

Affective instability, childhood trauma and major affective disorders

S. Marwaha¹, K. Gordon-Smith², M. Broome³, P.M. Briley⁴, A. Perry², L. Forty⁵, N. Craddock⁵, I. Jones⁵, L. Jones^{2*}

¹Division of Mental Health and Wellbeing, Warwick Medical School, University of Warwick Coventry, CV4 7AL, UK.

AND Affective Disorders Service (IPU 3-8), Caludon Centre, Coventry, CV2 2TE, UK.

² Department of Psychological Medicine, University of Worcester, WR2 6AJ, UK.

³ Department of Psychiatry, University of Oxford, OX3 4JX, UK.

⁴ School of Medicine, University of Nottingham, Nottingham, NG7 2UH, UK.

⁵ Institute of Psychological Medicine and Clinical Neurosciences, MRC Centre for Neuropsychiatric Genetics and Genomics, Cardiff University, CG10 3XQ, UK.

***Corresponding author:**

Professor Lisa Jones
Department of Psychological Medicine
University of Worcester
Henwick Grove
Worcester
WR2 6AJ
UK

Telephone: +44 (0)1905 54 2801

Fax: +44 (0)1905 85 5589

Email: lisa.jones@worc.ac.uk

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Abstract

Background Affective instability (AI), childhood trauma, and mental illness are linked, but evidence in affective disorders is limited, despite both AI and childhood trauma being associated with poorer outcomes. Aims were to compare AI levels in bipolar disorder I (BPI) and II (BP II), and major depressive disorder recurrent (MDDR), and to examine the association of AI and childhood trauma within each diagnostic group.

Methods AI, measured using the Affective Lability Scale (ALS), was compared between people with DSM-IV BPI (n=923), BP II (n=363) and MDDR (n=207) accounting for confounders and current mood. Regression modelling was used to examine the association between AI and childhood traumas in each diagnostic group.

Results ALS scores in descending order were BP II, BPI, MDDR, and differences between groups were significant ($p<0.05$). Within the BPI group any childhood abuse ($p=0.021$), childhood physical abuse ($p=0.003$) and the death of a close friend in childhood ($p=0.002$) were significantly associated with higher ALS score but no association was found between childhood trauma and AI in BP II and MDDR.

Limitations The ALS is a self-report scale and is subject to retrospective recall bias.

Conclusions AI is an important dimension in bipolar disorder independent of current mood state. There is a strong link between childhood traumatic events and AI levels in BPI and this may be one way in which exposure and disorder are linked. Clinical interventions targeting AI in people who have suffered significant childhood trauma could potentially change the clinical course of bipolar disorder.

[244 words]

Keywords Mood disorders, stressful events, affective symptoms, bipolar disorder, depressive disorder, affective instability

Introduction

The classical description of affective disorders is one in which there are manic and depressive phases in the case of bipolar disorders, or unipolar depressive episodes interspersed with periods of euthymia. Over the last few decades this conceptualisation has evolved, with the quantification of the significance of sub-syndromal affective states (Judd et al., 2002). More recently attention has turned to affective/mood instability (AI) throughout the illness course (Broome et al., 2015b), independent of whether the person is in a frank episode of mood disorder. This burgeoning interest is for several reasons. First, AI appears to be a prognostic marker for transition status in those at risk of bipolar disorder (Angst et al., 2003; Howes et al., 2011). Secondly, automated, persistent time series measurement of mood, analysed using advanced mathematical techniques has revealed a complex pattern of AI in the euthymic periods of people with bipolar disorder (Bonsall et al., 2012) reflecting an abnormality in affective reactivity (Henry et al., 2008). This may link to the possible neurobiological underpinnings of AI involving the amygdala and its connections (Broome et al., 2015a). Thirdly, greater affective lability and intensity during the inter-episode period prospectively explains impairment in home and work functioning over 1 month (Gershon and Eidelman, 2015) and longer term disability levels in bipolar disorder (Strejilevich et al., 2013).

AI is associated with suicidal thinking (Marwaha et al., 2013), hospitalisation and anti-psychotic use (Patel et al., 2015) even after controlling for the effects of diagnosis. AI has also been shown to be important in depression. It can occur in up to 60% of people with an established diagnosis of depression (Marwaha et al., 2013) and prospectively predicts depression inception, with this effect being mediated by sleep disturbance (Marwaha et al., 2015). Regulatory processes specific to sadness and strategies to recover from it (mood

repair) as well as increased emotional reactivity is seen in youths who subsequently develop depression (Kovacs and Lopez-Duran, 2010).

