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ORIGINAL ARTICLE

Adverse Childhood Experiences Among Inpatient Youths with Severe and Early-Onset Psychiatric Disorders: Prevalence and Clinical Correlates

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Abstract This study aimed to determine the prevalence and the clinical correlates of Adverse Childhood Experiences (ACEs) among 158 inpatient youths with two types of severe psychiatric disorders. ACEs were retrospectively collected with the ACEs scale and the List of Threatening Experiences Questionnaire in 77 patients hospitalized for a catatonic syndrome (average age 15.2 years) and 81 for a manic or mixed episode (average age 15.7 years). ACEs were frequent in youths suffering from bipolar disorder type I (BD-I) (58 %) and from catatonia (57 %), with around one quarter exposed to severe abuse (i.e., physical/sexual/emotional abuse or physical/emotional neglect). Youths with BD-I were more likely to be exposed to family violence compared to those with catatonia. Youths who had been exposed to ACEs did not exhibit a more severe presentation or a poorer response to treatment compared to others, either in the bipolar group or in the catatonic group.

Keywords Catatonia · Early-onset bipolar disorder · Adolescence · Abuse · Adverse life events

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Introduction

Child maltreatment and related experiences are common risk factors for poor mental health [1–5]. The notion of Adverse Childhood Experiences (ACEs), coined by Felitti et al. [6], has been recommended by the WHO to facilitate comparison between studies conducted to determine the impact of child adversity on mental and physical health. ACEs referred to abuse (emotional, physical, sexual), neglect (emotional, physical) and growing up in households with various stressors (such as domestic violence), relational stress (such as separation or divorce), excessive use of alcohol or drugs among members, or criminal behavior among parents [7]. Children or adolescents who have been exposed to ACEs have an increased risk for behavioral problems or internalized symptoms [4, 8]. There is also evidence that ACEs could impact the course of severe psychiatric disorders such as schizophrenia or bipolar disorder [9].

The role of abuse and maltreatment on the onset and the natural history of bipolar disorder has received much attention in recent years [9, 10]. Approximately 50 % of bipolar disorder patients have a history of severe trauma or abuse during childhood [9–12]. For example, early sexual abuse has been associated with an earlier age of bipolar disorder onset, a greater frequency of comorbidity, increased suicidal ideation and greater resistance to treatment [11]. However, results may be difficult to interpret due to study limitations. Firstly, most studies were conducted on outpatient samples and included sub-threshold forms of bipolar disorder (e.g., Bipolar Disorder-Not Otherwise Specified, or cyclothymia) [13–16]. Persistent mood swings and emotional lability, which may characterize these sub-threshold forms of bipolar disorder, have been associated with interpersonal trauma and post-traumatic stress [4]. For this reason, the relation between

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maltreatment and bipolar disorder in youths may be distorted by using a broader definition of the disorder or by focusing on the less severe presentation. Secondly, it has been raised that early adversity could mediate the relationship between genetic vulnerability and the early onset of the illness [17]. Then, the distinct clinical presentation and the poor prognosis of youths with bipolar disorder and ACEs could result from an earlier onset of the disease [4, 18]. Comparing the clinical feature of the first manic/mixed episode of youths with and without ACEs limits the impact of all possible confounders associated with an early onset (e.g., in terms of medication received or associated substance use).

Catatonia is as a psychomotor syndrome that can be associated with a variety of psychiatric and medical disorders. Pediatric catatonic episode has received increasing attention in recent decades [19, 20], in particular due to its potential severe and lethal consequences at this age with a 60-fold increase in the risk of premature death [21]. The historical and contemporary literature reviewed by Dhossche et al. [22] suggests that traumatic factors may play an important part in the onset of this disorder. Kahlbaum [23] mentioned in his seminal paper that stressful events frequently occurred prior to the onset of an episode. Kanner [24] reported that a traumatic event could trigger cataleptic manifestation in children. Some similarities have also been reported between the emotional and motor symptoms found during a catatonic episode and those found during an acute stress-reaction in children suffering from severe deprivation or abuse [25]. Some core motor symptoms of catatonia (i.e., immobility/stupor; staring; negativism; mutism; echopraxia) are also found in anaclitic depression described by Spitz in the case of deprived institutionalized children [26]. Similar features may also be found in the Pervasive Refusal Syndrome described among refugee children, and in quasi-autism syndrome in Romanian institution-reared children [27]. Moskowitz [28] suggested that the extreme withdrawal found in catatonia might take its evolutionary heritage from the immobilization reflex exhibited by primates during a fear-response. If the high rate of adverse events in youth with catatonic episodes is confirmed, it may help clinicians to recognize and manage this disorder more effectively. This is of considerable relevance as catatonia is a largely under-diagnosed disorder in youths [19, 20].

