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## Borderline Personality and Attention-Deficit Hyperactivity traits in childhood are associated with hypomanic features in early adulthood

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### Abstract

#### Background

There is limited understanding of the symptomatic development of bipolar disorder from childhood to early adulthood.

#### Aims

We assessed whether borderline personality disorder traits, ADHD, and emotional, behavioural and social difficulties during childhood were associated with hypomania assessed in young adulthood.

#### Method

We used data from the Avon Longitudinal Study of Parents and Children (ALSPAC), to examine associations between measures of childhood psychopathology and lifetime hypomanic features assessed at age 22-23 years using the Hypomania Checklist-32 (HCL-32; n = 3,372). We also conducted a factor analysis of the HCL to identify latent constructs underlying hypomania, and the extent to which childhood psychopathology was associated with these.

#### Results

We identified two factors of the HCL corresponding to energy/mood and risk-taking/irritability. There was evidence of association between childhood borderline personality disorder traits and both hypomania factors, with evidence that the association was stronger with the risk-taking/irritability factor. All individual borderline traits, with the exception of fear of abandonment, were associated with hypomania.

There was also evidence of association between most other measures of childhood psychopathology (ADHD, hyperactivity, conduct problems, peer relationship problems and reduced prosocial behaviour) and the risk-taking/irritability factor, but much less consistent evidence of association with the energy/mood factor.

### **Limitations**

The HCL cannot diagnose bipolar disorder and may be subject to reporting bias.

### **Conclusions**

A broad range of childhood psychopathologies may represent early markers of risk for hypomania. Further studies are required to understand the mechanisms underlying these associations, and to inform earlier detection of bipolar disorder.

**Key words** ALSPAC, cohort study, Borderline Personality Disorder, Bipolar Disorder, hypomania, ADHD.

## Introduction

Bipolar Disorder (BD) is a complex affective disorder with a prevalence of 1-2% (Merikangas et al., 2007; Merikangas et al., 2011). A diagnosis of BD depends on a history of mania or hypomania (Anderson et al., 2013), but the accurate detection of hypomania can be difficult because individuals are more likely to present for help with depression and often have poor recollection of manic symptoms (Ghaemi et al., 1995). The identification of early clinical markers of bipolar disorder may help with improving diagnosis and treatment, but there is currently uncertainty about the extent to which features of childhood psychopathology might be considered as reliable predictors for the later development of BD (Faedda et al., 2014; Faedda et al., 2015). Borderline personality disorder (BPD) and attention deficit hyperactivity disorder (ADHD) are relatively common comorbid diagnoses in people with BD and they share some clinical features in common. It is therefore possible that borderline personality disorder traits and/or features of ADHD in childhood might be predictive of BD in adulthood (Faedda et al. 2014).

In this study, we assess whether borderline personality disorder traits, a diagnosis of ADHD, or subscales of the Strengths and Difficulties Questionnaire (SDQ) (including hyperactivity, prosocial behaviour, emotionality, conduct problems and peer relationship difficulties) assessed during childhood might be early markers for hypomania within the prospective Avon Longitudinal Study of Parents and Children (ALSPAC) cohort. Specifically, we hypothesised that children with more BPD traits, ADHD, or higher hyperactivity subscale scores on the SDQ would have more features of hypomania assessed in early adulthood.

## Methods

### Participants

ALSPAC ([www.bris.ac.uk/alspac/](http://www.bris.ac.uk/alspac/)) was set up in April 1991, comprising children born in the South West of England (Avon) between 1<sup>st</sup> April 1991 and 31<sup>st</sup> December 1992 (Boyd et al., 2013). These children are considered representative of children in the UK (Golding et al., 2001). At the beginning of the study, ALSPAC contained 15,445 participants (Boyd et al., 2013) with extensive baseline information from the first trimester of pregnancy onwards. Following this, clinics, assessments, and questionnaires were conducted from birth regarding family circumstances and the child's health. After the age of 7, the children were able to attend face-to-face interviews, from which a number of assessments were conducted assessing a variety of measures. The study website contains details of all the data, searchable through the data dictionary ([www.bris.ac.uk/alspac/researchers/data-access/data-dictionary/](http://www.bris.ac.uk/alspac/researchers/data-access/data-dictionary/)). As with any cohort study of this kind, there has been a degree of attrition over time (see figure 1 for sample recruitment flow diagram). This study received ethical approval from the ALSAPC Law and Ethics Committee and Local Research Ethics Committees (<http://www.bristol.ac.uk/alspac/researchers/research-ethics/>).