Childhood trauma, including emotional and physical abuse, is commoner in people with bipolar disorder than the general population (Etain et al., 2010), and sexual abuse commoner in those with bipolar disorder in comparison to unipolar depression (Hyun et al., 2000). Childhood trauma is associated with greater number of manic or depressive episodes, suicidality and increased comorbidity with other psychiatric as well as medical disorders (Leverich and Post, 2006). The question arises as to how childhood trauma leads to an increased severity of bipolar disorder and poorer prognosis. In people with borderline personality disorder childhood abuse appears to generate emotional dysregulation, which ultimately manifests itself as a disorder (Crowell et al., 2009). We have previously shown that dysphoric mood disturbance (Marwaha and Bebbington, 2014), and more specifically AI, mediates the association between childhood sexual abuse and paranoia, auditory hallucinations and psychotic disorder (Marwaha et al., 2014a). Therefore initial evidence from other disorders suggests AI may be a worthwhile mediating mechanism for investigation in bipolar disorder also.

As far as the authors are aware there have been two previous studies examining AI and childhood trauma in people with bipolar disorder. Using a modest sample size (N=42) of people primarily with a diagnosis of bipolar disorder type I, Aas et al (2014) report a significant association between childhood trauma questionnaire (CTQ) scores and AI (Aas et al., 2014). They found the strongest associations were for emotional abuse followed by emotional neglect. In a larger study of 201 people with bipolar disorder both affective

intensity and lability were strongly correlated with CTQ score and this to a large extent was explained by the correlation between CTQ and emotional abuse (Etain et al., 2008).

In summary, at present nearly all studies in this field have had small to modest sample sizes. There is no study that has directly examined AI in bipolar disorder type I and type II, together with unipolar depression using the same assessment methods (Marwaha et al., 2014b) allowing an understanding of the characteristics of AI across these groups. Such a comparison is the next step in understanding whether AI is of particular importance in bipolar disorder or affective disorders in general. Detailed analysis of AI in bipolar disorders may also help to address the nosological debate regarding the overlap between bipolar disorder type II and borderline personality disorder (Bassett, 2012). Given the importance of childhood trauma we need to know whether the connection with AI spans the range of affective disorders and whether the link is general or specific to a particular type of childhood trauma. Such investigation could give clues as to the underlying pathologies and mechanistic trajectories in bipolar and unipolar mood disorders, thereby helping to identify novel targets for clinical interventions.

Aims of the study

We aimed to: a) compare the degree of AI in large samples of bipolar disorder type I and type II, and unipolar depression; and, b) report the prevalence of adverse childhood life events and examine the association between each of them and AI in both bipolar disorders and unipolar depression.

Methods

The study was part of an on-going programme of research into the genetic and non-genetic determinants of bipolar disorder and related mood disorders (UK Bipolar Disorder Research Network, BDRN; www.bdrn.org) which has UK National Health Service (NHS) Research Ethics Committee approval and local Research and Development approval in all participating NHS Trusts/Health Boards.

Recruitment of participants

Participants were recruited throughout the UK via both systematic and non-systematic recruitment methods. Systematic recruitment involved screening for potential participants through Community Mental Health Teams (CMHTs) and Lithium clinics. Non-systematic recruitment involved advertisements for volunteers on the research team website, in local and national media and through patient support organisations (such as Bipolar UK and Depression Alliance).

The research programme inclusion criteria required participants to be aged at least 18 years, able to provide written informed consent, meet DSM-IV criteria for major affective disorder and for their mood symptoms to have started before the age of 65 years. Individuals were excluded if they: (i) experienced affective illness only as a result of alcohol or substance dependence; (ii) experienced affective illness only secondarily to medical illness or medication; or (iii) were biologically related to another study participant. Those developing episodes of hypomania / mania secondary to anti-depressants were not excluded. Additional exclusion criteria for participants with unipolar depression were: (i) positive family history of bipolar disorder, schizophrenia, schizoaffective disorder or any other psychotic disorder in a

first- or second-degree relative; (ii) history of mood incongruent psychotic symptoms or psychotic symptoms outside of mood disturbance.

Psychiatric assessment

Participants were interviewed using the Schedules for Clinical Assessment in Neuropsychiatry (SCAN) (Wing et al., 1990) which provides detailed information about lifetime psychopathology. Psychiatric and general practice (primary care) case-notes where available, were also reviewed. Based on these data best-estimate lifetime diagnoses were made according to DSM-IV criteria. In cases where there was doubt, a diagnosis was made by at least two members of the research team blind and consensus was reached via discussion where necessary. Inter-rater reliability was formally assessed using 20 random cases. Mean kappa statistic was 0.85 for DSM-IV diagnosis. Team members involved in the interview and diagnostic procedures were all research psychologists or psychiatrists.

Measurement of affective instability

AI was measured using the Affective Lability Scale-Short Form (ALS-SF) (Oliver and Simons, 2004) which was sent to 5354 previously recruited BDRN participants as part of a questionnaire mail out with a reminder being sent one month later. 1959 responses were received (37%).

