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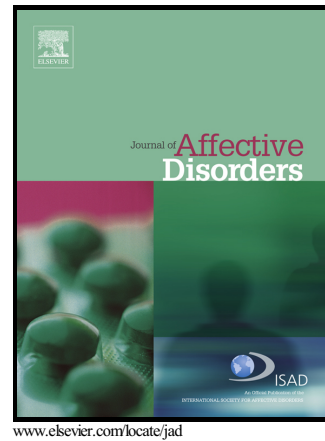
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Affective temperaments and concomitant alcohol use disorders in bipolar disorder.

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Abstract

Background: Alcohol misuse (AM) is more common in bipolar disorder (BD) than within the general population but the mechanisms of this association are unclear. We hypothesised that certain affective temperaments (including hyperthymic, cyclothymic, anxious, depressive and/or irritability) might represent 'fundamental states' contributing to risk of both AM and BD and we aimed to assess whether extremes of these five affective temperaments were associated with BD and concomitant AM status.

Methods: Our sample comprised 1420 individuals with BD who were recruited into a clinical-genetic study conducted by the Bipolar Disorder Research Network. Phenotypic assessments, including evaluation for AM and the 32-item TEMPS-A questionnaire, were conducted. Binary logistic regression was used to determine the effect of TEMPS-A scores on the likelihood of concomitant AM, with adjustment for confounders.

Results: Mean scores for four affective temperaments (hyperthymic, cyclothymic, depressive and irritable) were higher in cases (BD+AMs) than controls (BD only) (p<0.001). Hyperthymic and irritable temperaments in particular significantly increased the odds of concomitant AM within the BD sample after adjustment for potential confounders.

Limitations: The definition of AM was not directly based on formal diagnostic classification systems. A retrospective, cross-sectional design was used. Our findings may not generalize to other countries and cultures.

Conclusions: Higher scores on measures of hyperthymic and irritable temperament may contribute to the association between AM and BD. Assessing affective temperaments early in the course of BD may help to predict the development of an AM problem in vulnerable individuals.

Key words: bipolar disorder, alcohol misuse, affective temperament.

1. Background

Problems relating to alcohol use are common in bipolar disorder (BD), affecting almost one third of individuals (Di Florio et al., 2014), compared to 13%-25% of the general population (Kessler et al., 2005; Regier et al., 1990; Schuckit, 2009). Alcohol misuse (AM) is an important clinical issue because comorbid alcohol problems in people with BD are associated with treatment non-adherence, higher rates of suicide, and higher rates of other substance abuse disorders (Baldessarini et al., 2008; Oquendo et al., 2010).

Several potential mechanisms might explain the development of AM problems in people with BD. The self-medication hypothesis suggests that AM develops from the frequent use of alcohol to cope with the symptoms and distress associated with BD (Strakowski et al., 2000). There may also be important neurobiological and genetic mechanisms (Farren et al., 2012). For example, individuals with BD and individuals with AM both have reduced grey matter volumes within the anterior cingulate gyri relative to controls (Nery et al., 2011), there are shared genetic risk factors between BD and AM (Johnson et al., 2009), and shared abnormalities within neurotransmitter and neuropeptide systems (Rakofsky and Dunlop, 2013).

Affective temperaments are a collection of biologically determined and inherited traits (Greenwood et al., 2013). Certain affective temperaments may be characteristic for certain personalities or serve as a starting point for an episodic affective illness (Blöink et al., 2005) and temperament is thought to shape the way a person views and acts by interacting with environmental factors to shape personality (Moore et al., 2005). Affective temperaments may refer to subaffective trait expressions representing the earliest subclinical phenotypes of affective disorders which are present during euthymic periods of affective disorders (Maremmani et al., 2005). To date, there has been relatively little work on the possible role of affective temperaments in the investigation of risk factors for AM in people with BD.

