyre et al., 2022). Misdiagnosis rates are high in BD leading to inappropriate treatment and negative outcomes (Fritz et al., 2017; Wolkenstein et al., 2011). For instance, when misdiagnosed as unipolar depression, administering antidepressants to those with bipolar disorder tends to trigger manic episodes and lead to poorer prognosis (Awad et al., 2007; Goldman et al., 2022; McIntyre et al., 2022). Delayed diagnoses and treatment also lead to increased mortality (Duffy et al., 2019) and health care cost (Singh & Rajput, 2006)

BD runs in families, as shown by its high heritability estimates (Algorta et al., 2015; Bienvenu et al., 2011; Birmaher et al., 2009). Concordance rates are higher in monozygotic than dizygotic twins, showing that BD is strongly dependent on genetics (Edvardsen et al., 2008; O'Connell & Coombes, 2021). Further twin studies showed heritable estimates of 0.85 to 0.93 (Kieseppa et al., 2004; McGuffin et al., 2003). Therefore, children with a first-degree relative with BD are considered at extremely elevated risk of developing BD themselves.

Moreover, BD has recently been suggested to develop through progressive stages, suggesting that symptoms slowly develop before reaching the full-blown manifestation of the disorder (Vieta et al., 2018). Duffy et al. (2019) mapped out a potential trajectory of BD's emerging course: children with a familial risk of developing BD might first experience sleep and anxiety symptoms, then minor mood symptoms, before presenting a major depressive disorder, and eventually develop a first full-blown BD episode (Duffy et al., 2019). Moreover, a review by Vieta and colleagues also endorsed sleep problems, anxiety, and mood disorders as vulnerability markers of the development of bipolar disorder in the offspring of parents with BD (Vieta et al., 2018).

Environmental factors, such as the experience of traumatic stressful events in youth, are also implicated in the development of psychopathology (Gur et al., 2019). Though many studies emphasize the importance

of considering familial and developmental factors when diagnosing children at risk for BD, some have specifically investigated the impact of traumatic experience on the clinical course of this disorder. Traumatic experiences can be differentiated into interpersonal (i.e., consequences of other people's direct actions) and non-interpersonal (i.e., other life-threatening events, such as severe accidents or illness) (Hughesdon et al., 2021). Interpersonal traumatic experiences, such as abuse and neglect, are particularly correlated with the development of BD (T. Li et al., 2023a). These traumatic events are more likely to occur in individuals diagnosed with BD compared to control groups (T. Li et al., 2023a; Palmier-Claus et al., 2016; Yang et al., 2024). Additionally, the frequency of childhood adversity among individuals with BD is relatively high, ranging from 45% to 68% (Daruy-Filho et al., 2011; T. Li et al., 2023a). Therefore, examining the impact of interpersonal traumatic events on the early stages of development of BD, rather than only its course, may be crucial for recognizing it early and potentially preventing its onset.

Therefore, the aim of this study was to observe the development of early psychopathological behaviors (e.g. mood disorders and anxiety) that are considered to illustrate the emergent course of BD, in children at risk of developing BD and more specifically those who experienced an interpersonal traumatic event. The Adolescent Brain Cognitive Development (ABCD) longitudinal dataset was used to compare, at both baseline and two-year follow-up, the psychopathological behaviors between (1) at-risk children and controls and between (2) at-risk children who experienced an interpersonal traumatic event and those who did not. The hypotheses were that (1) at-risk children would present more anxiety and mood symptoms than the control group and (2) that these symptoms would be more frequent in children at risk who have experienced a traumatic event when compared to those who did not.

2. Methods

2.1. Participants

2.1.1. Data Set

The Adolescent Brain Cognitive Development (ABCD) study is the largest longitudinal study ongoing in the United States on brain development and child mental health (Garavan et al., 2018). At baseline, 11,880 participants aged 9-10, and their families, were recruited through schools. The ABCD study ensured that participants were representative of the U.S. population with regard to gender, ethnicity, education, income level, and living environment (Adolescent Brain Cognitive Development, 2024). The study has been designed to take place over 10 years, where every year participants are tested on multimodal assessments such as physical, social, emotional, environmental, behavioral, and neuroimaging measures.