The ALS-SF is an 18-item questionnaire measuring rapid changes from euthymic mood to other emotional states including elation, depression, and anger. It is generally assumed to measure aspects of temperament. Participants were asked to indicate how well each item described how they have been feeling over the past week on a scale of very unresponsive, rather unresponsive, rather responsive, very responsive (scored 1 to 4). In addition to having

a total score (ranging from 18-72), the ALS-SF has three subscale scores:

Anxiety/Depression (ranging from 5-20), Depression/Elation (ranging from 8-32) and Anger (ranging from 5-20). Investigation demonstrates the ALS has good psychometric properties in bipolar disorder (Aas et al., 2015)

Measurement of affective state at time of completion of the ALS-SF

ALS-SF score may be influenced by the mood state of an individual at the time of completion. Therefore two current mood state measures were administered at the same time as the ALS-SF, the Beck Depression Inventory (BDI) (Beck and Steer, 1987) and Altman Self-Rating Mania Scale (AMS) (Altman et al., 1997). The BDI is a self-report scale that measures the presence and severity of current depressive symptoms on a scale from 0 (no depressive symptoms) to 63 (severe depression). The self-report AMS measures the presence and severity of current manic symptoms from 0 (no manic symptoms) to 20 (severe mania).

Adverse childhood life events

Information about adverse childhood life events (ACLEs) was gathered using a bespoke instrument, Childhood Life Events Questionnaire (CLEQ), developed by the BDRN (see (Upthegrove et al., 2015) for further information). The CLEQ was administered verbally to all participants following the SCAN interview once there had been the opportunity for rapport to be established. Participants were asked if they experienced one or more of a list of 12 childhood events, not including abuse, before the age of 16 years. Case notes were also reviewed for any mention of ACLEs including abuse.

Participants also completed the Brief Life Events Questionnaire (BLEQ) asking about severe life events based on the list proposed by Brugha et al. (1985). An open question was added to

the questionnaire asking participants “Do you think that there is anything that has happened to you during your life which has contributed to you becoming unwell?” This was also examined for evidence of ACLEs including abuse. These sources of information were combined to code the presence or absence of the following types of ACLE occurring before the age of 16 years for each participant: (1) any abuse (sexual and/or physical and/or emotional), (2) sexual abuse, (3) physical abuse, (4) emotional abuse, (5) death of parent, (6) death of sibling, (7) death of a close friend, (8) divorce and/or separation of parents.

Sample

Participants were included in the current study if they had completed the ALS-SF measure and met DSM-IV diagnostic criteria for bipolar I disorder, bipolar II disorder or major depressive disorder recurrent.

Statistical analyses

The data were analysed quantitatively using SPSS software (version 20.0). Analyses of variance (ANOVAs) and chi-squared analyses were firstly conducted to compare the three diagnostic groups on a number of demographic variables and current mental state. Four separate analyses of covariance (ANCOVAs) to compare mean ALS-SF scores (total score, plus three subscale scores) between the diagnostic groups with possible demographic confounders and current mood state as covariates were conducted.

In order to address our second aim we calculated descriptive summaries for the frequency of each type of ACLE in those with each diagnosis, and the ALS-SF total score for those with and without each trauma within each diagnostic group. We also examined whether there was a dose–response effect of childhood trauma by testing whether a greater number of ACLEs

was associated with higher ALS-SF score within each diagnostic group using Pearson's correlation coefficients.

Multiple linear regressions within each diagnostic group were then conducted to assess the relationship between the type of ACLE and ALS-SF scores adjusting for possible confounders and current mood state. Probabilities used were two-tailed throughout, a value $p < 0.05$ was the minimum criterion for statistical significance for all analyses.

Results

The final sample for the current analyses was made up of the following DSM-IV diagnostic groups who had completed the ALS-SF: bipolar disorder I (BPI) (n=923); bipolar disorder II (BPII) (n=363); and, major depressive disorder recurrent (MDDR) (n=207).

Demographics and current mental state measures

The demographic characteristics and current mental state measures of each diagnostic group are presented in Table 1. There were significant differences ($p < 0.05$) between groups for sex, age at interview, highest level of education, recruitment method and on both current mental state measures (BDI and AMS). These variables were therefore controlled for in further analyses.

[TABLE 1 ABOUT HERE]

Adjusted mean total ALS-SF and subscale scores

After adjusting for current manic (AMS score) and depressive symptoms (BDI score), and potential demographic confounders (sex, age at interview, highest level of education, recruitment method), total ALS-SF scores differed significantly across groups [$F(2, 1387) = 10.407, p < 0.001$] (see Table 2). Scores were highest in the BPII group (mean 42), followed by the BPI group (mean 40), then the MDDR group (mean 37). All differences between groups were significant (BPI *versus* BPII, $p = 0.024$; BPI *versus* MDDR, $p = 0.001$; BPII *versus* MDDR, $p < 0.001$). The same adjustments were applied to analyses of the three ALS-SF subscales (see Table 2). Scores on each subscale differed significantly across the diagnostic groups [anxiety/depression: $F(2, 1387) = 3.072, p = 0.047$; depression/elation: $F(2, 1387) = 14.903, p < 0.001$; and, anger: $F(2, 1387) = 7.246, p = 0.001$]. In each case, the BPII group scored highest.

