

Link between childhood trauma and characteristics of bipolar disorders: A survey in Algiers

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Abstract:

Background: More than half of individuals with bipolar disorder (BD) report having experienced childhood maltreatment, including sexual and physical abuse. It appears that this early traumatic exposure impacts the clinical expression of the illness and its management. The objective of this study is to determine the link between childhood trauma and the characteristics of bipolar disorders in the Algerian population.

Materials and Methods: We conducted a descriptive cross-sectional study involving 144 bipolar patients, diagnosed according to the DSM-5 criteria for BD, over a period of 24 months, from January 2021 to December 2022. Sociodemographic, clinical, and evolutionary characteristics were collected by using a hetero-questionnaire. Clinical evaluation was performed by using the Young Mania Rating Scale, Hamilton Depression Rating Scale, and the Child Trauma Questionnaire (CTQ).

Results: The mean age of our patients was 41.3 ± 13 years. The majority were male, and over half were single. The average age of onset of the illness was 22.7 ± 4.8 years. The majority had an average of 4.60 ± 4.30 hospitalizations. Type I BD was overrepresented in 77.1% of cases. The prevalence of early maltreatment was 40.3% ($n=58$), with 19.3% reporting at least two subtypes. The overall CTQ score was 43.55 ± 53.5 . Childhood trauma history was significantly associated with early onset of the illness (at 21 years), family history of mental illness ($p=0.000$), suicidal behavior ($p=0.009$), psychotic disorders (delusions were more common than hallucinations, 77.1% vs 29.9%), and treatment resistance. However, no notable associations were found with the speed of mood episodes, anxious comorbidities, personality disorders and psychoactive substance use disorders.

Conclusion: Overall, our results are consistent with the existing literature. They confirm a high prevalence of childhood trauma that has a significant impact on the course of bipolar disorder in the Algerian population. It is important for clinicians to identify early maltreatment in patients, as it has an influence on the clinical expression of the illness and treatment response.

Key Word: Bipolar disorder, childhood trauma, treatment resistance.

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I. Introduction

The term childhood trauma is often used to refer to various forms of abuse and mistreatment that an individual has been exposed to during their childhood and adolescence¹⁻². Furthermore, the World Health Organization (2013)³ estimated the prevalence of sexual violence at 19.1%, physical violence at 22.9%, emotional violence at 29.1%, physical neglect at 16.3%, and emotional neglect at 18.4%. Given their significant frequency and the physical and psychological consequences they entail, childhood traumas are now recognized as a major public health issue by the High Authority of Health (HAS) in 2014⁴. Among the long-term psychological consequences, numerous studies suggest a significant impact of early trauma on the risk of developing psychiatric disorders in adulthood, such as bipolar disorders, schizophrenia, anxiety disorders, personality disorders, and substance use disorders. Moreover, more than 50% of bipolar individuals report having been victims of sexual or physical abuse during their childhood⁵⁻⁶. Indeed, the association between childhood maltreatment and the risk of developing bipolar disorder has been the subject of several literature reviews, including the two meta-analyses conducted by Palmier-Claus and Agnew-Blais and their collaborators⁷⁻⁸. These meta-analyses, based on several studies (19 and 30 studies respectively), found a risk of developing bipolar disorder more than 2.6 times higher in cases of early traumatic exposure. All types of maltreatment were involved and particularly emotional abuse. Beyond an increased risk of developing a mood disorder, the authors note that childhood maltreatment significantly and negatively impacts the clinical expression of the illness, its course, and its response to treatment⁷⁻⁸. The objective of our study was to determine the link between childhood trauma and the characteristics of bipolar disorders based on a survey conducted in Algiers.

II. Material And Methods

We conducted a descriptive cross-sectional study involving 144 bipolar patients hospitalized at the Specialized Psychiatric Hospital DRID Hocine in Kouba-Algiers, Algeria. The patients were included based on the diagnostic criteria for bipolar disorder outlined in the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5) ⁹. The study was carried out over a period of 24 months, from January 2021 to December 2022. Patients had to be 18 years of age or older. Patients with schizophrenia, schizoaffective disorder, schizophreniform disorder, and recurrent depressive disorders were excluded from the study. Prior to their participation, patients were provided with information about the purpose of the study, the respect for anonymity, and the confidentiality of data, in order to obtain their informed and voluntary consent to participate.