From 1993 to 2013, we prospectively followed up one sample of youths with catatonia (n = 77) [19, 21, 29–31] and another sample of youths with bipolar disorder type 1 (BD-I) (n = 81) [32–34]. In each group, we investigated their sociodemographic characteristics, clinical characteristics, associated medical and psychiatric conditions, developmental histories and treatment responses. We conducted a cross-sectional study to study and compare the prevalence of ACEs among inpatient youths with a catatonic episode and BD-I, and to determine whether the presence of ACEs was associated with specific clinical presentations and/or a poor response to treatment for each disorder.

Methods

Participants and Setting

We assessed all patients admitted to the Department of Child and Adolescent Psychiatry at University Hospital La Pitié-Salpêtrière, Paris, between 1993 and 2013 for a catatonic episode or BD-I. To obtain a diagnosis of catatonia, patients had to present at least two motor symptoms, or one motor symptom and one non-motor symptom indicative of severe behavioral and emotional impairment. To delineate catatonic signs we used the 14-item Bush–Francis catatonia rating scale (BFCRS) to which we added items for six symptoms taken from the historical description of pediatric catatonia [19, 29, 35]. Symptoms listed in the modified BFCRS included negative withdrawal symptoms (e.g., mutism, negativism, social withdrawal, refusal to eat), catalepsy (e.g., posturing, waxy flexibility), abnormal movements (e.g., mannerisms, stereotypes, automatic compulsive movements) and echo phenomenon (e.g., echolalia, echopraxia). The bipolar sample included all cases meeting a DSM-IV discharge diagnosis of BD-I (a manic or mixed episode). The Diagnostic Interview for Genetic Studies (DIGS) was administered to confirm the index episode [36]. In the catatonic group, we excluded the participation of patients who presented extra-pyramidal syndrome secondary to antipsychotics. No exclusion criteria were applied to the BD-I group. The procedure for the recruitment and clinical description of the samples has previously been reported both for the catatonic sample [19, 21, 30, 31] and for the BD-I sample [33, 37]. We included 81 subjects in the BD-I group, and 77 subjects in the catatonic group, aged from 9 to 19 years old. For 2 patients a manic episode was associated with catatonic features and these subjects were excluded from the analysis. Among youths with catatonia, 55 % (n = 41) had schizophrenia, 30 % (n = 22) a major depressive episode and 16 % (n = 12) an atypical developmental history (i.e., autistic spectrum disorder or intellectual disability). One subject with manic episode exhibited a neuropsychiatric manifestation of systemic lupus erythematosus; whereas 21 of the 75 catatonic subjects presented a medical condition (auto immune condition: n = 5; infectious encephalitis: n = 1; epileptic encephalopathy: n = 3; iatrogenic encephalopathy: n = 2; genetic and metabolic condition: n = 10). The studies were conducted according to the rules of the hospital ethics committee.

Measurement

We conducted a systematic assessment within the patients' first week of admission and repeated this assessment at discharge. Most patients were interviewed after the acute phase of their illness. All questionnaires were administrated by experienced psychiatrists who were trained in their use and who were blind to the diagnosis given at the index episode. The following information was examined:

1. Socio-demographic data (age, sex, family, social-economic status SES) were collected. SES was estimated by the clinician on the basis of parental income, parental education level, and adequate housing. SES was scored as high, low or intermediate.
2. A semi-structured interview was conducted to evaluate a patient's personal and family histories of psychiatric and medical disorders. Clinical examination was performed to search for a medical condition (e.g., neurological conditions, intoxication, auto-immune diseases) associated with the psychiatric disorder.
3. The modified BFCRS was completed to test for the presence and severity of catatonic symptoms [19, 29, 35] and the Young Mania Rating Scale (YMRS) to evaluate the severity of manic symptoms. Internal validity of these scales were reported as very good (for YMRS kappa = 0.93, for BFCRS kappa = 0.83) [38, 39]. We considered catatonia as chronic if the patient had catatonic symptoms after discharge from the index episode.
4. The Clinical Global Impression rating scales [40] were administrated to assess symptom severity at admission (Severity scale, CGI-S) and treatment response (Improvement scale, CGI-I) [41]. The CGI-S asks the clinician one question: "Considering your total clinical experience with this particular population, how mentally ill is the patient at this time?". Possible answers range from 1 (normal, not at all ill) to 7 (among the most extremely ill patients). CGI-I was completed at discharge to measure the change in the severity of the patient's illness. Scores range from 1 (very much improved) to 7 (very much worse). The validity of the CGI-S and CGI-I have been regarded as excellent [41]. The Global Assessment Functioning scale (GAF) was administrated to assess how subjects' symptom severity affected functioning at admission and at discharge.
5. Lifetime and current comorbid psychiatric diagnoses were assessed using the DIGS, version 2.0, a semi-structured diagnostic interview developed by the Human Genetics Initiative of the U.S. National Institute of Mental Health [36]. The DIGS elicits information necessary to diagnose psychotic, mood, anxiety, substance use and eating disorders by DSM-IV criteria. In cases of intellectual disability (ID) or autistic spectrum disorder (ASD), diagnoses were confirmed using the parental Autism Diagnostic Interview—Revised [42] and the Wechsler Intelligence Scales. Both scales are used routinely in the department.
6. Treatments, such as pharmacological treatments and electroconvulsive therapy (ECT), were recorded for each case. The efficacy of first-line treatment was reported using the CGI-I. In the catatonic group, benzodiazepines were considered as a first option. In the BD-I group, we estimated the response to the first psychotropic treatments lasting more than 1 week prescribed during hospitalization after the diagnosis, regardless of the type (i.e., antipsychotics, normothymics, anxiolytics) [31, 32]. The duration of the psychiatric episode, the duration of hospitalization, the type of disorder onset (e.g., <10 days = acute; ≥10 days = insidious) and the duration of the episode were noted.