[TABLE 2 ABOUT HERE]

Adverse childhood life events and association with ALS-SF scores

The frequency of each type of ACLE across the diagnostic groups is shown in Table 3. Having experienced any form of childhood abuse was reported most frequently by those with BPII followed by BPI, and then MDDR (21.8% *versus* 16.3% *versus* 5.3% respectively), and this pattern was replicated for individual categories of sexual, physical and emotional abuse. There was a significant difference in the prevalence of experiencing any abuse ($p < 0.001$), sexual abuse ($p = 0.001$), physical abuse ($p < 0.001$) and death of a close friend ($p = 0.017$) across the diagnostic groups.

[TABLE 3 ABOUT HERE]

Figure 1 displays the mean total ALS-SF scores of individuals within each diagnostic group according to the presence or absence of each type of ACLE. Mean ALS scores in those without and with the experience of any childhood abuse were: BPI 37.69 (95% confidence interval (CI): 36.77-38.61) *versus* 45.25 (CI: 42.97-47.53) respectively; BPII 44.40 (CI: 42.74-46.07) *versus* 47.13 (CI: 44.15-50.10); and, MDDR 37.05 (CI: 35.31-38.79) *versus* 35.27 (CI: 26.83-43.71). The number of ACLEs experienced was not significantly associated with ALS-SF total score in any diagnostic group.

[FIGURE 1 ABOUT HERE]

Results of the linear regression analyses examining the association between the presence of each type of ACLE and ALS-SF total score within each diagnostic group, controlling for potential confounders are shown in Table 4. Within the BPI group experiencing any abuse ($p=0.021$), physical abuse ($p=0.003$) and the death of a close friend ($p=0.002$) was significantly associated with higher total ALS-SF score. No ACLEs were significantly associated with a higher total ALS-SF score within the BPII and MDDR groups. Significant associations were found between abuse and death of a close friend and higher scores on all the ALS subscales within the BPI group (see Table 5).

[TABLES 4 & 5 ABOUT HERE]

Discussion

Main findings

This study addresses important gaps in our research knowledge; that is a direct comparison of the extent of affective instability in bipolar disorders and unipolar depression as measured by a standardised assessment and an examination of whether, and which, childhood traumatic events are linked to affective instability in adulthood as they are in other disorders.

The main findings are that level of affective instability is highest in bipolar disorder II, followed by bipolar disorder I, and unipolar depression, even after adjusting for current mood state. Secondly, this pattern persists within subscale scores of anger, anxiety-depression and depression-elongation with scores in these parameters. Thirdly, the rates of childhood traumas categorised as emotional, physical and sexual abuse, and nearly all other traumatic events, were highest in those with bipolar disorder II, followed by bipolar disorder I. Fourthly, in this large sample of people with affective disorders, childhood traumas such as experiencing any abuse, physical abuse and the death of a close friend were significantly associated with greater affective instability only in people with bipolar disorder I, no such links being found in bipolar disorder II or those with unipolar depression. So, whilst childhood traumatic events are commoner in bipolar disorder II, they only appear to be robustly associated with degree of affective instability in bipolar disorder I. Fifthly, the total number of traumatic childhood experiences was not associated with the degree of affective instability; there is no dose-response relationship operating in this link. Finally, a number of different traumatic childhood experiences, including death of a parent and parental divorce/separation, did not have an effect in explaining extent of affective instability in either bipolar disorders or unipolar depression.

Theoretical and clinical implications

It has previously been suggested that affective instability may be a core dimension of bipolar disorder, with levels being high in euthymia in comparison to controls (Henry et al., 2008)

and existing independent of manic or depressive episodes (Strejilevich et al., 2013).

Emerging evidence suggests there are specific gene variants that related specifically to emotional reactivity in BD (Mathieu et al., 2015). We found affective lability levels are higher in those with bipolar disorder than depression, discriminating between them even after controlling for current mood state. Whilst affective instability is transdiagnostic (Broome et al., 2015b) our findings add further support to the idea that affective instability may be a particularly important psychopathology in bipolar disorder. It may underlie some of the severe consequences of the illness, predicting chronicity and severity in youth with the disorder (Yen et al., 2015) and functional losses in those with established illness (Strejilevich et al., 2013).

Within major affective disorders levels of affective instability are highest amongst people with bipolar disorder II. Previous studies measuring affective instability using the ALS have suggested both bipolar disorder II and borderline personality disorder involve similar levels of affective lability, though there are differential patterns in the two disorders (Henry et al., 2001; Reich et al., 2012). Whilst we did not have a borderline personality disorder comparison group our results may in part be explained by comorbidity with borderline personality disorder, which is known to exist in 25-30% of people with bipolar disorders being highest in bipolar II (Mantere et al., 2006). These results may help to explain the difficulties that clinicians have in delineating bipolar disorder II and borderline personality disorder. However meeting criteria for both disorders does not negate the importance of affective instability in each of the diagnostic categories. Many pathologies are a feature of

different medical illnesses and this is the case for psychiatric disorders also. Greater affective instability in bipolar disorder II compared to bipolar disorder I may also be due to differences in the rate of co-morbid anxiety disorders or suicidal ideation/behaviour between the groups and should be investigated in future work.