Data Collection and Measurement Instruments

Sociodemographic data: age, gender, marital status, level of education, occupation, family history of mental illness, personal history of suicide attempts, childhood traumas, subtypes of childhood maltreatment, and comorbidities (anxiety disorders, personality disorders, and addiction).

Clinical and evolutionary data: age at first episode, current mood episode, duration of illness, number of hospitalizations, interval between hospitalizations, presence of psychotic symptoms, and history of treatment resistance. Regarding the assessment of clinical severity, we used three scales: the Young Mania Rating Scale ¹⁰, the Hamilton Depression Rating Scale ¹¹, and the Child Trauma Questionnaire (CTQ) (Bernstein et al., 2004) for the types of maltreatment ¹².

Statistical Analysis

All data collected from the pre-established questionnaire were entered into the SPSS software, version 26. Qualitative variables were expressed as percentages or frequencies, while quantitative variables were expressed as means, standard deviations, and ranges. The chi-square test was used to compare qualitative variables, and the Student's t-test was used to compare a qualitative variable with a quantitative variable. The significance level was set at 5% ($p \leq 0.05$).

III. Result

The sociodemographic and clinical characteristics are summarized in Tables 1 and 2.

Our study revealed a significant relationship between a history of childhood abuse and suicidal behavior ($p=0.013$) (Figure n°1), as well as a significant association between family history of mental illness ($p=0.000$). The most frequently implicated types of abuse were sexual, emotional, and physical abuse ($p=0.009$). However, sex and comorbidities (anxiety, personality disorders, and addictions) were not significantly associated with a history of childhood abuse ($p=0.453$).

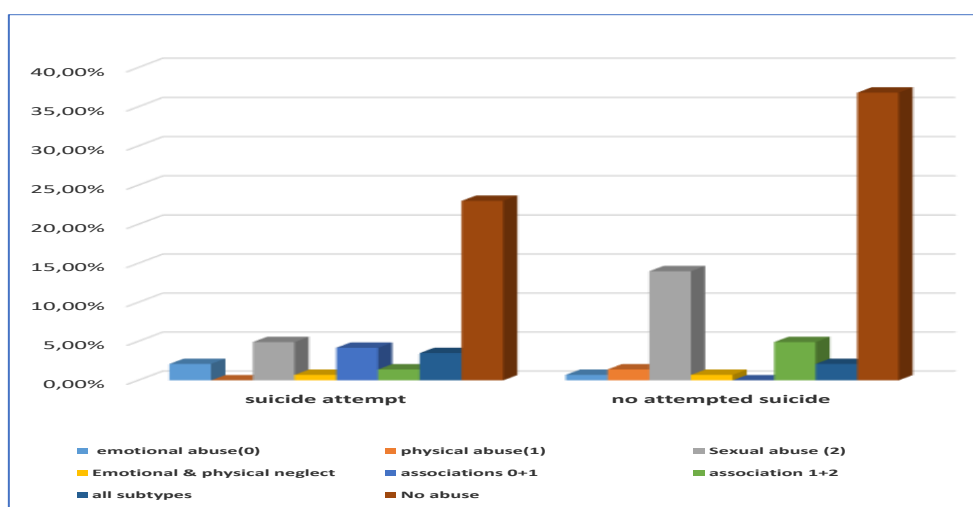


Figure n° 1: Distribution of 144 bipolar patients with or without attempted suicide by history of childhood trauma

Furthermore, the statistical analysis revealed that patients with a history of childhood trauma (sexual, physical, or emotional abuse) had a significant association with early onset of the disease ($p=0.000$) and psychotic symptoms ($p=0.007$). Delusions and hallucinations were particularly associated with sexual and

physical abuse ($p=0.000$). However, no significant association was found with the number of hospitalizations ($p=0.550$).