There has been some work on the possible role of affective temperaments in alcohol and substance misuse disorders. Pacini et al. (2009) found higher scores for depressive, cyclothymic and irritable temperaments in alcohol dependence compared to controls, and Vyssoki et al. (2011) found that higher cyclothymic scores influenced the age of onset of alcohol abuse and dependence and that methadone-treated individuals with heroin dependence had significantly higher cyclothymic and irritable scores (Maremmani et al.,

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2009). Irritable temperament may be a risk factor for drug misuse disorders in patients treated for alcohol dependence (Khazaal et al., 2013).High trait anxiety is a common feature in people with BD and AM (Levander et al., 2007) and there is also a relationship between hyperthymic temperament and substance misuse in people with BD (Azorin et al., 2011a; Harnic et al., 2010).

In this study, we aimed to assess *a)* whether certain affective temperaments were more strongly associated with BD and concomitant AM, compared to BD alone, and *b)* whether any of the associations persisted after accounting for a range of potential confounders. Our *a priori* hypotheses were that individuals with BD and AM would have higher scores on cyclothymic, hyperthymic, depressive or anxious temperaments on the Temperament Evaluation of Memphis, Pisa, Paris & San Diego auto-questionnaire (TEMPS-A), and that higher scores for these temperaments would be significant predictors of concomitant AM within a logistic regression model, which took account of confounding factors.

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2. Methods

2.1 Sample

The study sample were individuals with BD-I and BD-II recruited between 1996 and 2012 as part of an on-going programme of research conducted by the UK-based Bipolar Disorder Research Network (BDRN) into the genetic and environmental causes of mood disorders. Participants were recruited systematically from the case-loads of community mental health teams and non-systematically from advertisements in local and national media, through patient support organisations (such as Bipolar UK) and the study website (www.bdrn.org). Volunteers were excluded from the original study if they had only experienced affective illness secondary to alcohol, substance dependence, or a medical illness or medication, or if they were biologically related to another study participant. All participants were aged 18 years or over. This study was approved by the relevant NHS research ethics committees and had local Research and Developmental approval in all participating NHS Trusts/Health Boards.

The current study was carried out on a subset of 1420 participants with BD who had been rated according their alcohol consumption and had also completed the TEMPS-A questionnaire. Of the original sample which comprised data for 2160 individuals with bipolar disorder, 1 person was excluded because of missing data on alcohol intake, 658 were excluded due to missing data on TEMPS-A scores, and 55 individuals with a diagnosis of BD NOS and 26 individuals with schizoaffective disorder – bipolar subtype (SABP) were excluded, leaving a total sample of 1420 individuals with BD.

Using the Schedules for Clinical Assessment in Neuropsychiatry (SCAN) (Wing et al., 1990), all participants were interviewed by a trained research psychologist or psychiatrist. Psychiatric and general practice case-notes were also reviewed. Data from the clinical interview and case notes were then combined to make best estimate lifetime-ever diagnoses according to DSM-IV criteria and to rate lifetime-ever clinical characteristics. In cases where there was some doubt, diagnostic and clinical ratings were made by at least two members of the research team blind to each other's rating and consensus was reached via discussion when necessary. Inter-rater reliability was formally assessed using 20 random cases. Mean kappa statistics were 0.85 for DSM-IV diagnoses and ranged between 0.81 and 0.99 for other key

clinical categorical variables. Mean intra-class correlation coefficients were between 0.91 and 0.97 for key clinical continuous variables.

2.2 Measures

During the interview participants were asked about their lifetime alcohol intake and any associated problems. Based on their responses, and from information within case notes, AM was defined as consuming >14 units of alcohol (>8 standard US drinks) in women or >21 units of alcohol (>12 standard US drinks) in men at any point of life, with related impairments which included any one of: psychiatric/psychological problems, medical problems, financial problems, relationship problems, occupational problems, other problems or multiple problems. (A unit of alcohol refers to 8 g of ethanol. A US standard drink contains 14 g of ethanol).