Surprisingly there is only limited evidence from epidemiological studies regarding prevalence of childhood trauma in bipolar disorders. In this large sample of people with major affective disorders, the prevalence of significant childhood trauma, i.e., childhood abuse, was 16-22% in people with bipolar disorder, broadly in line with other studies (Conus et al., 2010; Romero et al., 2009) with smaller sample sizes. Trauma levels were higher in those with bipolar disorder than people with unipolar depression again replicating a smaller study (Hyun et al., 2000). Our findings of the comparison of childhood trauma between different subtypes of bipolar disorder are novel and suggest those with bipolar II are particularly frequently affected by childhood trauma. Possible explanations of the high rates of childhood trauma in bipolar disorders includes direct causality, predisposition to bipolar disorder increasing risk of experiencing abuse or the trans-generational transmission of childhood trauma in families affected by the illness (Etain et al., 2008). Each of these possibilities requires different interventional strategies.

Childhood trauma in the form of experiencing any form of abuse, or death of a close friend was associated with degree of affective instability in bipolar disorder I even after controlling for a number of important variables. Exposure to such events was particularly linked to current experiences of anger independent of mood state in the current study. This link is important as childhood trauma in bipolar disorder is associated with rapid cycling, suicidal behaviour, earlier onset (Garno et al., 2005; Leverich and Post, 2006; Post et al., 2014), post

traumatic stress disorder (Maniglio, 2013) increased number of depressive episodes (Etain et al., 2013), and more severe psychosis (Alvarez et al., 2011). All represent a worsening of clinical course (Daruy-Filho et al., 2011). Thus, clinical interventions targeting affective instability in people who have suffered significant childhood trauma could potentially change the clinical course of bipolar disorder.

Children who are subjected to traumatic events, show increased affective reactivity to stress and a diminished ability to regulate emotions (D’Andrea et al., 2012) and this may be due to induced changes in limbic reactivity or deficits in default mode network connectivity (Dvir et al., 2014). Data from a large (N=1065) prospective study of adolescents suggests emotional dysregulation leads to a multitude of psychiatric pathology but that it was not primarily a consequence of psychopathology (McLaughlin et al., 2011). A previous erudite literature review hypothesises a baseline genetic vulnerability on which the neurobiological effects of childhood traumatic events are superimposed in the developing child’s brain inducing affective dysregulation in people with bipolar disorder (Etain et al., 2008). Our results, whilst cross sectional, are consistent with this hypothesis suggesting a link between childhood trauma, affective dysregulation and bipolar disorder.

It is known that people with bipolar disorder who have suffered childhood trauma have more mood cycling within a 24-hour period (Leverich et al., 2002) and that they have higher scores indicating depressive, cyclothymic and anxious temperament in comparison to those who have not experienced childhood traumas (Kesebir et al., 2015) . The current study further defines this association in that whilst rates of affective instability were significantly higher in bipolar disorder II, the link between childhood trauma and affective instability only operated in bipolar disorder I. Indeed experiencing “any” childhood abuse increased the affective

instability levels of those with bipolar disorder I to levels similar to people with bipolar disorder II. Either childhood trauma is not mechanistically related to bipolar disorder II and unipolar depression in the same way as in bipolar disorder I or affective instability is in some way different in bipolar I, II and unipolar depression that is not captured by the affective lability scale.

A further explanation is to some extent supported by neuro-imaging research; that is, the nature of affect dysregulation is discrepant in bipolar I and II. In a relatively small study comparing healthy controls (N=20), euthymic participants with bipolar I disorder (n=16), and euthymic participants with bipolar II disorder (N=19) participants with bipolar I disorder showed abnormalities in functional and anatomical connectivity between prefrontal cortices and subcortical structures in emotion regulation circuitry. These deficits did not extend to people with bipolar II disorder, suggesting fundamental differences in the pathophysiology of bipolar disorder subtypes (Caseras et al., 2015).

Childhood trauma did not appear to be linked to affective instability in unipolar depression either. The ALS-SF primarily measures affect lability, but affect intensity may be more important at generating depression than lability (Gershon and Eidelman, 2015).

Limitations

This study had a number of limitations. Affective instability includes several aspects including lability, intensity and control (Marwaha et al., 2014b). The Affective Lability Scale (ALS), as its name suggests primarily measures affect lability and valence, although some questions can relate to intensity. The ALS is a self-report scale and as such will be subject to

retrospective recall bias, something which could be particularly significant when measuring affective instability in which dynamic oscillation is a key feature (Broome et al., 2015b).

