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## Autism and psychosis: Clinical implications for depression and suicide

Rachel Uptegrove<sup>a,b,c,\*</sup>, Ahmad Abu-Akel<sup>d</sup>, Katharine Chisholm<sup>a</sup>, Ashleigh Lin<sup>e</sup>, Sofia Zahid<sup>a</sup>, Mirabel Pelton<sup>a</sup>, Ian Apperly<sup>a</sup>, Peter C. Hansen<sup>a</sup>, Stephen J. Wood<sup>a,f,g</sup>

<sup>a</sup> University of Birmingham, School of Psychology, Edgbaston, Birmingham B15 2TT, United Kingdom

<sup>b</sup> University of Birmingham, Institute of Clinical Sciences, College of Medical and Dental Science, Edgbaston, Birmingham B15 2TT, United Kingdom

<sup>c</sup> Forward Thinking Birmingham and Birmingham and Solihull Mental Health Foundation Trust, 1 Printing House Street, Birmingham B4 6DF, United Kingdom

<sup>d</sup> University of Lausanne, Institute of Psychology, UNIL - Mouline, Géopolis - office 4129, CH-1015 Lausanne, Switzerland

<sup>e</sup> Telethon Kids Institute, The University of Western Australia, 100 Roberts Rd, Subiaco, WA 6008, Australia

<sup>f</sup> University of Melbourne, Centre for Youth Mental Health, 35 Poplar Rd, Parkville, VIC 3052, Australia

<sup>g</sup> Orygen, National Centre of Excellence in Youth Mental Health, 2a/2A Hartington Street, Glenroy, Victoria 3046, Australia

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### ABSTRACT

There is increasing recognition of the co-occurrence of autism and schizophrenia spectrum disorders. However, the clinical significance of this on outcomes such as depression and suicidal thinking has not been explored. This study examines the association of autism spectrum traits, depressive symptoms and suicidal behaviour in individuals with psychotic experiences.

In two cross sectional studies, individuals from a non-help seeking university student sample and patients with first episode psychosis (FEP) service completed standardized measures of autism spectrum traits, psychotic experiences, depressive symptoms and suicidal thinking.

In healthy non-help seeking students, increased autism traits and increased subclinical psychotic experiences were significantly associated with depressive symptoms; a significant interaction effect suggests their combined presence has a greater impact on depression. In FEP, high autism traits and positive symptoms were associated with increased depression, hopelessness and suicidality, however there was no significant interaction effect. In FEP a multiple mediation model revealed that the relationship between autism traits and risk for suicidality was mediated through hopelessness.

Young people with subclinical psychotic experiences and all patients with FEP should be screened for autism spectrum traits, which may have significant impact on clinical outcomes. Tailored interventions for patients with high levels of autistic spectrum co-morbidities in FEP should be a priority for future research.

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### 1. Introduction

Despite early recognition of similarities between autism and schizophrenia at the times of Bleuler and Kanner, historically these have been understood as two distinct disorders (Kolvin, 1971). Time course (onset in early childhood vs adolescent) and progression (stable vs progressive) are two possible distinguishing features (Chisholm et al., 2015; Wood, 2017). However, it is now recognised that autism spectrum disorder and schizophrenia spectrum disorders share not only some clinical similarities, but also a biological, particularly genetic, liability (Ruzzo and Geschwind, 2016). While autism has long been understood as occurring on a spectrum, with a continuum of severity and deficits identifiable from population to disorder level (Young et al., 2005), recently psychosis has also been suggested to exist on a continuum; positive

symptoms are reported in the general population, can be used to identify those at heightened risk of developing psychosis with the ultra-high risk paradigm, and are seen in schizophrenia and other severe mental illnesses (Yung et al., 2006).

At the population level, autistic and psychosis traits are evidentially co-occurring; using the Avon Longitudinal Birth Cohort, Sullivan et al. demonstrated that poorer pragmatic language, a key deficit in autism spectrum disorders, was associated with later psychosis and depression (Sullivan et al., 2016). In the same cohort, Siebald and colleagues showed that children aged 8 diagnosed with pervasive developmental disorders, which included the DSM-IV classification of Autism (Association and DSM-IV., 1994), had heightened risk of later psychotic experiences with an odds ratio of 8 (Siebald et al., 2016).

Within clinical populations, the two disorders co-occur at higher rates than would be expected by chance. There is a reported mean incidence of schizophrenia spectrum disorders of 13.8% in autism spectrum disorder populations, and a mean incidence of autism spectrum disorder of 24.1% in schizophrenia spectrum disorder populations

\* Corresponding author at: University of Birmingham, 25 Vincent Drive, Edgbaston, B16 2NF, United Kingdom.

E-mail address: [r.uptegrove@bham.ac.uk](mailto:r.uptegrove@bham.ac.uk) (R. Uptegrove).

(Chisholm et al., 2015). Shared clinical features of autism spectrum disorders and schizophrenia spectrum disorders also include difficulty with social communication, emotional expression, salience and restrictive behaviours (Abu-Akel et al., 2017a, b; Hommer and Swedo, 2015; Ruzzo and Geschwind, 2016). Depression is common in both autism spectrum disorder and schizophrenia spectrum disorders. It has been reported that 14–20% of young people with autism spectrum disorders have experienced a significant depressive episode by the age of 18 (Gotham et al., 2015). Likewise, up to 80% of patients with schizophrenia may experience significant depression (Upthegrove et al., 2010), and this has significant long-term consequences for autism spectrum disorders and schizophrenia, including suicide. Lifetime prevalence of completed suicide in schizophrenia is between 7 and 10% (Dutta et al., 2011; Häfner et al., 2005; Upthegrove et al., 2010), and the prevalence of suicidal behaviour in autism spectrum disorder is between 11 and 50% (Zahid and Upthegrove, 2017).