Participants completed the Beck Depression Inventory (BDI) and the Altman Mania Scale (AMS) to assess current depressive and mania symptoms. The TEMPS-A was also completed by each participant to assess five affective temperaments: cyclothymic, hyperthymic, irritable, depressive and anxious (Akiskal et al., 2005a). It has been found to have concurrent validity with the Temperament and Character Inventory (TCI) (Akiskal et al., 2005b), McCrae's Neuroticism-Extroversion-Openness Five Factor Inventory (NEO-FFI) (Blöink et al., 2005), and von Zerssen's Munich Personality Test (MPT) (Akiyama et al., 2005). A study of 178 Japanese white-collar workers demonstrated the stability of TEMPS-A scores over 6 years (Kawamura et al., 2010) suggesting that, unlike personality, temperament does not substantially change over time. The maximum possible scores were recorded for each of the domains are 12 points for cyclothymic, 8 for depressive, 8 for irritable, 8 for hyperthymic and 3 for anxious (Akiskal et al., 2005b).

2.3 Analyses

Data for the 1420 participants were divided into two groups according to the presence of AM: individuals with BD plus concomitant AM (BD with AM group; N = 821) and the comparison group BD without AM (BD without AM group; N = 599). These two groups were then compared according to their TEMPS-A scores for the 5 affective temperaments and a number of demographic and clinical characteristics, including age at interview, gender and lifetime history of cannabis use disorder(defined using an OPCRIT item based on diagnostic classification systems (McGuffin et al., 1991)), as well as scores on two current mood state measures completed by the participant at the same time as the TEMPS-A: the Beck

Depression Inventory (BDI) and the Altman Mania Scale (AMS). The Chi-squared (χ^2) test was used for categorical variables; the Student's t-test for continuous variables.

The potential effect of each TEMPS-A domain score on the odds of having a lifetime history of concomitant AM was investigated using binary logistic regression. Before constructing a logistic regression model, the collinearity between scores for domains was assessed using a Pearson correlation coefficient and a 2-tailed significance test. Since there was collinearity between almost all of the TEMPS-A domains when compared with the other four, it was appropriate to include all TEMPS-A domains in a single binary logistic regression model.

The final adjusted logistic regression model contained a number of clinical and demographic covariates to control for the effect of potential confounders in the relationship between BD, AM and TEMPS-A scores. They were identified from the factors previously studied. The continuous covariates were age at interview, Beck Depression Inventory (BDI) scores, Altman Mania Scale (AMS) scores. Age was included as the prevalence of AM is known to vary across the life-span (Grant and Dawson, 1997) which might have also affected alcohol consumption. BDI and AMS scores were included to control for the effect of current mood on TEMPS-A scores. The categorical covariates were gender, whether or not the participant had ever been a regular tobacco smoker and whether or not the participant reported a lifetime diagnosis of cannabis abuse or dependence (Strakowski et al., 2007). Gender was included because AM is more common in men (Cardoso et al., 2008). Smoking history was included because it is known to be associated with BD (Maremmani et al., 2011) and cannabis use was included because it is the most commonly abused drug in individuals with BD (Strakowski et al., 2007) and a Swedish study demonstrated that cannabis use is associated with a higher prevalence of hazardous alcohol use (Berge et al., 2014).

For a further 371 there was missing data for the other covariates (e.g. gender, age at interview and smoking status) in the adjusted logistic regression model, leaving a sample of 1049. The Hosmer-Lemeshow χ^2 test was used as a goodness-of-fit statistic and the c statistic was also used as a method of validating predicted probabilities (Peng et al., 2002). All statistical analyses were performed on SPSS, version 21.

3. Results

3.1 Demographic and clinical differences between BD with AM and BD without AM groups

There were significant differences on several demographic and clinical variables between the groups (table 1). Individuals in the BD with AM group were more likely to be female (p<0.001), were older at interview (p<0.001), more likely to have ever been a regular tobacco smoker (p<0.001), more likely to have a lifetime diagnosis of cannabis abuse or dependence (p<0.001), and had lower BDI scores (p<0.001) (table 1).