The response rate to the ALS-SF was 37%. Despite this relatively modest response rate which inevitably introduces some form of responder bias to the data, our analyses are based on a large, representative and well characterised sample of people with major affective disorders (N=1493). The ALS-SF was included in a mailshot with several other questionnaires; responders completed all questionnaires, which reduces the likelihood that decision to respond was particularly influenced by the inclusion of the ALS-SF. Information about childhood trauma was comprehensive with data collection triangulated from interview self-report and using information from casenotes. The analyses also controlled for current mood state, giving greater confidence about the associations between childhood trauma and affective instability that were found.

It is possible that we did not find an association between childhood abuse and higher ALS score in the bipolar disorder II group because of lack of statistical power due to the smaller sample size in that group. A *post hoc* power calculation showed that the power of the study to detect the observed difference in ALS score between those with (N=79) and without (N=284) a history of childhood abuse (47.13 *versus* 44.40 respectively, a difference of 2.73 points) in the bipolar disorder II group was 35%. However, if we had observed a difference of the magnitude observed in the bipolar disorder I group (7.56 points), the power of the comparison within the bipolar disorder II group would have been over 95%.

Future research

This study uses cross sectional data to test the association between childhood trauma and affective instability in those with major affective disorders. Further studies are required in order to more securely ascertain direction of effect; these are likely to require formal path analytic statistical techniques to investigate whether affective instability mediates the association between childhood traumatic events and bipolar disorder diagnosis and its outcomes. Such analyses ideally, will require data from longitudinal cohort studies. If affective instability, in those longitudinal studies is confirmed as being part of the pathway from childhood trauma to bipolar disorder, then intervention studies targeting affective instability will be warranted. Whilst in this study we used the ALS to thoroughly assess affective instability, this primarily focuses on affect change. In-depth assessment of fluctuations of mood over time using ecological momentary assessment could further illuminate the associations found.

In summary, affective instability is greater in bipolar disorder than unipolar disorder and this adds support to the idea that affective instability is an important dimension in bipolar disorder. Childhood rates of abuse are highest in those with bipolar disorder II. There is a strong link between childhood traumatic events and affective instability levels in bipolar disorder I and this may be one way in which exposure and disorder are linked.

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Table 1. Demographics and current mental state by diagnostic group

	BP I	BP II	MDDR	
Total number of individuals	923	363	207	
Females % (<i>n</i>)	75.0 (692)	73.8 (268)	66.7 (138)	$p = 0.049$ BPI>MDDR
Mean age at interview, in years (SD)	49.0 (11.5)	46.5 (12.1)	50.0 (10.4)	$p < 0.001$ BPI+MDDR>BP II
Completed higher education % (<i>n</i>)	46.6 (415)	45.6 (161)	30.5 (61)	$p < 0.001$ BPI+BP II>MDDR
Professional occupation % (<i>n</i>)	59.5 (522)	59.4 (202)	63.6 (131)	NS
Systematically recruited % (<i>n</i>)	22.1 (201)	20.9 (75)	38.0 (78)	$p < 0.001$ MDDR>BPI+BP II
Mean BDI score (95% CI)	13.35 (12.64 – 14.06)	18.55 (17.25 – 19.85)	16.29 (14.78 – 17.79)	$p < 0.001$ BP II>MDDR>BP I
Mean AMS score (95% CI)	3.29 (3.07 – 3.51)	4.39 (3.96 – 4.81)	2.33 (1.94 – 2.72)	$p < 0.001$ BP II>BPI>MDDR

Ns vary due to missing data. BPI = bipolar I disorder, BP II = bipolar II disorder, MDDR = major depressive disorder recurrent, BDI = Beck Depression Inventory, AMS = Altman Mania Scale, CI = confidence interval.

Table 2. Mean ALS-SF scores, adjusted for potential demographic confounders¹ and current mental state², by diagnostic group

	BP I (n=923)	BP II (n=363)	MDDR (n=207)	
Total ALS-SF (95% CI)	39.99 (39.26 – 40.71)	41.60 (40.42 – 42.77)	37.08 (35.55 – 38.60)	$p < 0.001$ BP II > BP I > MDDR
Anxiety/depression subscale (95% CI)	11.74 (11.49 – 11.99)	12.34 (11.94 – 12.74)	11.82 (11.29 – 12.34)	$p = 0.047$ BP II > BP I
Depression/elation subscale (95% CI)	18.60 (18.23 – 18.97)	19.28 (18.68 – 19.88)	16.58 (15.80 – 17.36)	$p < 0.001$ BP I + BP II > MDDR
Anger subscale (95% CI)	9.65 (9.40 – 9.90)	9.98 (9.57 – 10.39)	8.68 (8.15 – 9.22)	$p = 0.001$ BP I + BP II > MDDR

BP I = bipolar I disorder, BP II = bipolar II disorder, MDDR = major depressive disorder recurrent, ALS-SF = Affective Lability Scale-Short Form, CI = confidence interval.