2.1.2 Family History

The main inclusion criterion for this study's at-risk group was for participants to have at least one first-degree relative with BD. Familial history was identified using the "ABCD Parent Family History Summary Scores" data. It includes a summary score of all that was reported by the caregiver on lifetime occurrences of different psychological issues in first- and second-degree biological relatives of the participants. Variables of interest were those that assessed whether "mania problems" were experienced by the father, mother, or siblings. In total, 625 participants were considered at-risk at baseline, and 545 were identified at the two-year follow-up. Adopted children were not uniformly excluded from the current study since these assessments specifically referred to biological first-degree relatives.

2.2. Measures

The ABCD study used the Kiddie Schedule for Affective Disorders and Schizophrenia- Lifetime Version (Kaufman et al., 1997) to assess mental health diagnoses and symptoms in children. The K-SADS-PL is a highly reliable semi-structured interview that assesses the manifestation of past and present psychopathological disorders in children, according to the Diagnostic and Statistical Manual for Mental Disorders 5^{th} edition (DSM 5) criteria. These interviews were administered both with the parent and the child, and a total score was calculated. Of interest to this study were the syndromes relating to mania/hypomania, depression, and anxiety.

2.3. Procedures

At baseline, 626 children with at least one first-degree relative who was reported to have experienced mania problems were classified into the at-risk group. This at-risk group was matched by sex and age to a control group with no first-degree relatives with mania problems. Within the at-risk group, participants were further divided into trauma and no-trauma subgroups based on whether they had experienced at least one of the nine interpersonal traumatic events according to the KSADS PTSD measure (Figure 1). Consequently, 198 children were classified in the trauma subgroup and 438 in the no-trauma subgroup. Due to missing data, only 555 children from the at-risk group were included in the two-year follow-up. At two-year follow-up, children who endorsed at least one interpersonal traumatic event either at baseline or at the follow-up were classified into the trauma subgroup, leading to 205 children in the trauma subgroup and 350 in the no-trauma subgroup at follow-up. The different traumatic events experienced by the children at baseline and follow-up are shown in **Figure 1** .

The KSADS-PL was used to assess whether participants experienced manic, depressive, and/or anxious symptoms. Anxiety disorders of interest were social anxiety disorder (SAD) and generalized anxiety disorder (GAD) because all others (panic disorder (PD), agoraphobia, and separation anxiety disorder) were not endorsed. The ABCD dataset included a summary score of the different psychopathologies' symptoms with a Boolean scoring method. Scores were divided into "past" and "present" timepoints indicating the time at which the KSADS-PL was administered within the ABCD study. This study only included the "present" timepoint.

2.4. Statistical Analysis

Statistical analyses were conducted using the R studio software (R version 4.4.1: 2024-06-14, (RStudio Team, 2024)). The at-risk and control groups were matched on sex and age using the MatchIt package and these were compared using the chi-square and Mann-Whitney U test, respectively, to confirm the matching procedure and compare the trauma sub-groups (Ho et al., 2011) .

Two statistical tests were conducted to compare depression, mania, SAD, and GAD symptomatology between the at-risk and control groups, and between the trauma and no-trauma subgroups. First, a Mann-Whitney U test assessed differences in the number of symptoms experienced across the various syndromes. This test was chosen for its ability to handle non-normally distributed data. Second, a chi-square test was conducted to determine if there was a significant difference in the proportion of children experiencing at least one symptom across the syndromes, depending on their group classification. These analyses were performed at both baseline and at a two-year follow-up.

3. Results

Demographic characteristics are outlined in **Table 1** .

3.1. At-Risk Versus Control

As shown in **Table 2** , at baseline, the at-risk group reported a significantly greater number of manic symptoms compared to the control group (p =0.04). At follow-up, the at-risk group experienced a significantly greater number of depressive (p =0.003), SAD (p =0.003), and GAD (p =0.033) symptoms. Although there was a trend towards a greater number of manic symptoms, at follow-up, in the at-risk group compared to the control group, this difference was not statistically significant (p =0.083).

As per **Table 3** , there was a trend seen in greater number of at-risk children who experienced at least one manic symptom at baseline (p =0.06). At follow-up, the number of children in the at-risk group who experienced at least one depressive, SAD, and GAD symptom was significantly greater than the control group (p= 0.005,p= 0.005, and p= 0.054 respectively).

3.2. Trauma Versus No Trauma

At both baseline and follow-up, there were no statistically significant differences in the number of symptoms

experienced between the trauma and no trauma subgroups across the four syndromes (**Table 4**). Furthermore, there was no significant difference in the number of children who experienced at least one symptom in any of the syndromes between the two groups (**Table 5**).

