



# Autistic and schizotypal traits and global functioning in bipolar I disorder

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## ARTICLE INFO

### Keywords:

Autism  
Global functioning  
Psychosis  
Schizophrenia  
Schizotypy

## ABSTRACT

**Objective:** To determine the expression of autistic and positive schizotypal traits in a large sample of adults with bipolar I disorder (BD I), and the effect of co-occurring autistic and positive schizotypal traits on global functioning in BD I.

**Method:** Autistic and positive schizotypal traits were self-assessed in 797 individuals with BD-I recruited by the Bipolar Disorder Research Network. Differences in global functioning (rated using the Global Assessment Scale) during lifetime worst depressive and manic episodes (GASD and GASM respectively) were calculated in groups with high/low autistic and positive schizotypal traits. Regression analyses assessed the interactive effect of autistic and positive schizotypal traits on global functioning.

**Results:** 47.2% (CI=43.7–50.7%) showed clinically significant levels of autistic traits, and 23.22% (95% CI=20.29–26.14) showed clinically significant levels of positive schizotypal traits. In the worst episode of mania, the high autistic, high positive schizotypal group had better global functioning compared to the other groups. Individual differences analyses showed that high levels of both traits were associated with better global functioning in both mood states.

**Limitations:** Autistic and schizotypal traits were assessed using self-rated questionnaires.

**Conclusions:** Expression of autistic and schizotypal traits in adults with BD I is prevalent, and may be important to predict illness aetiology, prognosis, and diagnostic practices in this population. Future work should focus on replicating these findings in independent samples, and on the biological and/or psychosocial mechanisms underlying better global functioning in those who have high levels of both autistic and positive schizotypal traits.

## 1. Introduction

Bipolar disorder (BD) is a major affective disorder characterised by chronically recurring episodes of mania (or hypomania) and depression, which in their severe forms may present with psychotic symptoms, such as hallucinations or delusions (Weissman et al., 1996). This complex condition is often exacerbated by the presence of one or more comorbid conditions, in addition to a number of clinical factors such long duration of illness (Altamura et al., 2010, 2015). While BD, schizophrenia spectrum disorders (SSD) and autism spectrum disorders (ASD) are considered distinct conditions, there is evidence for an overlap between BD and SSD (Altamura et al., 2014; Carroll and Owen, 2009; Moller, 2003), as well as between ASD and BD (Carroll

and Owen, 2009; Stahlberg et al., 2004). Indeed, BD has a number of genetic, symptomatological and epidemiological overlaps with SSD (Laursen et al., 2009; Lichtenstein et al., 2009; Murray et al., 2004), and psychosis has been recognised as an important dimension in the psychopathology of BD (van Os and Kapur, 2009). In addition, schizotypy, which encompasses a set of personality traits that reflect subclinical expression of schizophrenia (Ettinger et al., 2015), is recognised as genetically related to SSD and is considered an endophenotype common to both SSD and BD (Ettinger et al., 2014; Mahon et al., 2013; Schurhoff et al., 2005). Schizotypy has been reported at elevated rates in individuals with BD compared to healthy controls, although this was conducted in a relatively small BD sample (N=92) (Heron et al., 2003).

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Furthermore, there is growing evidence of an association between ASD and BD (Cross-Disorder Group of the Psychiatric Genomics, 2013; Vannucchi et al., 2014). ASD is defined by its cardinal impairments in social interaction, language and communication, and restricted behaviour and interests. To date, the majority of reports of ASD-BD comorbidity are in ASD samples, with prevalences ranging from 6% to 21.4% (Vannucchi et al., 2014). Only two studies have assessed ASD in BD samples: in youths (aged 7–17 years, N=157), 30% met diagnostic criteria for ASD (Joshi et al., 2013); and in a small sample of adults (N=56), 50% had high levels of autistic traits as measured with the Social Responsiveness Scale (Matsuo et al., 2015). Thus, the extant literature reporting the expression of autistic or schizotypal traits in BD has been limited by small samples, and requires replication in large, well-characterised, adult samples of BD.