Table 1: Socio-demographic characteristics and background

Variables	(n) %	Variables	(n) %
Mean Age (M±SD)* (year) = 41,3±12,9		Schizophrenia and bipolar disorder	(1) 0,7
Gender		No family history	(79) 54,9
Mal	(88) 61,1	Personal history	
female	(56) 38,9	Childhood trauma	
Marital status		- Yes	(58) 40,3
Single	(81) 56,3	- No	(86) 59,7
Married	(48) 33,3	Subtypes of maltreatment	
Divorced	(13) 9,0	- Emotional abuse	(4) 2,8
widow	(2) 1,4	- Physical abuse	(2) 1,4
Educational level		- Sexual abuse	(27) 18,8
Illiterate	(4) 2,8	- Emotional and physical neglect	(2) 1,4
Primary	(5) 3,5	- Emotional and physical abuse	(6) 4,2
College	(37) 25,7	- Physical and sexual abuse	(9) 6,3
Secondary	(54) 37,5	- All subtypes	(8) 5,6
Academic	(44) 30,6	- No abuse	(86) 59,7
Professional status		Suicide attempt	
Senior manager	(14) 9,7	- Yes	(57) 39,6
Middle manager	(29) 20,1	- No	(87) 60,4
Low manager	(31) 21,5	Comorbidities:	
Without profession	(58) 40,3	Anxious	(13) 9
Other (Student)	(12) 8,3	Personality disorders	(16) 31,9
Family history of mental illness		Substance use disorder	
Schizophrenia	(32) 22,2	- Yes	(69) 47,9
Bipolar disorder	(37) 25,7	- No	(75) 52,1

(M±SD)*: mean ± standard deviation

Table 2 : Clinical Characteristics

Variables	M ± SD*	(n) %
Mean age of onset of BD (M ±SD)*(years)	22,71±4,81	
Mean age of onset of BD (M ±SD)*(years):		
- with history of early trauma	21,00±4,57	
- with no history of early trauma	23,90±4,64	
Average duration of BD evolution (M± SD) (years)	16,11±11,20	
Average number of hospitalizations (M ±SD) (years)	4,60±4,30	
Mean interval between hospitalizations (M ±SD) (years)	2,80±1,50	
Diagnosis of bipolar disorder (BD)		
BD type I		(133) 92,4
BD type II		(11) 7,4
BD with or without psychotic characteristics (CP)		
Without (CP)		(31) 21,5
With (CP)		(113) 78,5
- Congruent with mood		(70) 48,6
- Not congruent with mood		(43) 29,9
Existence or no hallucination		
- No		(101) 70,1
- Yes		(43) 29,9
Existence or no delusion		
- No		(33) 22,9
- Yes		(111) 77,1
Clinical evaluation		
- Overall CTQ score**	43,55±53,5	
- Total HDRS score (M ±SD)	13,40±8,20	
- Young Total Score (M ±SD)	24,42±10,56	

(M ±SD)*: Mean ± standard deviation;_CTQ**_: Child Trauma Questionnaire

IV. Discussion

Prevalence

The prevalence of childhood trauma history in this study, as assessed by the overall Child Trauma Questionnaire (CTQ) score (43.55 ± 53.5), was 40.3% ($n=58$) among bipolar patients, with 19.3% reporting at least two subtypes of early maltreatment. Our results are consistent with previous studies examining the link between early trauma and bipolar disorders, which have reported prevalence rates ranging from 40% to 55%⁵⁻⁶.¹³. Etain and al. (2013)⁵ reported a prevalence rate of 49.6%. Similarly, Sala and al. (2014)⁶ found that 54.3% of patients with bipolar disorder type I and 428 with bipolar disorder type II reported at least one subtype of

childhood trauma in a study of 1,172 bipolar patients. In line with these findings, comparative studies have shown a higher prevalence of early trauma in bipolar patients compared to healthy controls¹⁴⁻¹⁶. For instance, a comparative study by Jansen and al. (2016)¹⁶ reported higher early trauma rates, as assessed by the CTQ, in bipolar disorder compared to healthy controls (53.9% vs. 17%). Similarly, Watson and al. (2014)¹⁴ compared 60 bipolar patients to 55 healthy controls and found that the total CTQ score was higher in the bipolar group compared to the healthy controls (44.4% vs. 31.2%; $p < 0.001$).