[Insert table 1 here]

3.2 Differences in TEMPS-A scores

The mean scores for four of the TEMPS-A domains (cyclothymia, depressive, irritable, hyperthymic) were significantly higher in the BD with AM group (p<0.001) (table 2).

[Insert table 2 here]

3.3 Unadjusted logistic regression model

In an unadjusted logistic regression model, without potential confounders, the following led to significant odds ratios for concomitant AM: increasing irritable TEMPS-A score (OR=1.265; 95% CI: 1.186-1.349) and increasing hyperthymic TEMPS-A score (OR=1.090; 95% CI: 1.036 to 1.147) (table 3). The unadjusted model fitted to the data well (Hosmer-Lemeshow χ^2= 6.010; *p*= 0.646 i.e. p>0.05) and the *c* statistic value of 0.698 suggested that the accuracy of the unadjusted logistic regression model in predicting the presence of AM within this sample was poor (Hanley and McNeil, 1982).

[Insert table 3 here]

3.4 Adjusted logistic regression model

With adjustment for potential confounders the same two affective temperaments remained significant predictors of AM: increasing irritable score (OR=1.221; 95% CI: 1.129 to 1.321) and increasing hyperthymic score (OR=1.097; 95% CI: 1.030 to 1.168) (table 4). Several potential confounders in the model were also significant predictors of increases or decreases in the odds of AM (table 4): older age (OR = 0.980; 95% CI: 0.969-0.992) and female sex compared to male (OR = 0.637; 95% CI: 0.465-0.873) led to significantly decreased odds

(table 4). The following led to significantly increased odds of AM: current or previous regular tobacco smoking (OR = 2.539; 95% CI: 1.915-3.368) and a lifetime history of cannabis abuse or dependence (OR = 2.275; 95% CI: 1.314-3.938) (table 4). The adjusted model fitted to the data well (Hosmer-Lemeshow χ^2= 6.320 p=0.611) and the *c* statistic value of 0.730 suggested that the accuracy of the adjusted logistic regression model in predicting the presence of concomitant AM within this sample was fair (Hanley and McNeil, 1982).

4. Discussion

The aim of this study was to assess whether certain affective temperaments were associated with concomitant AM in individuals with BD and whether higher scores on any of the affective temperaments were associated with an increase in the likelihood of BD individuals having concomitant AM. Although several of the TEMPS-A domain scores were higher in the BD with AM group, only higher scores on the irritability and hyperthymic TEMPS-A domains were significant predictors of AM in our sample of individuals with BD, after controlling for confounding factors.

It is notable that a history of tobacco smoking and cannabis abuse or dependence led to higher odds ratios for concomitant AM than irritable and hyperthymic TEMPS-A scores. Therefore, affective temperaments are clearly not the only factors associated with AM in people with BD and so cannot be considered in isolation and must be viewed as part of the wider psychopathology of AM in people with BD.

BDI scores were lower in the BD with AM group than for the BD alone group. Differences in TEMPS-A scores might explain this. Given the higher mean hyperthymic TEMPS-A scores (p<0.001) in the BD with AM group, this might be explained by a lower expression of depression symptomatology due to a temperamental predisposition to slightly elevated mood. Moreover, the irritable TEMPS-A scores were higher in the BD with AM group (p<0.001) which is of interest because irritable temperament is associated with mixed states (Iasevoli et al., 2013; Roettig et al., 2007) and atypical depressive features such as hypomanic symptoms and novelty seeking (Parneix et al., 2014).

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4.1 Limitations

Several possible limitations are acknowledged. The definition for AM in this study does not allow for the consideration of a formal diagnosis of alcohol abuse and alcohol dependence. Nevertheless, we believe that our definition of AM is pragmatic and clinically intuitive and it is noteworthy that our findings are based on a very large sample size for a study of this kind.