¹ Sex, age at interview, highest level of education, recruitment method.

² BDI and AMS scores.

Table 3. Frequency of adverse childhood life events across the diagnostic groups

	BP I (n=923)	BP II (n=363)	MDDR (n=207)	
Any abuse % (n)	16.3 (150)	21.8 (79)	5.3 (11)	$p < 0.001$ BP II > BP I > MDDR
Sexual abuse % (n)	10.1 (93)	13.5 (49)	3.4 (7)	$p = 0.001$ BP I + BP II > MDDR
Physical abuse % (n)	8.8 (81)	11.6 (42)	1.4 (3)	$p < 0.001$ BP I + BP II > MDDR
Emotional abuse % (n)	3.1 (29)	3.6 (13)	1.4 (3)	$p = 0.335$
Death of a parent % (n)	7.2 (66)	7.7 (28)	8.7 (18)	$p = 0.736$
Death of a sibling % (n)	4.6 (42)	2.5 (9)	2.4 (5)	$p = 0.118$
Death of a close friend % (n)	10.1 (93)	15.7 (57)	11.1 (23)	$p = 0.017$ BP II > BP I
Divorce or marital separation of parents % (n)	15.3 (141)	19.3 (70)	12.1 (25)	$p = 0.059$

Ns vary due to missing data. BP I= bipolar I disorder, BP II=bipolar II disorder, MDDR=major depressive disorder recurrent.

Table 4. Linear regression analyses for the association between ALS-SF total scores and the presence of adverse childhood life events within each diagnostic group controlling for potential demographic confounders¹ and current mental state²

	Total ALS-SF B Coefficient (95% CI) <i>p</i> -value		
	BP I (n=923)	BP II (n=363)	MDDR (n=207)
Any abuse	2.36 (0.36 – 4.36) 0.021	0.72 (-2.26 – 3.69) 0.635	-0.52 (-6.87 – 5.84) 0.873
<i>Sexual abuse</i>	0.78 (-1.68 – 3.24) 0.534	1.87 (-1.70 – 5.43) 0.304	2.72 (-5.16 – 10.59) 0.497
<i>Physical abuse</i>	3.94 (1.33 – 6.55) 0.003	-0.27 (-4.10 – 3.55) 0.888	-2.12 (-14.17 – 9.93) 0.729
<i>Emotional abuse</i>	3.88 (-0.25 – 8.01) 0.066	3.35 (-3.62 – 10.32) 0.346	2.63 (-9.38 – 14.65) 0.666
Death of a parent	-1.62 (-4.41 – 1.18) 0.257	-0.61 (-5.14 – 3.93) 0.792	-2.18 (-7.52 – 3.16) 0.422
Death of a sibling	0.32 (-3.07 – 3.71) 0.853	0.90 (-7.12 – 8.91) 0.826	-2.36 (-11.81 – 7.09) 0.623
Death of a close friend	3.75 (1.36 – 6.14) 0.002	1.80 (-1.59 – 5.20) 0.297	0.23 (-4.38 – 4.84) 0.921
Divorce or marital separation of parents	0.98 (-1.04 – 3.01) 0.341	0.46 (-2.71 – 3.63) 0.776	-1.64 (-6.19 – 2.91) 0.477

Ns vary due to missing data. BPI= bipolar I disorder, BPII=bipolar II disorder, MDDR=major depressive disorder recurrent, ALS-SF= Affective Liability Scale-Short Form. Figures in **bold** indicate $p < 0.05$.

¹ Sex, age at interview, highest level of education, recruitment method.

² BDI and AMS scores.

Table 5. Linear regression analyses for the association between ALS-SF subscale scores and the presence of adverse childhood life events within the bipolar I disorder group (n=923) controlling for potential demographic confounders¹ and current mental state²