The interplay between BD, SSD and ASD or expression of their traits may have significant consequences on global functioning in patients with BD. Global functioning, a measure of illness severity, provides an overall picture of an individual's combined psychological, social and occupational functioning, such as how adaptive the patient is in dealing with social and interpersonal problems (Endicott et al., 1976). Poor functioning has been reported in individuals with schizotypal personality disorder (Henry et al., 2008; Skodol et al., 2002), schizophrenia (Robertson et al., 2013) and ASD (Engstrom et al., 2003; Kastner et al., 2015). Hence a combined worsening effect may be expected in BD patients with high levels of co-occurring autistic and schizotypal traits. A recent study evaluated the effect of co-occurring autistic and positive schizotypal (i.e. relating to psychotic-like experiences) traits on the ability to appreciate the perspective of others (or *mentalising*) in the general population (N=201) (Abu-Akel et al., 2015). It showed that while autistic and positive schizotypal traits independently induced perspective-taking errors, their interaction was associated with fewer errors, reflecting an improvement in mentalising abilities. The authors proposed that this unexpected finding may be explained by the diametric model (Crespi and Badcock, 2008), which postulates that ASD and SSD have opposing effects on mentalising abilities, whereby autism is associated with reduced or no mentalising, and schizophrenia with dysfunctional overmentalising. While global functioning is not a test of mentalising per se, it has been shown to be associated with socio-cognitive abilities (Bo et al., 2015) and improve following mentalising-based treatments (Bateman and Fonagy, 2008). To-date, no study has investigated the effect of co-occurring autistic and schizotypal traits on an outcome of clinical value in a psychiatric population.

Thus the present study has two main objectives: (1) to determine the expression of autistic and positive schizotypal traits in a large sample of adults with BD, and (2) to examine whether co-occurring autistic and positive schizotypal traits interact to affect global functioning in this population. The assessment of positive schizotypy only, rather than the general construct of schizotypy (comprising both positive and negative traits), is based on evidence that autistic and schizotypal traits cannot be distinguished by the presence or absence of negative traits, due to similarities in impaired social and communicative functioning (Spek and Wouters, 2010). Moreover, given that ASD is more prevalent in males compared to females (Lehnhardt et al., 2016), the expression of autism traits in our sample was analysed for male and female patients separately.

Investigating the prevalence of autistic and schizotypal traits in BD has management implications for individuals with BD, and may contribute to understanding the aetiology of BD. Moreover, isolating and characterising the expression of autistic and schizotypal traits is important to understanding the nature of their effect on the course, outcome and treatment of the index condition (i.e. BD).

## 2. Methods

### 2.1. Participants

Participants were recruited by the Bipolar Disorder Research Network (BDRN) to an on-going programme of research into the genetic and non-genetic causes of BD. The study has UK National Health Service (NHS) Research Ethics Committee approval and local Research and Development approval in all participating NHS Trusts/Health Boards. Participants were recruited systematically via NHS mental health services, and non-systematically via advertisements on the BDRN website, in general practitioner surgeries and local media, and patient support organisations (such as Bipolar UK). Participants are included in the BDRN study if they meet the following criteria: i) capable of providing written informed consent; ii) aged at least 18 years; iii) meet DSM-IV criteria for a major affective disorder; and, iv) due to the study's genetic focus, UK/Ireland White ethnicity. The exclusion criteria are individuals who: i) have only experienced affective illness secondary to alcohol or substance abuse, medical illness or medication; ii) have a cognitive impairment that affects their ability to complete the measures; and, iii) are biologically related to another BDRN participant. After complete description of the study to the participants, written informed consent was obtained. The present analysis was performed on a subset of BDRN participants with DSM-IV bipolar I disorder who completed measures of both autistic spectrum and schizotypal traits (N=797).

### 2.2. Assessments

Lifetime clinical data were compiled by trained research psychologists and psychiatrists using the Schedules for Clinical Assessment in Neuropsychiatry (SCAN) semi-structured interview (Wing et al., 1990), and available psychiatric case notes. Data were combined for each participant, and lifetime best-estimate diagnostic and key clinical ratings (such as age of illness onset and lifetime presence of psychosis) were made based on pre-specified guidelines. Specifically, following SCAN guidelines, the worse episode ('peak of the disorder' or most severe episode) of each of depression and mania was decided in consultation with the participant. In very rare cases where there was discrepancy between the participant's chosen episode and their medical case-notes, a consensus decision was made with the clinical team about the worst episode.

### 2.3. Global functioning

The Global Assessment Scale (GAS) (Endicott et al., 1976) was used to rate global functioning during lifetime worst depressive and manic episode separately (GASD and GASM, respectively). Scores range 1–100, with higher scores reflecting higher functioning. All ratings, including GASD and GASM, were made independently by at least two members of the research team and consensus reached. Inter-rater reliability was formally assessed using 20 random cases. Mean kappa statistics were 0.85 for DSM-IV diagnoses, and 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, including GASD and GASM.

### 2.4. Autism and schizotypal traits

Autism and schizotypal traits were self-rated using the Autism-Spectrum Quotient (AQ-Short) (Hoekstra et al., 2011) and Kings Schizotypy Questionnaire (KSQ) (Jones et al., 2000). Participants were administered the KSQ at the end of the clinical interview, and AQ-Short was subsequently administered via a questionnaire mail-out.

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