### Main outcome: Hypomanic features

Hypomania features were assessed via postal and online questionnaires using the Hypomania Checklist 32 (HCL-32) when the cohort were 22-23 years of age. In total, 9,359 participants were invited to complete the HCL-32, of whom 3,448 (37%) returned the questionnaire. The HCL-32 is a self-rating questionnaire designed for a lifetime history of hypomanic symptoms. It has been used extensively, in clinical and non-clinical settings and is validated as a screening tool for bipolar disorder type II (Angst et al., 2011; Carta et al., 2006; Forty et al., 2009; Meyer et al., 2014).

A Rasch analysis for unidimensionality of the HCL-32 was recently conducted within a sample of 389 individuals with DSM-IV BD from the Bipolar Disorder Research Network (Court et al., 2014). Four items were identified as redundant and could be excluded. In our study we have therefore used only 28 items from the HCL-32 to calculate a dimensional measure of hypomania (Court et al. 2014).

Furthermore, in line with previous literature, we also examined presence of hypomania as an outcome, which was defined as a threshold score of  $\geq 14/32$  on the HCL, plus a duration of 2-3 days or more, and a response of either negative, or negative/positive impact of highs on family life, social life, work life and leisure (Angst et al., 2005; Angst et al., 2011).

*Insert figure 1*

## Childhood predictors: borderline personality disorder traits, ADHD and SDQ sub-scales

### Assessment of borderline personality disorder traits

At age 11 years, the cohort was interviewed to assess their experience of borderline personality disorder traits over the preceding two years. The interview was conducted by trained psychologists using the Childhood Interview for DSM-IV Borderline Personality Disorder (CI-BPD), a semi-structured interview designed to assess BPD traits in latency-age children and adolescents, which has been adapted for use in this cohort (Zanarini et al., 2004). The CI-BPD is based on the borderline module of the Diagnostic Interview for DSM-IV Personality Disorders (Zanarini et al., 1996). The convergent validity of the CI-BPD has been shown to be significantly associated with clinician diagnosis and other measures of borderline personality disorder reported by patients and parents (Sharp et al., 2012). It contains nine borderline personality disorder traits (anger symptoms, affective instability, emptiness, identity disturbance, paranoid ideation, abandonment, suicidal behaviour, impulsivity and intense interpersonal relationships). Judgements were made by a trained assessor and rated as absent, probably present or definitely present (coded as 0, 1 and 2 respectively). To meet criteria for definitely present, the trait had to be present at least 25% of the time (or daily). A probably rating required the trait to be present regularly but not as often as definitely.

Individuals in the present study were classified as being 'high risk for borderline personality disorder' if they were rated 'probably' or 'definitely' on 5 or more of the nine items, as used previously (Wolke et al., 2012). We also derived a score for borderline personality disorder traits by summing the 9 items (range from 0-18) and then standardised this score.

## Assessment of childhood ADHD status

The presence of ADHD was assessed in 8,219 children using the Development and Wellbeing Assessment (DAWBA) based on parent ratings when the children were aged 91 months (7.6 years) (see figure 1) (Goodman et al., 2000). This assessed the presence of psychiatric disorders including ADHD, which was rated as absent or present (coded as 0 and 1 respectively).

## SDQ subscales

We also examined all five SDQ subscales (hyperactivity, prosocial behaviour, emotionality, conduct problems and peer relationship difficulties). The SDQ had been completed by parents when their children were aged 115 months (9 years) (see figure 1). Each SDQ raw score was standardised for ease of interpretation (Goodman, 1997).