4. Discussion

The broader aim of this study was to add to the body of literature exploring early signs of development of BD, to aid in increasing early detection of BD and improving preventative measures. Specifically, it aimed to investigate early psychopathological behaviors in children at-risk of developing BD and to explore the association of interpersonal trauma with these behaviors. Using this large dataset, it was observed that the at-risk group experienced a higher number of manic symptoms compared to the control group at baseline, and more depressive, SAD, and GAD symptoms at the two-year follow-up. Additionally, the number of children endorsing at least one depressive, SAD, or GAD symptom was significantly greater in the at-risk group than in the control group at the two-year follow-up. Surprisingly, there was no statistically significant difference in the expression of psychopathological symptoms between the trauma and no-trauma subgroups within the at-risk group.

4.1. At Risk Versus Control Groups

At baseline, the at-risk group had a significantly higher number of manic symptoms endorsed and a higher number of children who had experienced at least one manic symptom. This finding is somewhat surprising given previous literature has observed that manic symptoms usually manifest at later stages in life (Duffy et al., 2019), raising the question of whether the current study accurately captured manic symptoms in this population. Some of the manic symptoms addressed in the semi-structured clinical interviews were irritability, decreased need for sleep, pressured speech, increased thoughts, flight of ideas, agitation, and distractibility. These symptoms are commonly present in attention hyperactivity disorder (ADHD), a neurodevelopmental disorder characterized by inattention, hyperactivity, and impulsivity (Y. Li et al., 2023). There is considerable overlap between these two disorders, and studies have explored ways to distinguish between them (Barden et al., 2023). While this study focuses on the number of symptoms rather than diagnoses, it is possible that ADHD symptoms may have contributed to the observed statistically significant differences in manic symptoms between the at-risk and control groups at baseline. That is, ADHD is much more frequent at the age tested (9-10 years), with an estimated prevalence of 10 to 10.5% among US children and adolescent (Y. Li et al., 2023).

The higher numbers of symptoms and incidences for depression and anxiety within the at-risk group at follow-up are in line with and contribute to previous literature (Duffy, 2018; Duffy et al., 2019; Faedda et al., 2019; Vieta et al., 2018). Specifically, this research aligns with Duffy et al.'s (2019) results and hypothesized trajectory of emerging disorders, given at-risk participants showed a greater number of depressive and anxious symptoms when they were older (11-12) at two-year follow-up, than at baseline (9-10). Furthermore, as per the literature, children with a predisposition to bipolar disorder seem to experience more depressive symptoms and episodes than healthy controls (Duffy, 2018), and half of patients who eventually meet diagnostic criteria for BD have experienced mood symptoms or episodes of major depressive disorder in their youth (Faedda et al., 2019).

4.2. Trauma Versus No Trauma Groups

When comparing the trauma and no-trauma at-risk subgroups, no statistically significant differences were found in the number of symptoms or incidences across all psychopathologies examined. However, this does not discount the potential role of trauma in the early developmental signs of BD. Existing literature provides substantial evidence linking interpersonal trauma and childhood trauma to the development, persistence, and recurrence of BD (Hillegers et al., 2004; T. Li et al., 2023a; Nierenberg et al., 2023; Watson et al., 2014; Wrobel et al., 2023). Therefore, it was unexpected to observe that having experienced an interpersonal traumatic event did not appear to be associated with differential early developmental signs of BD in this study.

It is also important to address that offspring children and adolescents of parents with BD are susceptible to the development of not only BD, but also other psychopathologies as well, such as depression and anxiety (DelBello & Geller, 2002). That is, even the no trauma group is still susceptible to developing BD and other psychopathologies which might account for why there was no statistically significant difference between the trauma and no trauma sub-groups. Also, the low number of children who experienced anxiety symptoms, ranging from two to seventeen, might also justify the observation that there was no statistically significant difference in the anxiety symptoms between the trauma and no trauma groups.

Previous research has typically investigated childhood trauma using retrospective cohorts (T. Li et al., 2023a; Palmier-Claus et al., 2016; Watson et al., 2014), which rely on individuals' recollections of their experiences. It is interesting to consider how a person's lived experience and personal history might shape their perceptions of trauma and its impact, potentially influencing clinical trajectories over time. Factually, patients with BD seem to have higher emotional memory which is associated with the high recall of traumatic or emotionally adverse events in those populations (Fijtman et al., 2020). This study investigated the *prospective* effects of traumatic events on early developmental signs of BD.