List of Threatening Experiences Questionnaire

All medical and paramedical entries in the chart of all patients in both cohorts were reviewed by XB for direct references to childhood abuse, maltreatment or other traumas. Information obtained during the hospitalization and outpatient follow-up were examined. The experience of life-events in the 6 months prior to admission was reported using the List of Threatening Experiences Questionnaire (LTQ) [43]. This instrument was designed to detect events carrying a significant long-term threat and particular salience for mood disorders [44]. Previous analyses have shown that the LTQ successfully captures 83 % of the life events covered in the more extensive life-event interviews [43]. LTQ has previously been used in pediatric samples (excluding questions referring to professional activities) [45]. The events included: serious illness or injury to a participant or his/her close relative, death of a close friend or relative, the break-up of a steady relationship, suspension from school, problems with the police, and serious conflicts with a close friend. A random subsample of 22 cases (Catatonia: n = 11; BD-I: n = 11) was blindly reviewed by AC. The inter-rater agreement metrics were low: Kappa = 0.26; Intra-Class Correlation = 0.26. By consulting each medical chart, we noticed that differences between raters were due to disagreement regarding the dating of events related to retrospective assessment.

Adverse Childhood Experiences Scale

Childhood events were assessed using the Adverse Childhood Experiences (ACE) scale which consists of 10

questions pertaining to those aged 18 or younger [6]. The ACE scale includes five categories of childhood abuse: psychological abuse (2 questions), physical abuse (2 questions), contact sexual abuse (2 questions), emotional neglect (2 questions) and physical neglect (2 questions). In addition, the ACE inquiries about four categories of exposure to household dysfunction during childhood: parental separation or divorce (1 question), exposure to substance abuse (1 question), mental illness (1 question), violent treatment of the mother or stepmother (3 questions), and incarceration (1 question). We used the subscales previously defined by Felitti et al.: a major ACE was endorsed for one or more positive answer to the first five items of the scale (i.e., physical abuse and/or psychological abuse and/or sexual abuse and/or physical or emotional neglect); and exposure to household dysfunction for at least one positive answer to the last five items (i.e., exposure to parental separation or divorce and/or parental substance abuse and/or parental mental illness and/or familial violence such as violent treatment of mother or stepmother and/or parental incarceration). The inter-rater agreement metrics were good to excellent: Kappa = 0.59; Intra-Class Correlation = 0.88. To further investigate the concurrent validity of ACE, we searched for correlation between ACE and social outcomes from official data (e.g., reports to child-protection agencies; home educative assistance). As expected, ACE strongly correlated with the social outcome variables.

Statistical Analyses

Comparisons of categorical data between participants in each group were conducted using Pearson's Chi square or Fisher's Exact Test. Comparisons of numeric variables between groups were conducted using the Student Test and the Wilcoxon's Rank-Sum Test. Differences were considered as significant at $p \leq 0.05$. Subjects with comorbid BD-I and a catatonic episode were excluded from analysis (n = 2). A history of ACE was not available for five subjects in the catatonic group. The main clinical characteristics of the subjects were comparable between those included in the analysis and those who were not. The first objective was to determine the prevalence of ACE in each group and to describe the types of adverse events. The second objective was to compare the clinical characteristics and response to treatment in each group with and without major ACE. Dichotomizing into presence or absence of severe childhood abuse regardless of the nature of maltreatment facilitates the interpretation of findings and follows current recommendations taking into account the high rate of correlation between abuse categories [46]. However, as categorical approach may be associated with a substantial loss of information while modeling a dimensional construct such as maltreatment; we ensured that the main findings were consistent when the ACE score was used as a continuous quantitative variable. Analyses comparing the sub-type of abuse or the nature of adverse events presented in each group have to be regarded as mainly exploratory. Corrections for multiple testing were not performed given that we estimated that the costs of type II error outweigh the costs of type I error in this context. R-software was used to conduct all of the analyses. Given that patients were enrolled over a long period, we compared subjects recruited during the first decade versus the second one to ensure the absence of bias related to study duration.

Results

We prospectively included 75 patients with catatonia and 81 patients with BD-I from 1993 to 2013. Table 1 summarizes the main socio-demographic and clinical characteristics of our sample. Of note, for catatonic participants, neither severity measures (GAF admission $p = 0.433$, CGI-S $p = 0.489$, BFCRS total score $p = 0.264$) nor efficacy measures (Δ-GAF: $p = 0.113$, % of benzodiazepine responders: $p = 1.0$) differed between subjects hospitalized before versus after 2003. Similarly, in the bipolar group neither severity measures (GAF admission: $p = 0.558$, CGI-S: $p = 0.778$, YMRS total score: $p = 0.771$) nor efficacy measures (Δ-GAF: $p = 0.410$, efficacy of first-line pharmacological treatment: $p = 0.999$) differed according to the period of hospitalization.