## Statistical analyses

Statistical analysis was performed using Stata version 14 (<http://www.stata.com/>). Linear regression was used to compare associations between our exposures (BPD traits, ADHD and SDQ sub-scale scores) and outcome (hypomania score). A Kernel density plot of the residuals showed normal distribution of the residuals and tests for heteroskedasticity showed homogeneity within the sample. Alpha level used was 0.05.

## HCL-28 Confirmatory factor analysis

Previously, several studies used exploratory factor analysis to determine underlying structure of the HCL in general population samples (Brand et al., 2011; Holtmann et al., 2009) and clinical samples (Angst et al., 2005; Wu et al., 2008). Confirmatory factor analysis (CFA) was conducted in MPlus v7 (Muthén and Muthén, 2015). CFA was used to confirm the factor structure of 28 items of the HCL-32 completed by 2,996 individuals. Using the WLSMV (mean and variance adjusted weighted least squares) estimator, 2 factors were derived based on 19 items representing the energy/mood

dimension of the HCL-28 and 9 items representing the risk-taking/irritability dimension of the HCL-28.

Linear regression was used to examine the relationship between the childhood predictors and the HCL-factors within MPlus. A Wald test was used to compare the childhood predictors and energy/mood factor and childhood predictors and risk-taking/irritability factor models.



## Results

Compared to the whole ALSPAC sample (those without data on the HCL), our study sample had a smaller proportion of males (56.15% vs 35.26%;  $p < 0.001$ ), higher maternal social class ( $p < 0.001$ ), greater maternal age (27.9 years vs 29.7 years;  $p < 0.001$ ), a higher proportion of mothers who had a degree (9.99% vs 21.50%;  $p < 0.001$ ) and smaller proportion of mothers who had depression (20.65% vs 18.38%;  $p = 0.006$ ). There was no evidence that ethnicity differed between the whole ALSPAC cohort (those who had not completed the HCL) and our study sample (see table 1).

*Insert table 1*

### Borderline personality disorder traits and hypomania

We found strong evidence of an association between borderline personality disorder traits in childhood and hypomania in young adulthood, with each standard deviation (SD) change in borderline personality traits score associated with an increase in HCL score of 0.07 SD (95%CI 0.04, 0.10;  $R^2 = 0.0075$ ;  $p < 0.001$ ). Individuals in the 'high-risk' borderline personality disorder group had a mean HCL score of 16.16 (SD 5.7) compared to 14.6 (SD 5.7) ( $p = 0.003$ ) in the non high-risk group (see table 2).

*Insert table 2*

We also examined the association between each of the nine individual borderline personality disorder traits and HCL score, to determine whether individual traits were driving the association between the borderline personality disorder score and hypomania. Anger, affective instability, paranoid ideation, identity disturbance and intense interpersonal relationships all showed evidence of association, with weaker evidence for impulsivity, emptiness, and suicidality. There was no evidence to support any association with abandonment (see table 3).

*Insert table 3*

## Confirmatory Factor Analysis (CFA) of the HCL items

As shown in appendix 1, we identified two latent variables that best described the 28 HCL items. The first factor encompassed items relating to 'energy/mood' in the HCL, and the second factor described items that are more strongly related to 'risk-taking/irritability'.

We tested whether the borderline personality disorder score was differentially associated with the two HCL factors, and found evidence that it was more strongly associated with the risk-taking/irritability factor than with energy/mood factor, using confirmatory factor analysis (see table 2).

## ADHD and SDQ scores in childhood and hypomania in young adulthood

A DSM-IV diagnosis of ADHD in childhood was not associated with an increase in HCL score in young adulthood. There was also no evidence of association between SDQ sub-scale scores for hyperactivity, emotionality, conduct problems or peer problems with HCL score, but individuals who scored lower on the prosocial subscale had a higher HCL score (see table 4).

*Insert table 4*

When examining associations with the HCL factors we found evidence that ADHD in childhood, conduct problems and peer problems, were associated with the risk-taking/irritability factor. Hyperactivity was associated with both an increase in the risk-taking/irritability factor and, less strongly, a decrease in the energy/mood factor, whilst a lower level of prosocial behaviour was associated with an increase in both factors (see table 5).