We have previously shown that depression, positive symptoms and hopelessness are known precursors of self-harm and suicide in schizophrenia spectrum disorders (Upthegrove et al., 2014). However, the role of autism spectrum disorder traits as a potential pathway to depression and suicidality in schizophrenia spectrum disorders has not been explored to date.

While there has been a considerable amount of recent recognition of the co-occurrence of autism spectrum disorder and schizophrenia spectrum disorders, and how this might inform aetiological understanding, the evidence of the clinical significance of this co-occurrence has yet to develop. This knowledge is needed for evidence-based treatment and management decisions. This study aims to determine the importance, in terms of depression and suicidal behaviour, of autism traits in individuals within the spectrum of psychotic experiences. Given that both disorders are associated with depression and suicidal behaviour, we predict that depression and suicidal behaviour would be increasingly prevalent when autistic spectrum traits and psychosis co-occur.

Hypotheses:

- Autism traits and subclinical psychotic experiences are associated with increased levels of depressive symptomatology in a healthy, non-help seeking population.
- Autism traits are associated with positive symptoms and their combined presence increases depression and hopelessness in people with first episode psychosis.
- Autism traits in people with first episode psychosis increase the risk of suicidality over and above other known risk factors.

## 2. Materials and method

### 2.1. Sample 1: healthy, non-help seeking

Data were collected from 381 University students. Participants were recruited through the University of Birmingham Research Participation Scheme for a course credit or small honorarium. Participants self-reported that they had no history of psychiatric illness, epilepsy, neurological disorders or brain injury (including self-report of any formal diagnosis of ASD, epilepsy, traumatic brain injury, and/or other known neurological or neurodevelopmental condition), and no current or past alcohol and/or substance abuse problems. The University of Birmingham Research Ethics Committee approved the study, and written informed consent was obtained from all participants.

Participants completed the CAPEp (Community Assessment of Psychotic Experiences: positive psychotic-like experiences), which is a 20-item positive scale questionnaire (Stefanis et al., 2002). The assessment of positive psychotic-like experiences was assessed with the CAPEp rather than the full Community Assessment of Psychotic Experiences (CAPE) as previous literature suggests that negative psychotic

experiences maybe confounded by the presence of autistic traits/autism spectrum disorders (Spek and Wouters, 2010).

Participants also completed the AQ (The Autism-Spectrum Quotient) (Baron-Cohen et al., 2001), a 50-item questionnaire which examines 5 domains along the autism spectrum: social skills; attention switching; attention to detail; communication; and imagination. While the AQ is not a diagnostic instrument, it is a well-validated self-report measure with a Cronbach's Alpha of 0.81 (Hurst et al., 2007). A score of >32 is regarded as indicative of autism spectrum disorder and people with autism spectrum disorder rarely score below 26 (Baron-Cohen et al., 2001).

Finally, participants completed the CESD-R (The Center for Epidemiologic Studies Depression Scale-Revised) to assess the presence of depressive symptomatology (Van Dam and Earleywine, 2011).

### 2.2. Sample 2: first episode psychosis

Ninety-nine participants with treated first episode psychosis were recruited from Birmingham Early Intervention Services, a community based clinical program with responsibility for the assessment and treatment of patients with first episode psychosis. Birmingham Early Intervention Services see approximately 200 new patients each year, referred from primary and secondary care services. Patients within the service receive antipsychotic medication, care-coordination and psychological interventions as needed.

Ethical approval was given by UK National Research Ethical Committee (NRES), Reference Number 13/WM/0213. Inclusion criteria included age of 16–35 years with a diagnosis of first episode of psychosis in keeping with ICD-10 F20–23, F25–29, F30.2, F31, F32.3. Exclusion criteria included a lack of capacity to consent, unable to communicate verbally in English, and known neurological disorder (including but not limited to epilepsy, traumatic brain injury and learning disability). Patients meeting inclusion and exclusion criteria were approached by their clinical team, and no parameters were set for length of treatment.

Participants completed; SBQ-R (The Suicide Behaviours Questionnaire-Revised) (Osman et al., 2001) which consists of 4 questions that assess different aspects of suicidality. It examines lifetime suicidal ideation and suicide attempt, the frequency of suicidal ideation over the last year, the threat of suicide attempt, and the likelihood of attempting suicide in the future (Osman et al., 2001); AQ (The Autism-Spectrum Quotient) (Baron-Cohen et al., 2001); PANSS (Positive and Negative Syndrome Scale) (Kay et al., 1987), to capture current severity of symptoms on the basis of the standard semi-structured interview. Positive symptoms were assessed by PANSS positive (PANSS-P) subtotal. Depression was rated using PANSS items G1–3 and G6 (PANSS-D), which has been shown to have validity and good correlation with other depression measures used in psychosis (Lako et al., 2012); BHS (Beck Hopelessness Scale) (Beck and Steer, 1988), a 20-item tool designed to measure three major aspects of hopelessness; feelings about the future, loss of motivation, and expectations.

### 2.3. Statistical analysis

Inspection of the data suggests that the distribution of all scores in both the healthy and clinical samples were within the accepted range, of  $-/+ 2$  skewness, for parametric analyses (Gravetter and Wallnau, 2014).

#### 2.3.1. Sample 1

The association of the participants' standardized AQ and CAPEp scores and their interaction with the CESD-R scores was examined in a linear regression model using Generalized Linear Models (GLMs), controlling for age and gender. Interactions were probed using the MODPROBE method for SPSS where the effect of one predictor on the outcome measure examined at the mean, 1 s.d. below the mean and 1 s.d. above the mean of the other predictor. This procedure does not

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