Prevalence of Adverse Events in Youth with Severe Psychiatric Disorders

Table 2 summarizes the adverse experiences found among the youths with BD-I and among those with catatonia. The sum score of the ACE questionnaire was comparable between the two groups ($M = 1.64$, $SD = 1.9$ in the catatonic group; $M = 1.86$, $SD = 1.99$ in the BD-I group; $p = 0.259$). A history of severe maltreatment was found in 24 % of subjects in the catatonic group and 21 % of those with BD-I. The most frequent abuse reported was sexual abuse, followed by severe neglect, and less frequently psychological abuse and physical abuse. At least one report had been sent to child-protection agencies for 17 % of the patients in the catatonic group and for 14 % of the patients in the BD-I group. A placement in foster care had occurred in the case of 11 % of youths in both the catatonic group and in the bipolar group. There was not a significant difference between the two groups in terms of stressful life events: 31 subjects in the catatonic group had experienced

Table 1 Demographic and clinical characteristics of children and adolescents with catatonia and bipolar disorder

	Catatonic group (n = 75)	Bipolar group (n = 81)	*p*
Socio-demographic characteristics			
Gender, female, n (%)	26 (35 %)	46 (57 %)	0.006*
Age (years) (mean ± SD)	15.17 ± 2.95	15.70 ± 1.89	0.181
Socio-economic status, good and middle, n (%)	51 (68 %)	51 (63 %)	0.778
Clinical characteristics			
Onset (≤10 days), n (%)	36 (47 %)	30(37 %)	0.278
Duration, acute, n (%)	43 (57 %)	na	–
GAF admission (mean ± SD)	19.26 ± 8.55	22.90 ± 7.80	0.008
GAF discharge (mean ± SD)	51.73 ± 14.69	63.93 ± 12.93	0.001**
CGI-S (mean ± SD)	6.74 ± 0.45	6.01 ± 0.70	0.001**
CGI-I (mean ± SD)	1.61 ± 0.97	1.91 ± 0.60	0.068
YMRS (mean ± SD)	na	22.16 ± 6.01	
BFCRS (mean ± SD)	21.87 ± 7.50	na	
Etiology			
Medical condition, n (%)	21 (27 %)	1 (1 %)	0.001**
Developmental history (ASD, ID), n (%)	12 (17 %)	8 (11 %)	0.163
Treatment			
Use of ECT, n (%)	11 (15 %)	2 (2 %)	0.014*
Efficacy of first line pharmacological treatment, n (%)	66 (88 %)	60 (80 %)	0.039

na not available, *GAF* Global Assessment of Functioning scale, *CGI-S* Clinical Global Impressions-Severity of Illness scale, *CGI-I* Clinical Global Impressions-Improvement scale, *BFCRS* Bush and Francis Catatonia Rating Scale, *YMRS* Young Mania Rating Scale, *ECT* electroconvulsive therapy, *ASD* autistic spectrum disorder; catatonia was considered as chronic if subjects had catatonic symptoms after discharge from the index episode

* $p \leq 0.05$; ** $p \leq 0.001$

such an event in the last 6 months (44 %), compared to 35 subjects in the bipolar group (43 %) ($p = 1.000$). Exposure to familial violence was twice as likely to be found among the youths with BD-I, as opposed to those in the catatonic group (33 vs. 17 % respectively, $p = 0.038$).

Clinical Features and Treatment Outcomes in Youths Presenting Severe Psychiatric Disorders with and Without Adverse Childhood Experiences

The clinical features and treatment outcomes are presented in Table 3 for the catatonic group and in Table 4 for the BD-I group. The severity of the symptoms and the functional impairments did not significantly differ between the subjects with and without major ACE in both groups. The frequency of medical condition associated and the rate of developmental disorder comorbid were comparable in the youths suffering from catatonia, with and without major ACE. Similar findings were observed in the BD-I group. In the catatonic group, a longer duration of hospital stay was noted in the subjects with major ACE, compared to those without major ACE ($M = 27.5$ days, $SD = 14.2$, vs. $M = 18.5$ days, $SD = 11.8$ respectively; $p = 0.020$). This was not observed in the BD-I group. Youths with BD-I, who had experienced major ACE, presented a better response to treatment which was measured by comparing the difference between their GAF score at entrance and at discharge to subjects without major ACE ($M = 47.2$, $SD = 9$ vs. $M = 39.7$, $SD = 12.7$ respectively; $p = 0.034$). The effectiveness of the first-line pharmacological treatment (94 vs. 71 % respectively; $p = 0.051$) also tended to be higher among these youths. However, in the catatonic group no difference in the response to treatment was found between those with a major ACE and those without.