Data on the self-reported AM measure may have been limited by a reluctance of participants to admit to their true alcohol consumption. AM might therefore have been more prevalent within this sample than our results suggest. It is also possible that there was a selection bias whereby participants with a lower level of alcohol consumption were more likely to provide complete responses to the questions on alcohol use.

Moreover, given that the study was cross-sectional, there are no data on the onset of BD or AM, making it difficult to comment on temporal relationships between AM and BD. This requires further investigation in the future in order to allow for a better understanding of the relationship between affective temperaments and the psychopathology of BD and AM.

The self-report TEMPS-A questionnaire used in this study was the shortened 39-item version which only has 3 items for anxious temperament. This may represent a limitation, particularly considering the high prevalence of anxiety in concomitant BD with AM (Levander et al., 2007).

There was no control group in this study (individuals without BD). It is therefore not known whether the temperament profiles of individuals with BD plus AM differ from non-BD individuals with AM. Although the final model was reasonably good at discriminating between those who did or did not meet the criteria for AM, the fact that it was not a perfect fit could be due to other factors, such as the use of other drugs.

There were some additional limitations of the dataset used in this study. Firstly, given the highly significant effect of tobacco smoking and cannabis misuse on the odds of AM, it would have been useful to include a measure of the use of other substances as possible confounders. For example, cocaine is known to be used more commonly by people with BD than the general population (Cerullo and Strakowski, 2007). Secondly, there were no data on factors related to BD such as family history, suicide and self-harm, impulsivity, conduct disorders, history of mixed states and illness course, as well as factors relating to AM such as hospitalizations and symptoms of alcohol dependence.

One issue regarding the generalizability of these results is that participants were excluded in the original study if they had only experienced affective illness as a result of alcohol or substance use. This is a potential limitation because there may be differences in the temperament profiles between people who experience AM before or after the onset of affective illness. Further prospective work will be required to clarify this.

Finally, all participants in this study were of White UK ethnicity. Some evidence suggests that the high prevalence of AM in individuals with BD may be predominantly a Western issue: a retrospective chart review found that only 8.2% of a Taiwanese sample of 158 people with BD had AM, a figure that is similar to the rest of the Taiwanese population (Tsai et al., 1997).

4.2 Research implications

Our findings may provide insights into the developmental origins of AM in BD. For example, a developmental model suggests that AM, substance abuse disorder and antisocial personality disorders may all arise as externalizing psychopathologies which are related to underlying endophenotypic liabilities, childhood disruptive disorders and the environment (Iacono et al., 2008). This model proposes that interactions between these factors might predict an individual's susceptibility to externalising psychopathology. BD may represent another risk factor that interacts within this model to predispose an individual to AM (Lara and Akiskal, 2006). Since temperament is regarded as an innate and enduring trait, it might be part of this model of AM.

Another potential mechanism relates to behavioural traits associated with affective temperaments. People with a hyperthymic temperament tend to be more outgoing, confident, upbeat, jocular and fun loving (Akiskal et al., 2005a). Excessive alcohol use may represent an attempt by hyperthymic individuals to maximise these behavioural traits. In contrast, people with an irritable temperament tend to be critical, grouchy, dissatisfied, angry, violence-prone and sexually jealous (Akiskal et al., 2005a). Such traits may be more pronounced during periods of high mood in people with BD, with the result that individuals with BD and an irritable temperament may choose to use alcohol to attenuate the negative impact of these behaviours. Furthermore, people with hyperthymia have been found to have higher scores under Type I of the Lesch Alcoholism Typology (Vyssoki et al., 2011) which suggests that they may use alcohol to reduce withdrawal symptoms. This could represent another means by which hyperthymic temperament leads to the development of AM in

people with BD.