Sociodemographic characteristics and family/personal history

– Sociodemographic characteristics

Considering the sociodemographic data of our sample, the clinical population consisted of 144 bipolar patients, the majority of them were male. Over half of the patients were unmarried and in their forties, with secondary or university education. More than half were employed. These results were consistent with some studies in the literature involving individuals with bipolar disorder, regardless of whether they had experienced childhood trauma⁷⁻⁸. However, our study did not find a significant relationship between gender and early trauma, which is in line with the New York study by Garino et al. in 2005¹⁷. On the other hand, some studies, including the study by Etain et al. in 2013⁵, reported higher CTQ scores among women compared to men (scores of 43.48 vs 40.78; $p = 0.025$).

– Personal and family history

A history of family mental illness was found in our bipolar patient population in 58% of cases. Patients with a family history of mental illness were significantly associated with a history of sexual, physical, and emotional abuse ($p=0.000$), and they had an earlier onset of the illness (21 years). Our results are consistent with the study by Post et al. in 2016¹⁸, which included 968 patients with bipolar disorder type I and II. They found that patients with a family history of mental illness and traumatic experiences (sexual, physical, and emotional abuse) had an earlier onset of the illness (22 years) compared to those without a family history.

Furthermore, early trauma is consistently associated with suicidal behaviors in the course of bipolar disorder. However, according to the results of the study by Sugoy et al. in 2012¹⁹, this factor is non-specific to suicide in bipolar disorder. On the other hand, the results of other studies⁷⁻⁸ show that bipolar patients with a history of childhood trauma have a higher incidence of suicidal behaviors. Additionally, the total CTQ score is higher in patients with a history of suicide attempts. In line with this, the results regarding the subtypes of trauma show that they are all associated with the risk of suicide attempts, particularly sexual, physical, and emotional abuse^{5,15}, which is consistent with the findings of our study, as we found a significant association with sexual abuse followed by physical and emotional abuse ($p=0.009$).

In our sample, the majority of our patients had at least one comorbidity. This comorbidity rate is consistent with figures often cited in the literature (over 80%), ranging from 65% to 75%²⁰⁻²¹. However, some authors^{5, 7-8} have mentioned that comorbidities are higher in bipolar patients with a history of early trauma compared to those without. Contrary to these results, our study did not find a significant association between childhood trauma and various comorbidities, including anxiety disorders, pathological personality, or substance use disorders.

Clinical characteristics

– Age at first episode

Several studies^{4, 15, 17} have highlighted the link between early onset of the illness and a history of early trauma. Indeed, the age at onset of bipolar disorder was three years earlier (22.1 vs. 25.7 years) for individuals who experienced a single subtype of trauma, and six years earlier (19.6 years) for those who reported at least three subtypes of trauma among patients with bipolar disorder type I and II. Some authors have reported that the earlier the onset of the illness, the higher the number of traumas experienced²². This finding was confirmed by our study, as the onset of symptoms was significantly earlier in bipolar patients with a history of early trauma (a difference of three years) compared to those without a history of trauma (21 years vs. 24 years, respectively).

– Type of bipolar disorder

The present study found a predominance of bipolar disorder type I, significantly more frequent in the manic phase than in the depressive phase. These results are consistent with some studies in the literature^{21, 23-24}. Sala et al. 2014⁶ compared bipolar disorder types based on a history of childhood maltreatment and found a higher prevalence of childhood maltreatment in bipolar disorder type I patients, while the results of another study²⁵ found higher rates of maltreatment in bipolar disorder type II patients. On the other hand, other authors have not found a difference between the two types^{7, 14-15}, including the meta-analysis by Palmier-Claus et al. 2016⁷ which did not find a significant difference between bipolar disorder type I and type II, which is consistent with our study.