Discussion

The first objective of this study was to determine the prevalence of ACE in two severe and early-onset psychiatric disorders in children and adolescents (i.e., catatonia and BD-I). The rate of ACEs was similar and strikingly high in both groups with more than half of the subjects presenting at least one ACE. Also, youths with BD-I appeared to be more frequently exposed to family violence than those with catatonia. The second objective was to compare the severity of each disorder between the subjects

Table 2 Adverse life experiences among children and adolescents with catatonia and severe bipolar disorder

	Catatonic group (n = 70)	Bipolar group (n = 81)	*p*
ACE scale			
1. Psychological abuse	4 (6 %)	6 (8 %)	0.581
2. Physical abuse	5 (7 %)	2 (3 %)	0.358
3. Sexual abuse	9 (13 %)	9 (12 %)	0.811
4. Emotional neglect	5 (7 %)	6 (8 %)	1
5. Physical neglect	4 (6 %)	4 (5 %)	1
6. Parental separation or divorce	10 (14 %)	13 (17 %)	0.866
7. Exposure to parental substance abuse	7 (10 %)	9 (12 %)	0.975
8. Exposure to parental mental illness	33 (47 %)	30 (38 %)	0.368
9. Exposure to familial violence (e.g., violent treatment of mother)	12 (17 %)	26 (33 %)	0.038*
10. Incarceration	2 (3 %)	2 (3 %)	1
Major ACE	17 (24 %)	16 (21 %)	0.755
Exposure to household dysfunction	40 (57 %)	42 (54 %)	0.813
Positive answer to at least one ACE item	40 (57 %)	47 (58 %)	0.828
Total ACE score	1.64 (1.94)	1.86 (1.99)	0.259
LTQ scale			
1. Serious illness, injury or an assault	12 (17 %)	4 (5 %)	0.036*
2. Serious illness, injury or assault of close relative	10 (14 %)	7 (9 %)	0.451
3. Death of first-degree relative	3 (4 %)	12 (15 %)	0.045*
4. Death of a close family friend or other relative	5 (7 %)	12 (15 %)	0.188
5. Break up of a steady relationship	2 (3 %)	7 (9 %)	0.224
6. Serious problem with a close friend, neighbour or relatives	2 (3 %)	0 (0 %)	0.444
7. Problems with the police involving a court appearance	0 (0 %)	1 (1 %)	1
8. Valued item lost or stolen, bullying	0 (0 %)	1 (1 %)	1
Total LTQ score	0.53 (0.68)	0.58 (0.75)	0.816
Any recent life event (at least one in the last 6 months)	31 (44 %)	35 (43 %)	1
Administrative source			
Report to child-protection agencies	12 (17 %)	11 (14 %)	0.776
Home educative assistance	8 (11 %)	7 (9 %)	0.823
Foster care placement	8 (11 %)	8 (11 %)	1

* $p \leq 0.05$; mean (standard deviation) for total score

with and without a history of major ACEs. In these samples, neither the BD-I nor the catatonic group presented a significant difference in clinical presentation according to the presence of major ACEs. The effectiveness of treatment was comparable in the subjects with and without major ACEs among youths with catatonia; however, it was higher in the subjects with both BD-I and a history of ACEs.

Prevalence of Adverse Events in Youth with Severe Early-Onset Psychiatric Disorders

These findings are consistent with previous studies stressing the high prevalence of ACEs in many psychiatric disorders in children and adolescents: e.g., in bipolar disorder [9, 11, 13, 15, 46–48], in anxiety [1, 8], or in depression [1, 3, 6]. In general, maltreated individuals with a psychiatric disorder tended to have an earlier age of onset, greater symptom severity, more comorbidity, an increased risk for suicide, and a poorer response to treatment than non-maltreated individuals with the same diagnoses [3]. It has been suggested that childhood maltreatment could be a strong, but non-specific, risk factor for the onset of psychiatric disorder in childhood [3, 5, 48]. In addition, the presence of ACEs has been associated with a wide range of cognitive and affective impairments involved in the domains of internalizing and externalizing symptoms, rather than with an increase in individuals' liabilities to one specific disorder [5]. The longlasting consequences of early environmental stressors may be underpinned by structural and functional brain differences which involve the autonomic

Table 3 Demographic, clinical characteristics and treatment response in catatonic group with and without major adverse childhood events