An irritable temperament has been associated with anger (Akiskal et al., 2005a), which is in turn associated with a range of neurochemical effects including increased dopamine activity, increased glutamate activity and decreased adenosine activity (Lara and Akiskal, 2006). Glutamate is known to be effected by alcohol (Chastain, 2006) and there is indirect evidence that it might be involved in the pathophysiology of BD because lamotrigine, a commonly used treatment for bipolar depression, has anti-glutaminergic properties (Rakofsky and Dunlop, 2013). It is therefore also possible that the glutamate system is part of the mechanism linking irritability, bipolarity and propensity to alcohol abuse.

There is a high correlation between cyclothymic and irritable temperaments and it has been suggested that these two temperaments could be considered as operating as one construct (Walsh et al., 2012). Several studies have identified a relationship between cyclothymic and irritable temperaments in people with BD (Pompili et al., 2014; Rybakowski et al., 2014; Tunc et al., 2014), with effects on the clinical course and expression of BD (Azorin et al., 2011b; Iasevoli et al., 2013; Perugi et al., 2012), on the history of suicide attempts (Tunc et al., 2014), and on the presence of comorbid eating disorders (Rybakowski et al., 2014). Irritability is also associated with Type IV of the Lesch Alcohol Typology, whereby individuals seem to drink alcohol to cope with mood swings and heightened levels of depression, fear and irritation (Schlaff et al., 2011). Although cyclothymic scores were higher in the BD with AM group, we did not find that they predicted AM in our regression models.

To some extent our findings might also be explained by impulsivity traits, such as novelty seeking, which are known to be increased in BD patients with comorbid alcohol misuse problems (Nery et al., 2008; Nery et al., 2013). In addition, impulsivity is correlated with irritable temperament and might increase the expression of impulsive traits leading to AM problems (Tatlidil Yaylaci et al., 2014).

It is important to note that some of the other covariates included in the adjusted logistic regression model were also significant predictors of an increase in odds of AM. A history of tobacco smoking and cannabis abuse or dependence both significantly increased the odds of concomitant AM, while increasing age and female gender significantly decreased odds. These findings are somewhat unsurprising given the known associations between alcohol

use disorders, male sex and BD (Cardoso et al., 2008; Nery et al., 2014). There is prior literature that demonstrates that younger people with BD are more likely to have substance use disorders; this may also apply to alcohol misuse (Maremmani et al., 2011; Strakowski et al., 2007). The odds ratios for some of these factors were higher than for TEMPS-A scores. Nevertheless, the association between TEMPS-A scores and AM might be more stable over time and might not be altered by certain factors such as age. While it is possible that the association between affective temperament and AM might be driven by other factors that have not been measured in this study, such as disinhibition, this study demonstrates that affective temperaments might represent a part of the wider picture of the psychopathology of addictions in mood disorders.

4.3 Clinical implications

Our findings may provide some insight for the development of better treatments for AM in individuals with BD. Goldstein and Bukstein (2010) have reported a delay between the onset of BD and subsequent substance use disorders. Given that affective temperaments are considered innate and enduring, an evaluation of these temperaments early in the course of BD may help clinicians target interventions to those who are more likely to develop an AM, for example, those scoring highly on hyperthymia and irritability.

4.4 Future work

Prospective cohort studies are required to assess potential causal pathways between TEMPS-A scores and AM in people with BD while controlling for some factors not assessed in this study. Similarly, future work could investigate the relationship between affective temperaments assessed when BD is first diagnosed and the later development of AM, in order to establish whether an evaluation of temperament is clinical practice is clinically useful. Moreover, since these results may not generalize to people who are not of a UK-based White ethnicity, future work in other countries and cultures is warranted.

4.5 Conclusions

In summary, we have identified different patterns of affective temperaments between individuals with BD and AM versus BD individuals without AM. In particular, higher scores for hyperthymic and irritable TEMPS-A contributed to greater risk of concomitant AM within our sample. These findings are potentially relevant to our understanding of potential biological mechanisms of alcohol abuse comorbidity in bipolar disorder and may help to inform early intervention approaches (Goldstein and Bukstein, 2010).