– **Number of hospitalizations and intervals between hospitalizations**

Furthermore, the results of some studies also suggest that bipolar patients with a history of early trauma have a higher number of hospitalizations with shorter intervals between episodes compared to bipolar patients without a history of early trauma^{5, 7-8}. In contrast to these studies, our results demonstrated that the number of hospitalizations and the intervals between hospitalizations were not significantly associated with early trauma, which is consistent with the findings of the study by Etain et al. 2013 and Palmier-Claus et al. 2016^{5, 7}.

– **The presence or absence of psychotic features**

Our results also confirm that the majority of patients experienced an average of 2.7 ± 2.2 mood episodes with congruent or incongruent psychotic features. These symptoms were significantly more prevalent during manic episodes. Delusions were more common than hallucinations, with rates of 77.1% versus 29.9%, respectively. These findings are consistent with studies demonstrating a significant number of bipolar patients experiencing at least one mood episode with psychotic features, particularly during manic phases²⁶⁻²⁷. The results also revealed that delusions and auditory-verbal hallucinations were considered the psychotic symptoms most correlated with a history of early trauma, especially sexual abuse. Our results align with several studies^{6, 26, 28} that have found a significant association between the Childhood Trauma Questionnaire (CTQ) score and higher scores of delusional ideas in bipolar patients. Other studies have found a significant link between sexual abuse and hallucinations, particularly auditory hallucinations³⁰⁻³¹. In contrast to other studies, that found women to be more prone to hallucinations compared to men^{14, 15}, our results did not find a connection between hallucinations and bipolar women with a history of early trauma. For some authors, a history of childhood maltreatment appears to significantly and negatively impact the clinical expression, course, and management of bipolar disorder. A meta-analysis of 19 studies found a 2.63-fold higher risk (95% CI: 2.00-3.47) of developing a mood disorder in individuals exposed to early traumatic experiences unrelated to post-traumatic stress²⁵. Additionally, a literature review and meta-analysis conducted by Agnew-Blais and Danese in 2016⁸ found that patients with a history of childhood maltreatment had a greater number of manic episodes with more severe psychotic symptoms. A majority of authors have reported more severe positive symptoms, particularly auditory hallucinations and delusional ideas, in patients with a history of childhood maltreatment^{27, 28}, as observed in our study. The severity of positive symptomatology may be correlated with the intensity of traumatic exposure, suggesting a dose-response effect²⁹. Regarding the causal relationship between traumatic history and the emergence of mood disorders with psychotic features, some authors have proposed the hypothesis of specific gene-environment interactions that may mediate this association (e.g., nucleotide polymorphisms of the FKBP5 gene)³⁰⁻³³. However, this association is not specific to bipolar disorders and is shared with other psychiatric disorders, including schizophrenia.

– **Therapeutic response**

Finally, the impact of early trauma on the response to mood stabilizers treatments, antipsychotics, and antidepressants used in these patients remains little known, although some authors have mentioned resistance to certain molecules³⁴⁻³⁵. These findings are consistent with those our study, as one-third of patients (n=45; 31.25%) with a history of childhood trauma did not respond adequately to treatments.

Limitations of the Study and Perspectives

The results of the present study should be considered preliminary, and more prospective comparative studies between bipolar disorder with a history of childhood trauma and bipolar disorder without a history of childhood trauma are needed to confirm the findings presented in this paper.

Conflict of Interest Statement

The authors declare no conflicts of interest related to this article

V. Conclusion

Overall, in the present study, the sociodemographic and clinical characteristics associated with early trauma in Algerian patients with bipolar disorder align with those previously described in the literature. Indeed, we conclude that there is a significant association between childhood maltreatment and the risk of developing bipolar disorder in adulthood. The role of sexual abuse appears to be predominant in our study. The presence of these antecedents has consequences on the exacerbation of certain disease characteristics. The history of childhood trauma has a specific relation to the early onset of the disorder, the increased suicide risk, the severity of mood episodes with psychotic features, and the issue of treatment resistance. However, rapid cycling was not necessarily related to maltreatment. The significance of childhood trauma justifies the importance of addressing and providing support for children who experience it, aiming to prevent bipolar disorders in adulthood.