	No major ACE (n = 53)	Major ACE (n = 17)	*p*
Socio-demographic characteristics			
Gender, female, n (%)	12 (23 %)	9 (53 %)	0.043*
Age (mean ± SD)	15.6 ± 2.9	13.9 ± 2.3	0.027*
Socio-economic status, good and middle, n (%)	38 (72 %)	7 (41 %)	0.013*
Clinical characteristics			
Onset (≤10 days), n (%)	23 (43 %)	9 (53 %)	0.536
GAF admission (mean ± SD)	19.2 ± 6.2	21.8 ± 13.2	0.489
GAF discharge (mean ± SD)	51.4 ± 15.3	54.1 ± 13.0	0.600
CGI-S (mean ± SD)	6.7 ± 0.5	6.9 ± 0.3	0.230
CGI-I (mean ± SD)	1.7 ± 1	1.5 ± 0.8	0.424
BFCRS (mean ± SD)	22.3 ± 6.8	18.6 ± 6.8	0.082
Etiology			
Medical condition, n (%)	16 (30 %)	3 (18 %)	0.495
Developmental history (ASD, ID), n (%)	17 (32 %)	6 (35 %)	1
Treatment response			
Δ-GAF (mean ± SD)	31.2 ± 12.7	32.0 ± 12.8	0.562
Duration of stays (days) (mean ± SD)	18.5 (11.8)	27.5 (14.2)	0.020*
Use of ECT, n (%)	7 (13 %)	1 (6 %)	0.743
Effectiveness of first line pharmacological treatment, n (%)	44 (83 %)	15 (88 %)	0.500

GAF Global Assessment of Functioning scale, *CGI-S* Clinical Global Impressions-Severity of Illness scale, *CGI-I* Clinical Global Impressions-Improvement scale, *BFCRS* Bush–Francis Catatonia Rating Scale, *ASD* autistic spectrum disorder, *ID* intellectual disability, *Δ-GAF* difference between the GAF score at discharge and at admission

* $p \leq 0.05$

nervous system (ASN) and the hypothalamic–pituitary–adrenal (HPA) axis [49, 50]. Epigenetic modifications in stress-response systems and neurotrophic factors may embody the effect of such environmental factors on the brain's development [51].

This is the first study in which the prevalence of abuse/maltreatment has been examined in children and adolescents with catatonia. Our findings are consistent with previous case studies suggesting that childhood adversities could occur at a high rate in youths with catatonia [22, 52]. There is still much left to do in order to understand the role that such events may play in the development of certain types of catatonia. Fink and Taylor [53] and Mann et al. [54] suggested that extreme emotional stress experienced in a context of ACEs might durably affect the threshold for limbic activation. Higher amygdala reactivity might, therefore, disrupt the connection between the frontal motor cortex and the basal ganglia regions involved in the automatic motor activity provoking perceptual-motor dissociation in catatonia (e.g., the tonic immobility found during catalepsy or stupor). Interestingly, the rate of ACEs was roughly comparable in the youths with catatonia whatever the etiology (i.e., with or without an organic etiology). This finding is in line with the hypothesis that ACE could predispose [28] or precipitate [21, 22] catatonia in vulnerable children.

The prevalence of abuse/maltreatment in youths with BD-I should be interpreted with regard to rates found in other clinical studies conducted in pediatric samples. Based on retrospective chart review, Marchand et al. [15] found that 53 % of inpatient youths with BD-I had experimented maltreatment. In the COBY study, approximatively 20 % of youths with bipolar spectrum disorders reported physical or sexual abuse [55].

Exposure to Family Violence and Risk of Early-Onset of Psychiatric Disorder

Exposure to family violence was high in both diagnostic groups but was marginally higher in the BD-I group (33 %) than in the catatonic group (17 %). This is in line with previous studies where difficulties in the parent–child relationship are reported among families with a child with bipolar disorder [14]. Considering the cross-sectional design of this study, we cannot make any causal assumption based on this result. Several hypotheses have been made to explain the high rate of familial violence in children and adolescents with bipolar disorder. First of all,

Table 4 Demographic, clinical characteristics and treatment response in BD-I group with and without major adverse childhood events

	No major ACE (n = 61)	Major ACE (n = 16)	*p*
Socio-demographic characteristics			
Gender, female, n (%)	32 (53 %)	11 (69 %)	0.377
Age (mean ± SD)	15.9 ± 1.9	15.1 ± 1.7	0.117
Socio-economic status, good and middle, n (%)	42 (69 %)	6 (38 %)	0.046*
Clinical characteristics			
Acute onset, n (%)	24 (39 %)	4 (25 %)	0.548
GAF admission (mean ± SD)	23.1 ± 7.9	20.6 ± 6.8	0.269
GAF discharge (mean ± SD)	62.7 ± 13.8	67.8 ± 9.5	0.184
CGI-S (mean ± SD)	6 ± 0.7	6.1 ± 0.6	0.514
CGI-I (mean ± SD)	2 ± 0.6	1.8 ± 0.6	0.402
YMRS (mean ± SD)	21.9 ± 6.1	23.6 ± 6.1	0.327
Etiology			
Medical condition, n (%)	1 (2 %)	0 (0 %)	1
Developmental history (ASD, ID), n (%)	12 (20 %)	5 (31 %)	0.42
Clinical characteristics			
Mixed episode, n (%)	24 (39 %)	3 (19 %)	0.269
Psychotic features, n (%)	38 (62 %)	8 (50 %)	0.725
Treatment response			
Δ-GAF (mean ± SD)	39.7 ± 12.7	47.2 ± 9	0.034*
Duration of stays (days) (mean ± SD)	80.4 ± 51.4	81.2 ± 49.7	0.957
Use of ECT, n (%)	1 (2 %)	1 (6 %)	0.716
Effectiveness of first line pharmacological treatment, n (%)	43 (71 %)	15 (94 %)	0.051