Furthermore, previous studies often used the Childhood Trauma Questionnaire (CTQ), which assesses emotional abuse, physical abuse, sexual abuse, emotional neglect, and physical neglect. Specifically, BD's clinical course has been most strongly correlated with trauma related to emotional abuse and emotional neglect (T. Li et al., 2023a; Rowe et al., 2024; Watson et al., 2014). It is important to note that the traumatic events assessed using the PTSD measure in this study do not overlap with these categories. This discrepancy may largely account for the unexpected result of no statistically significant differences in the number of symptoms or incidences of psychopathologies between the trauma and no-trauma groups.

Interestingly, the rate of participants who self-reported having experienced a childhood traumatic event was as high as 78% in previous studies (Rowe et al., 2024). In the current study, the percentage of children who claimed they had experienced a traumatic event was only 30% at baseline and 37% at two-year follow-up. Children may have been reluctant to share their traumatic experiences, particularly since five of the nine interpersonal traumatic events inquired about involved their family or home environment, to which they would be returning. Therefore, this study might not have an accurate representation of children who actually experienced trauma.

4.3. Limitations

This study had a few limitations. First, the at-risk group was primarily chosen to have at least one first-degree relative with a history of mania. However, the assessment of mania for first-degree relatives was based on self- or other-report, and not confirmed by a structured interview. Second, as discussed, this ABCD study is collecting prospective data and the children's report on their recent traumatic experiences might be underestimated. Third, as this study did not explore all potential diagnoses and used symptoms rather than diagnostic criteria, the overlap between manic and ADHD symptoms warrants caution when interpreting the results.

4.4. Future Directions

This study contributes to the growing body of literature investigating early onset signs of bipolar disorder (BD). It aligns with previous research suggesting that BD has a progressive nature, with psychopathological symptoms appearing before the first full-blown manic episode (Duffy et al., 2019; Vieta et al., 2018). Even though this study bore non-significant results in the comparison of the trauma and the no trauma subgroups, research must be conducted to investigate the impact of interpersonal trauma on early developmental signs of BD. Retrospectively, childhood interpersonal traumatic events have been shown to lead to earlier development and worse prognosis of BD (T. Li et al., 2023b; Palmier-Claus et al., 2016). Therefore, more longitudinal studies are necessary to further explore the progression of BD in at-risk children and to investigate the effect of interpersonal trauma on its development.

Sustaining this line of inquiry is crucial because it provides insight on early developmental sign of BD.

Clinicians will need to exercise caution when diagnosing at-risk children or adolescents with depression or anxiety. Furthermore, adapted care, such as psychoeducative and psychosocial interventions, should be administered in such scenarios (Cotton et al., 2020). This could potentially reduce misdiagnoses of individuals manifesting BD and lead to improved prognoses.

not-yet-known not-yet-known

not-yet-known

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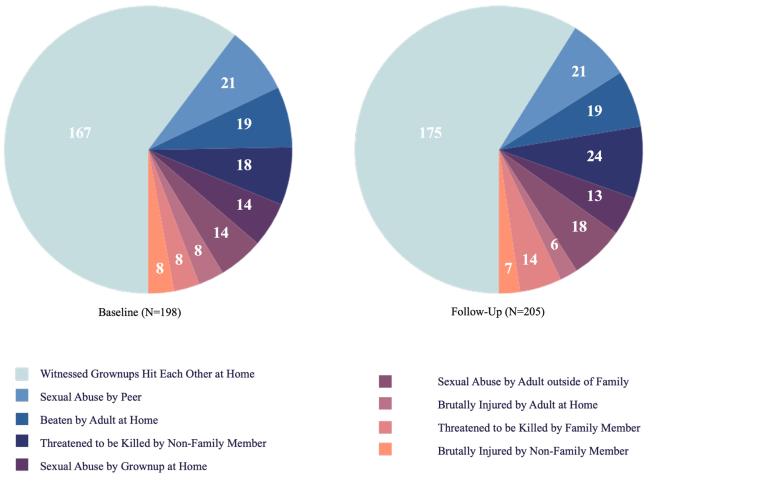
Figure 1

Number of Traumatic Events Experienced by children at Baseline and Two-Year Follow-Up



Note. Children might have experienced one or more traumatic events, which is why which is why the total number of events exceeds $N_{baseline}$=198 and $N_{follow\text{-}up}$=205

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Tables.docx available at https://authorea.com/users/839982/articles/1230389-exploring-behavioral-patterns-in-youth-predisposed-to-bipolar-disorder-and-the-role-of-interpersonal-trauma-using-the-adolescent-brain-cognitive-development-abcd-dataset