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Table 1. Demographic and clinical characteristics

Features	BD + AM (N=821)	BD alone (N=599)	*p* value (χ² or t-test)
Male sex – no. (%)	273 (33.3%)	128 (21.4%)	<0.001 [a]
Female sex – no. (%)	548 (66.7%)	471 (78.2%)	<0.001 [a]
Age – yrs (mean±SD)	49.0±12.5	44.7±11.4	<0.001 [b]
Smoking status, ever been regular tobacco smoker – no. (%)	467 (65.7%)	173 (38.7%)	<0.001 [a]
BD-I, DSM-IV – no. (%)	609 (74.2%)	447 (74.6%)	0.854 [a]
BD-II, DSM-IV – no. (%)	212 (25.8%)	152 (25.4%)	0.854 [a]
Cannabis abuse or dependence – no. (%)	125 (18.6%)	19 (4.2%)	<0.001 [a]
Current Beck Depression Inventory (BDI), total score – (mean±SD)	11.8±10.7	14.1±11.7	<0.001 [b]
Current Altman Mania Scale (AMS), total score – (mean±SD)	3.7±3.7	3.5±3.6	0.336 [b]

[a] Chi-squared (χ²) test, [b] t-test.

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Table 2. TEMPS-A scores

TEMPS-A domain	BD with AM	BD without AM	*p* value (t-test)
Cyclothymia TEMPS-A score – (mean±SD)	7.4±3.9	6.2±4.0	<0.001
Depressive TEMPS-A score – (mean±SD)	2.7±2.4	2.2±2.2	<0.001
Irritable TEMPS-A score (mean±SD)	3.0±2.3	1.8±1.9	<0.001
Hyperthymic TEMPS-A score (mean±SD)	4.1±2.4	3.3±2.2	<0.001
Anxious TEMPS-A score (mean±SD)	1.3±1.2	1.3±1.1	0.331

Table 3. Affective temperaments and lifetime history of concomitant AM.

Covariate	Odds Ratio	95% C.I. for OR		p value
		Lower	Upper	
Cyclothymic TEMPS-A	1.016	0.981	1.051	0.375
Depressive TEMPS-A	0.998	0.940	1.058	0.934
Irritable TEMPS-A	1.265	1.186	1.349	0.000
Hyperthymic TEMPS-A	1.090	1.036	1.147	0.001
Anxious TEMPS-A	0.919	0.828	1.021	0.116

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Table 4. Affective temperaments and lifetime history of concomitant AM (adjusted for potential confounders).

Covariate	Odds Ratio	95% C.I. for OR		p value
		Lower	Upper	
Cyclothymic TEMPS-A	0.987	0.944	1.033	0.583
Depressive TEMPS-A	0.986	0.912	1.066	0.728
Irritable TEMPS-A	1.221	1.129	1.321	0.000
Hyperthymic TEMPS-A	1.097	1.030	1.168	0.004
Anxious TEMPS-A	0.970	0.851	1.105	0.646
Age at interview	0.980	0.969	0.992	0.001
Gender (Reference category – male)	0.637	0.465	0.873	0.005
Have you ever been a regular Smoker?	2.539	1.915	3.368	0.000
Lifetime history of cannabis abuse or dependence	2.275	1.314	3.938	0.003
Current Beck Depression Inventory (BDI) score	0.994	0.979	1.010	0.479
Current Altman Mania Scale (AMS) score	0.981	0.943	1.021	0.352

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Highlights

- A large sample of 1420 individuals with bipolar disorder were assessed with respect to affective temperaments and lifetime alcohol misuse comorbidity.
- Mean scores for four affective temperaments (hyperthymic, cyclothymic, depressive and irritable) were higher for individuals with bipolar disorder plus alcohol misuse, compared to individuals with bipolar disorder only.
- Hyperthymic and irritable temperaments in particular significantly increased the odds of bipolar disorder plus alcohol misuse comorbidity.
- Assessing affective temperaments early in the course of bipolar disorder may help to predict the later development of alcohol misuse.