GAF Global Assessment of Functioning scale, *CGI-S* Clinical Global Impressions-Severity of Illness scale, *CGI-I* Clinical Global Impressions-Improvement scale, *YMRS* Young Mania Rating Scale, *ASD* autistic spectrum disorder, *ID* intellectual disability, *Δ-GAF* difference between the GAF score at discharge and at admission

* $p \leq 0.05$; ** $p \leq 0.001$

given the heritable traits associated with the genetics of bipolar disorder, certain aspects of parental psychopathology could be the expression of a bipolar trait more frequently found among relatives, such as impulsivity [56]. Unaffected parents of youths with bipolar disorder may be prone to presenting impulsive behaviors, including reactive aggressions. Especially as higher genetic loading is reported in early onset bipolar disorder compared to later onset [57]. In line with this, a high rate of mental health challenges has been found among parents of youths with BD-I in this study. Secondly, some aspects of family functioning may facilitate an earlier development of bipolar disorder and might, therefore, be frequently noted among youths with the disorder [58–60]. For example, Geller et al. [58] found that a low rate of maternal warmth in families with pediatric bipolar disorder predicted an earlier recurrence of mood episodes over eight years among child and preadolescent bipolar patients. Miklowitz et al. [59] reported an association between highly critical attitudes among parents of bipolar teenagers and a more deteriorative course of illness over 2 years in a treatment program. Furthermore, Schenkel et al. [60] observed that the parent–child relationships in families whose youths presented pediatric bipolar disorder were characterized by significantly less warmth, affection, and intimacy; they also presented more quarreling and forceful punishment compared to other youths. Finally, children with bipolar disorder may experience more negative life-events as a result of the behaviors associated with their symptoms [13]. In turn, such negative life events could affect their relationships with their parents. Future studies are warranted to replicate the high rate of family dysfunctions in children with catatonia and bipolar disorder.

Clinical Features and Treatment Outcomes in Youths with Severe Psychiatric Disorders Who Experienced Adverse Events

A history of major ACEs was not associated with distinct clinical features among bipolar youths and among those with catatonia. These findings are not consistent with previous studies conducted in adults [9, 12, 48, 61].

Unexpectedly, the treatment effectiveness for BD-I was higher in youths with a history of major ACEs compared to those without. The discrepancies with regard to the previous report may stem from the specificities of the sample recruited, i.e., inpatient children and adolescents referred to a university hospital for resistant or severe psychiatric disorder. Considering the high rate of comorbidity between anxiety disorder and bipolar disorder in youth [62], specifically in clinical samples, we cannot exclude that some subjects also presented symptoms of post-traumatic stress disorders. Such symptoms may respond to non-specific approaches during hospitalization (e.g., supportive psychotherapy, familial counseling). The better response to treatment may also result from the separation of the youth from their environment and thus from the exposure to ongoing stressors. Some authors have also suggested that the poorer response to treatment found in youths with bipolar disorder and a history of ACEs might be mediated by an early onset of the disorder [17]. If this is held to be true, selecting only youths with an early-onset bipolar disorder may partially decrease the effect of ACEs on the poor medical response. In this study, no data were available regarding prior or ongoing psychotherapies.

Clinical Implications

First, the high prevalence of household dysfunction found among youths with severe psychiatric disorders and its impact on the long-term prognosis stressed in previous studies advocate the consideration of a broad definition of abuse in child psychopathology. Second, the identification of a somatic cause of a disorder does not exclude the presence of environmental factors with important impact on the course of the disorder. A history of maltreatment appears more frequently in the childhood of adults suffering from many somatic diseases (e.g., obesity, hypertension or diabetes mellitus) compared to the rest of the population [6, 63]. The interplay of the HPA and SNA axis in both affective regulation and many physiological systems may play a role in the higher risk of children with severe adverse events to develop various somatic and psychiatric pathologies. Lastly, in this study, the presence of major ACEs was associated with a longer duration of hospitalization in the catatonic group. It could be hypothesized that a longer duration of hospitalization could facilitate the recovery of children presenting ACEs compared to other youths. Consequently, it would explain that no significant difference was found in treatment effectiveness between maltreated and non-maltreated children. However testing such hypotheses would require specific analyses and cannot be concluded from the present data. In our experience, a long period of hospitalization is important in this context as it enables the clinicians to carefully explore the family's strengths and weaknesses, to contact the different agents involved, to reinforce family compliance, and to better tailor subsequent outpatient care according to the patient's individual, familial, social, and educational needs. Indeed, childhood maltreatment could be seen as only one component of a broader range of difficulties in a vulnerable family (e.g., poor parenting, family psychopathology or low socio-economic status) [64]. The negative impact of ACEs extends beyond the increased risk of developing a disorder by presenting itself at each stage of the disorder (e.g., in accessing health care, understanding information about the disorder or following treatment recommendations).