References

- [1]. Morgan C, Fisher H. Environment and schizophrenia: environmental factors in schizophrenia: childhood trauma - a critical review. *Schizophr Bull.* 2007; 33:3–10.
- [2]. Felitti VJ, Anda RF, Nordenberg D, Williamson DF, Spitz AM, Edwards V, et al. Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults. The Adverse Childhood Experiences (ACE) Study. *Am J Prev Med.* 1998; 14(4):245–58.
- [3]. World Health Organization (2013). European report on preventing child maltreatment.
- [4]. High Authority of Health (HAS). Child maltreatment: identification and conduct to be held. Report of elaboration. Paris service documentation. 2014; 114 pages.
- [5]. Etain B, Aas M, Andreassen OA, Lorentzen S, Dieset I, Gard S, and al. Childhood trauma is associated with severe clinical characteristics of bipolar disorders. *J Clin Psychiatry.* 2013; 74(10):991–8.
- [6]. Sala R, Goldstein BI, Wang S, Blanco C. Childhood maltreatment and the course of bipolar disorders among adults: epidemiologic evidence of dose-response effects. *J Affect Disord.* 2014; 165:74–80.
- [7]. Palmier-Claus, J. E., Berry, K., Bucci, S., Mansell, W., Varese, F. Relationship between childhood adversity and bipolar affective disorder: systematic review and meta-analysis. *The British Journal of Psychiatry.* 2016; 209(6), 454–459.
- [8]. Agnew-Blais, J., and Danese, A. Childhood maltreatment and unfavourable clinical outcomes in bipolar disorder: a systematic review and meta-analysis. *The Lancet Psychiatry.* 2016; 3(4), 342–349.
- [9]. American Psychiatric Association. Diagnostic and statistical manual of mental disorders (DSM-5). American Psychiatric Pub. 2013
- [10]. Young RC, Biggs JT, Ziegler VE, Meyer DA. Young Mania Rating Scale. In: *Handbook of Psychiatric Measures.* Washington, DC: American Psychiatric Association. 2000: 540–542.
- [11]. Hamilton M. «A rating scale for depression», dans *Journal of Neurology, Neurosurgery and Psychiatry.* 1960: 56–62.
- [12]. Bernstein DP, Stein JA, Newcomb MD, Walker E, Pogge D, Ahluvalia T, and al. Development and validation of a brief screening version of the Childhood Trauma Questionnaire. *Child Abuse Negl.* 2003; 27 (2):169–90.
- [13]. Brown GR, McBride L, Bauer MS, Williford WO, Cooperative Studies Program 430 Study Team. Impact of childhood abuse on the course of bipolar disorder: a replication study in U.S. veterans. *J Affect Disord.* 2005 ; 89(1–3):57–67
- [14]. Watson S, Gallagher P, Dougall D, Porter R, Moncrieff J, Ferrier IN, and al. Childhood trauma in bipolar disorder. *Aust N Z J Psychiatry.* 2014; 48(6) :564–70.
- [15]. Janiri D, Sani G, Danese E, Simonetti A, Ambrosi E, Angeletti G, and al. Childhood traumatic experiences of patients with bipolar disorder type I and type II. *J Affect Disord.* 2015; 175:92–7.
- [16]. Jansen K, Cardoso TA, Fries GR, Branco JC, Silva RA, Kauer-Sant’Anna M, and al. Childhood trauma, family history, and their association with mood disorders in early adulthood. *Acta Psychiatr Scand.* 2016 ; 134(4):281–6
- [17]. Garino JL, Goldberg JF, Ramirez PM, Ritzler BA. Impact of childhood abuse on the clinical course of bipolar disorder. *Br J Psychiatry.* 2005 ; 186 :121–5
- [18]. Post RM, Altschuler LL, Kupka R, McElroy SL, Frye MA, Rowe M, and al. Age of onset of bipolar disorder: Combined effect of childhood adversity and familial loading of psychiatric disorders. *J Psychiatr Res.* 2016; 81:63–70.