*Insert table 5*

## Childhood traits and categorical hypomania

When using clinically-defined hypomania as an outcome, results for the borderline personality traits score, ADHD and SDQ peer problems and emotionality subscales were substantively the same. There was stronger evidence for association with SDQ conduct problems, but no association with prosocial behaviour. Evidence of association for the individual borderline personality disorder traits also varied, the most notable exceptions being stronger evidence for association with traits of abandonment and suicidal ideation (see appendix 2).

## Discussion

Within this large birth cohort, we found that both a higher borderline personality disorder traits score and 'high risk' status for borderline personality disorder at age 11 years was associated with higher hypomania scores and an increased odds of being classed as having hypomania in young adulthood. In particular, features of anger, paranoid ideation, intense interpersonal strongly associated with hypomania scores. Neither a diagnosis of ADHD in childhood nor any of the SDQ subscales (with the possible exception of prosocial behaviour) were associated with hypomania in young adulthood.

In keeping with previous factor analyses of the HCL-32, we identified a two factor model of hypomania, relating to 'energy/mood' items and 'risk taking/irritable' items. Childhood borderline personality disorder traits scores were more strongly associated with the 'risk taking/irritable' factor than the 'energy/mood' factor. Furthermore, we found strong evidence of association between diagnosis of ADHD in childhood and the 'risk-taking/irritability' factor. This factor was also associated with conduct and peer relationship problems, hyperactivity and with reduced prosocial behaviour in childhood.

Our findings were similar when examining clinically-defined hypomania as an outcome, although evidence for association with the 'fear of abandonment' and 'suicidal ideation' borderline personality traits, and with conduct problems, was stronger, whilst there was no evidence of association with reduced prosocial behaviour.

## Findings in the context of previous work

### Borderline personality traits and hypomania

Factor structure of hypomania was first studied by Hantouche et al. (2003) using a clinical population from the French multi-centre study EPIDEP. They found a 2-factor structure of hypomania; one of positive/"sunny side" features and the other of negative/"dark side" features. Sunny side features included features of more drive and energy, extremely happy mood, less sleep and increased social activity, which corresponds to our 'energy/mood' factor. Conversely, dark side hypomania included features of excessive shopping and spending, more irritable, easily distractible, increased sex drive

and increased consumption of coffee/cigarettes/alcohol, which corresponds to our 'risk-taking/irritable' factor (Hantouche et al., 2003). Similar factors were found using the HCL-32 in clinical samples (Angst et al., 2005; Vieta et al., 2007; Wu et al., 2008).

Similarly, Brand et al. (2011) assessed the factor structure of hypomania assessed using the HCL-32 in a non-clinical sample and reported a 2-factor-structure corresponding to sunny side ('energy/mood') and dark side ('risk-taking/irritable') factors reported by Hantouche et al. (2003). Those who scored most highly on the dark side factor were more likely to have increased negative coping strategies, social withdrawal and a reduced quality of life (Brand et al., 2011). Our results suggest that borderline personality disorder traits are more strongly associated with the 'risk-taking/irritability' (dark side) of hypomania, rather than with the energy/mood (sunny side) of hypomania.

The clinical and nosological overlap between borderline personality disorder and bipolar disorder is an area of intense debate (Akiskal, 2004; Paris, 2007; Paris and Black, 2015; Paris et al., 2007). In clinical settings, approximately 10% of individuals with bipolar disorder also satisfy criteria for borderline personality disorder and vice versa (Zimmerman et al., 2013). Further, individuals who are comorbid for bipolar disorder and borderline personality disorder tend to have a more severe form of bipolar disorder (Parker et al., 2016). It is clear that to some extent these two conditions share both diagnostic and aetiological features in common, although the precise nature of this is not understood.