Strengths and Limits

The results of this study should be interpreted in the context of its limitations. The number of patients in both groups is low despite the 20-year recruitment period. This is probably due to the relatively low prevalence of catatonia and BD-I in youth [19, 34, 65, 66]. Considering that participants were enrolled over a 20 year period, we ensured that the main findings were comparable between the subjects recruited over the first decade and those admitted in the second one. Lack of statistical power due to a large number of variables and small sample size precluded the use of multivariate analysis. There were more females in the bipolar group (57 %) than in the catatonic group (35 %). This is in line with previous literature but possibly introduces a gender bias in the analyses. Age and SES were comparable between the groups. Moreover, the naturalistic design of the study would not allow an assessment of treatment efficacy under blind conditions. Evaluation of ACEs in childhood during hospitalization was based on chart review and conduct retrospectively. To limit the potential biases we measured validity comparatively to official records (administrative data from child protection agencies was systematically sought during hospitalization). Such review of psychiatric records has been used to explore adverse events in bipolar disorder in previous studies [15, 67, 68]. In particular, ascertainment of ACEs by chart review may lead to under-estimation of certain kinds of abuse [69]. Given the long duration of hospitalization and the multiplicity of interviews, the data were regarded as adequate for a preliminary investigation [68]. Regarding the retrospective use of LTQ and the ACE scale, inter-rater agreement was low for LTQ but acceptable for ACE. An accurate evaluation of the starting point of recent life events was difficult considering that data were collected by chart review which may partly explain the low inter-rater agreement of the LTQ in this study. By contrast, the ACE scale did not refer to any specific time window.

Moreover, since our main results and clinical implications are related to significant associations with the ACE, the good metrics are rather reassuring. Lastly, the lack of a control group with less severe psychiatric disorders (e.g., anxiety) make it more difficult to interpret the prevalence of the adverse life events among youths with catatonia and bipolar disorder.

The strengths of the study are: (1) the prolonged duration of hospitalizations—providing us precise and numerous nurse and medical notes, (2) the homogeneity of the sample in terms of clinical characteristics (typical and severe forms of BD-I), (3) the fact that this sample of pediatric catatonic patients is the largest in the literature and, (4) the recruitment of participants over a 20-year period.

In this clinical study, ACEs were frequent in inpatient children and adolescents suffering from BD-I and those with catatonia. A history of severe abuse and neglect was noted in almost one-quarter of the youths for both disorders. Almost half of the subjects of both groups had experienced recent life-events. Having a history of major ACEs was not associated with more symptoms, a higher rate/level of functional impairments, or a lower response to treatment when compared to not having such a history. Future studies are warranted to replicate the high rate of family violence in children with catatonia and bipolar disorder, to assess whether specific types of ACEs are associated with specific early-onset psychiatric disorders and to assess the effects of preventive interventions.

Summary

ACEs are regarded as a group of psychosocial risk factors for child psychopathology. This relationship has been well demonstrated for youths with internalizing and/or externalizing psychiatric disorders. There is now a growing literature on their negative effects on the natural course of childhood-onset and adolescent-onset chronic psychiatric disorders. This study aimed to determine the prevalence and the clinical correlates of ACEs among 158 inpatient youths with bipolar disorder type I (BD-I) or a catatonic episode. For BD-I, the study would help to determine if the poorer prognosis of bipolar adults with ACEs also exist for pediatric form. Such results would help to better understand *how* and *when* the natural course of the disease is affected in those with ACEs. This is the first study exploring the prevalence of ACEs in catatonic youths. The role play by ACEs in the pediatric form of catatonia was raised based on a historical description of catatonia and the putative neurobiological mechanisms involving fear-response.

ACEs were retrospectively collected with the Adverse Childhood Experiences scale and the List of Threatening Experiences Questionnaire in 77 patients hospitalized for a catatonic syndrome (average age 15.2 years) and 81 for a manic or mixed episode (average age 15.7 years). ACEs were frequent in youths suffering from bipolar disorder type I (BD-I) (58 %) and from catatonia (57 %), with around one quarter exposed to severe abuse (i.e., physical/sexual/emotional abuse or physical/emotional neglect). Youths with BD-I were more likely to be exposed to family violence compared to those with catatonia. Youths who had been exposed to ACEs did not exhibit a more severe presentation or a poorer response to treatment compared to others, either in the bipolar group or in the catatonic group.

The prevalence of ACEs in youths with BD-I is in line with previous studies in inpatients sample, especially the higher rate of family dysfunction. Our data support the notion that ACEs could progressively impact the course of the BD over the clinical follow-up while no major difference exists in the clinical symptoms and treatment response of a first acute manic episode in hospitalization. In line with adults, this data support the view of pediatric catatonia as a syndrome whose clinical symptoms and treatment response did not significantly differ according to etiology. The combination of various risk factors (i.e., ACEs and somatic condition) in the same subject supports the development of a multidisciplinary approach for caring these patients.

Compliance with Ethical Standards

Conflict of interest On behalf of all authors, the corresponding author states that there is no conflict of interest.

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