- [19]. Sugaya L, Hasin DS, Olsson M, Lin K-H, Grant BF, Blanco C. Child physical abuse and adult mental health: a national study. *J Trauma Stress.* 2012. 25(4):384–92.
- [20]. Fountoulakis KN: *Bipolar Disorder an Evidence-Based Guide to Manic Depression.* Springer-Verlag, Berlin, 2015
- [21]. Goodwin FK, Jamison KR. *Manic-Depressive Illness. Bipolar Disorders and Recurrent Depression,* 2nd. ed. Oxford University Press, New York, 2007
- [22]. Golmard J-L, Scott J, Etain B, Preisig M, Aubry J-M, Henry C, and al. Using admixture analysis to examine birth-cohort effects on age at onset of bipolar disorder. *Acta Psychiatr Scand.* 2016 ; 133(3) :205–13
- [23]. Caldieraro MA, Sylvia LG, Dufour S, Walsh S, Janos J, Rabideau DJ, and al.: Clinical correlates of acute bipolar depressive episode with psychosis. *J Affect Disord.* 2017 ; 217:29–33
- [24]. Dell’Osso B, Camuri G, Cremaschi L, and al. Lifetime presence of psychotic symptoms in bipolar disorder is associated with less favorable socio-demographic and certain clinical features. *Comprehensive Psychiatry.* 2017; 76: 169–176.
- [25]. Marwaha S, Gordon-Smith K, Broome M, Briley PM, Perry A, Forty L, and al. Affective instability, childhood trauma and major affective disorders. *J Affect Disord.* 2016 ; 190 :764–71
- [26]. Dell’Osso B, Holtzman JN, Goffin KC, Portillo N, Hooshmand F, Miller S, and al. American tertiary clinic-referred bipolar II disorder compared to bipolar I disorder: More severe in multiple ways, but less severe in a few other ways. *J Affect Disord.* 2015; 188:257–62.
- [27]. Annet H, Bergen V, Verkooijen S and al). The characteristics of psychotic features in bipolar disorder. *CAMBRIDGE University Press. Psychological Medicine.* 2018: 1–13.
- [28]. Muenzenmaier, K. H., Seixas, A. A., Schneeberger, A. R., Castille, D. M., Battaglia, J., & Link, B. G. Cumulative effects of stressful childhood experiences on delusions and hallucinations. *Journal of Trauma & Dissociation.* 2015; 16(4), 442–462.
- [29]. Etain B, Lajnef M, Bellivier F, Henry C, M’bailara K, Kahn JP, and al. Revisiting the association between childhood trauma and psychosis in bipolar disorder: A quasi-dimensional pathanalysis. *J Psychiatr Res.* 2017; 84:73–9.
- [30]. Hammersley P, Dias A, Todd G, Bowen-Jones K, Reilly B, Bentall RP. Childhood trauma and hallucinations in bipolar affective disorder: preliminary investigation. *Br J Psychiatry.* 2003; 182:543–7.
- [31]. Upthegrove R, Chard C, Jones L, Gordon-Smith K, Forty L, Jones I, and al. Adverse childhood events and psychosis in bipolar affective disorder. *Br J Psychiatry.* 2015; 206(3):191–197.
- [32]. Alemany, S., Moya, J., Ibáñez, M. I., Villa, H., Mezquita, L, and al. Childhood trauma and the rs1360780 SNP of FKBP5 gene in psychosis: a replication in two general population samples. *Psychological medicine.* 2016; 46(1), 221–223.
- [33]. Collip, D., Myin-Germeys, I., Wichers, M., Jacobs, N., Derom, C., Thiery, E., and van Os, J. FKBP5 as a possible moderator of the psychosis-inducing effects of childhood trauma. *The British Journal of Psychiatry.* 2013; 202(4), 261–268
- [34]. Misiak B, Krefft M, Bielawski T. and al. Toward a unified theory of childhood trauma and psychosis: A comprehensive review of epidemiological, clinical, neuropsychological and biological findings *Neurosci Biobehav Rev.* 2017. 75, 393–406
- [35]. Kaufman J and Torbey S. Child maltreatment and psychosis. *Neurobiology of Disease,* November 2019; Volume 131, 104378