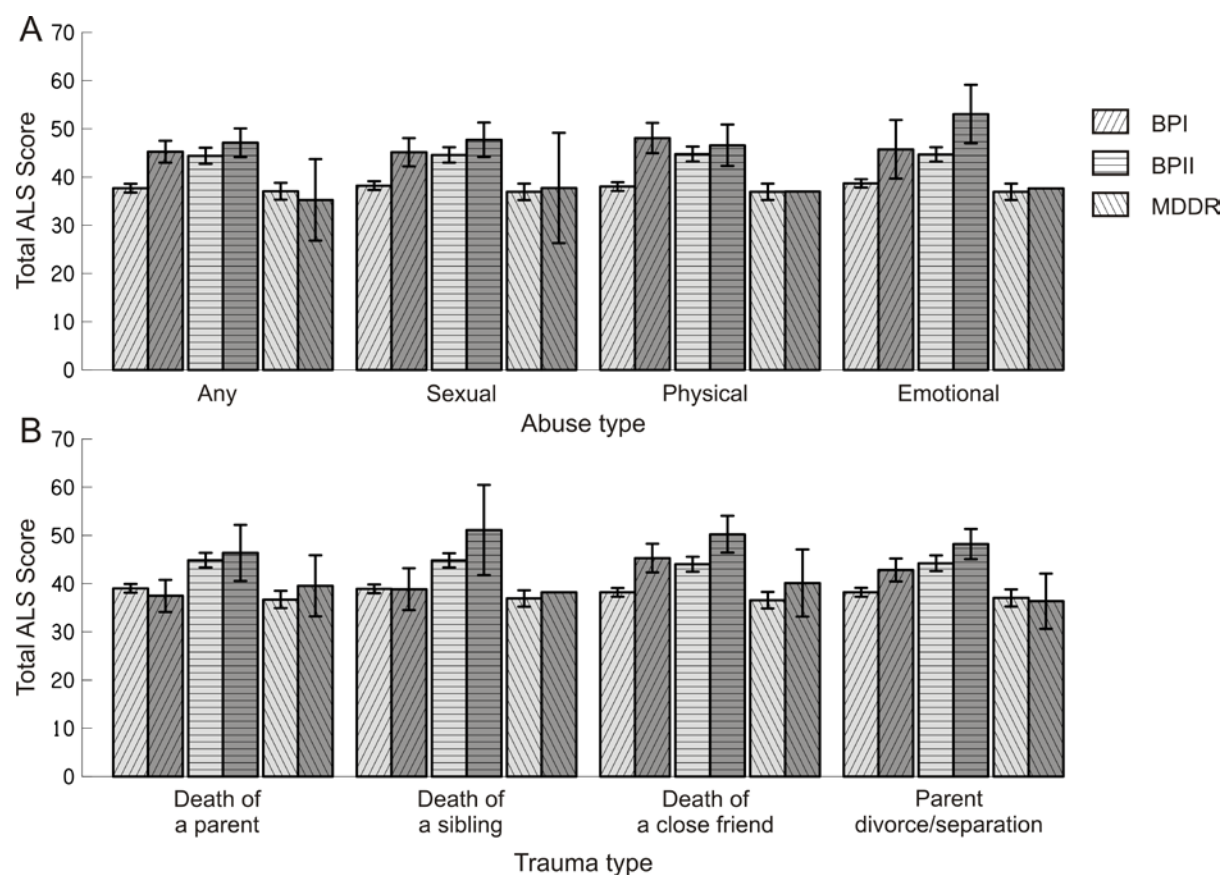
	Anxiety/Depression B Coefficient (95% CI) <i>p</i> -value	Depression/Elation B Coefficient (95% CI) <i>p</i> -value	Anger B Coefficient (95% CI) <i>p</i> -value
Any abuse	0.39 (-0.30 – 1.07) 0.269	0.96 (-0.07 – 1.99) 0.069	1.02 (0.33 – 1.70) 0.004
<i>Sexual abuse</i>	-0.18 (-1.02 – 0.66) 0.682	0.08 (-1.19 – 1.35) 0.905	0.88 (0.03 – 1.72) 0.042
<i>Physical abuse</i>	0.96 (0.06 – 1.85) 0.036	1.67 (0.32 – 3.02) 0.015	1.31 (0.41 – 2.21) 0.004
<i>Emotional abuse</i>	0.71 (-0.70 – 2.13) 0.321	2.27 (0.13 – 4.40) 0.037	0.90 (-0.53 – 2.32) 0.218
Death of a parent	-0.82 (-1.78 – 0.13) 0.090	-0.25 (-1.69 – 1.20) 0.737	-0.55 (-1.51 – 0.42) 0.267
Death of a sibling	-0.07 (-1.22 – 1.09) 0.910	0.19 (-1.57 – 1.94) 0.835	0.20 (-0.97 – 1.37) 0.734
Death of a close friend	1.32 (0.50 – 2.14) 0.002	1.30 (0.06 – 2.54) 0.040	1.13 (0.31 – 1.96) 0.007
Divorce or marital separation of parents	0.25 (-0.44 – 0.94) 0.480	0.33 (-0.71 – 1.38) 0.531	0.40 (-0.30 – 1.10) 0.260

Ns vary due to missing data. ALS-SF= Affective Liability Scale-Short Form. Figures in **bold** indicate $p < 0.05$.

¹ Sex, age at interview, highest level of education, recruitment method.

² BDI and AMS scores.

Figure 1 Mean total ALS-SF score (\pm 95% confidence intervals¹) associated with the absence (light colour) or presence (dark colour) of each adverse childhood life event by diagnostic group



BPI= bipolar I disorder, BPII=bipolar II disorder, MDDR=major depressive disorder recurrent, ALS-SF= Affective Liability Scale-Short Form

¹ Error bars omitted where a small sample size led to a very wide confidence interval.

Graph A: Childhood abuse.

Graph B: Childhood traumas (non-abuse).

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