Some authors have reported that certain borderline personality disorder traits are more strongly associated with bipolar disorder type II than major depression. In a small study from Italy, Benazzi and colleagues found that the 'affective instability' component of borderline personality disorder (symptoms of affective instability, unstable interpersonal relationships, unstable self-image, chronic emptiness and anger) but not an impulsivity component (paranoia, suicidal ideation, impulsivity and fear of abandonment) was associated with bipolar disorder type II (Benazzi, 2006). This is consistent with our finding that "affective instability" borderline personality disorder traits were more strongly associated with hypomania scores than "impulsivity" traits. We did not find an association between the borderline personality disorder trait of abandonment and hypomania score and only weak evidence of association for suicidality, though both of these traits showed stronger association with the categorical measure of hypomania. This suggests that these traits might be particularly related to levels of functional impairment or chronicity of symptoms that contribute to define a group more strongly aligned to clinical hypomania disorder.

There are several possible explanations which may explain why we found evidence of an association between borderline personality disorder traits and higher hypomania scores. One possibility is that borderline personality disorder and bipolar disorder are distinct psychopathologies but share common etiological mechanisms, for example childhood trauma (McDermid et al., 2015) or pleiotropic genetic effects (Song et al., 2015; Witt et al., 2014). It is also possible that childhood characteristics measured using the BPD interview are capturing early signs of bipolar disorder in some participants, for example affective instability occurring as a precursor to hypomania (Faedda et al., 2015). The assessment of borderline personality disorder traits could also be indexing mixed state depression, which has previously been shown to be a predictor of future bipolar disorder (Sani et al., 2014). Although both the HCL and BPD interview measures have been shown to have good validity (Holtmann et al., 2009; Sharp et al., 2012) such misclassification bias is hard to rule out. Causal effects of BPD on bipolar disorder are also possible, for example secondary to substance use (Strakowski and DelBello, 2000) that might occur more commonly in people with BPD traits (e.g. those with greater impulsivity (Faedda et al., 2014) as a means of coping with distressing emotional states (Van den Bosch et al., 2003).

### ADHD and hypomania

We are not aware of any studies examining the relationship between childhood ADHD and hypomania as an outcome in early adulthood. However, a number of studies have previously reported that illness onset (Sachs et al., 2000) , or onset of affective symptoms (Ryden et al., 2009) in adult patients with bipolar disorder was significantly earlier in those who had childhood ADHD. A study by Henin and colleagues found that individuals with DSM-IV adult bipolar disorder had significantly higher rates of childhood disruptive disorders including ADHD, oppositional defiant disorder and conduct disorder, compared to adults without a mood disorder (Henin et al., 2007), although the selection of controls, requiring the absence of ADHD in their children, may have biased this comparison. Whilst we failed to find evidence of association between ADHD diagnosis and HCL score, ADHD was strongly associated with the HCL 'risk-taking/irritability' factor. It is possible that the lack of association with the total HCL score could be attributed to a greater number of HCL items corresponding to 'energy/mood', rather than 'risk-taking/irritability', and thus diluting the association with the total score. It is possible that the risk-taking aspect of hypomania and ADHD share a common aetiology. It is also possible that ADHD leads to an increased risk of hypomania, for example secondary to the psychotogenic effects of substance misuse (Hidalgo-Mazzei et al., 2015) that occurs more commonly in adolescents with ADHD (Lee et al., 2011).

## SDQ and hypomania

The relationship between childhood psychopathology, assessed using the SDQ and hypomania assessed using the HCL-32 has previously been studied in a German general population sample of adolescents. This study suggested a 3-factor structure to the HCL-32. They found that peer problems were negatively associated with an 'active/elated' factor of the HCL-32 that most closely approximates to our 'energy/mood' factor. They also reported associations between conduct problems and a 'disinhibited/stimulation' factor, that most closely approximates our 'risk taking/irritability' factor. Finally, associations between hyperactivity and peer problems scales with an 'irritable/erratic' factor which most closely approximates our 'risk-taking/irritability' factor (Holtmann et al., 2009).

There are several similarities in findings between our study and that of Holtmann et al. (2009). Firstly, we also found no evidence of an association between our 'energy/mood' or our 'risk-taking/irritability' factors and emotional difficulties. A possible explanation for this lack of finding may be due to only current psychopathology being captured by the SDQ, which could in turn miss any previous negative emotional difficulties experienced by the children. Secondly, those with more conduct problems have stronger associations with our 'risk-taking/irritability' factor than our 'energy/mood' factor. This finding may reflect overlapping symptoms between the HCL ("I am more easily distracted") and conduct problems ("I am easily distracted"). An explanation for the discrepancy of our findings regarding peer relationship difficulties might be attributed to the different ages of our samples (university students versus children). University students are more likely to have complete brain maturation (Sowell et al., 1999), compared to children who are still developing and have not yet completed the first phase of synaptic pruning which would typically start around puberty (Gogtay et al., 2004). Another possible explanation for our findings specifically, may be attributed to completion of the SDQ by the parents. Behavioural problems may have been underestimated by some of the parents which could increase the likelihood of finding no association with some SDQ subscales and hypomania.

## Strengths and Limitations

There are a number of strengths of this study. ALSPAC is considered representative of the UK general population in terms of ethnicity, social class and educational attainment, and although attrition has resulted in changes to the sample characteristics, our findings are likely to be fairly generalizable to the population as a whole. There were a number of differences in socio-demographic and background characteristics between our final study samples and the original ALSPAC cohort, which could potentially introduce selection bias as a result of missing data and sample attrition. Although methods such as multiple imputation can minimise problems of selection bias, these methods are not straightforward and rely on a number of assumptions, most notably that data are missing at random. Multiple imputation to deal with missingness has previously been reported to have little impact on selection bias in the association between early life exposures and childhood psychopathology in this cohort (Wolke et al., 2009).

The assessment of ADHD at age 7.6 years and SDQ at age 9 years, approximately 15 years and 13 years respectively before the assessment of hypomanic features means that we can be confident that the associations we observed represent change in risk of hypomania in relation to childhood psychopathology rather than a result of recall of childhood psychopathology that is biased by the presence of hypomanic symptoms. Although participants were not screened for hypomania during childhood it seems unlikely that presence of hypomania or bipolar disorder in children led to the associations observed.

However, there are also a number of limitations. Our primary outcome of interest was the dimensional score for lifetime hypomanic features from the HCL-28, selected from the original HCL-32 questionnaire (Angst et al., 2005). Though this measure does not allow a DSM-IV/ICD-10 diagnosis of bipolar disorder to be made, the score may be used to assess propensity to bipolar disorder, particularly pertinent in a population where a first episode of mania/hypomania is unlikely to have occurred given the age of the participants (Leboyer et al., 2005). Whilst the clinical relevance of findings is limited by the absence of a diagnosis, dimensional constructs have clear advantages over categorical approaches for understanding the aetiology of psychiatric disorders, as exemplified in the Research Domain Criteria (Cuthbert and Insel, 2013).

Whilst the HCL has been validated as a screening tool for bipolar disorder in many clinical settings (Angst et al., 2011; Carta et al., 2006; Forty et al., 2009; Meyer et al., 2014), the HCL-32 is a self-report measure and it is therefore possible that bias has occurred in reporting, particularly in relation to questions asking about sexual activity, risk-taking and alcohol use.

Whilst we defined a group of children as being at ‘high risk’ of borderline personality disorder at age 11 years, it is not possible to diagnose a personality disorder at this age, and we do not know the proportion of ‘high risk’ children who met criteria for this diagnosis in adulthood. However, the CI-BPD has previously been shown to be significantly associated with clinician diagnosis, demonstrating convergent validity (Sharp et al., 2012), even though individual borderline personality traits may correlate with other markers of psychopathology (e.g. fear of abandonment and separation anxiety that has also been associated with bipolar disorder (Bruckl et al., 2007).

## Conclusions

In this prospective study, we found that those children who had more borderline personality disorder traits had higher hypomania scores in adulthood. When examining underlying factors of the HCL, we found BPD traits strongly associated with hypomania outcomes, irrespective of how we defined these (i.e. score, factors, clinical), whereas associations for ADHD, hyperactivity, conduct, peer and prosocial less were primarily with the risk-taking/irritability factor, and less consistent with other hypomania outcomes examined. Further work is needed to determine to what extent associations between childhood psychopathology and adult hypomania are explained by common genetic or non-genetic effects, and to understand any causal mechanisms that might inform prevention strategies for bipolar disorder.

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*Insert appendix 1*

*Insert appendix 2*