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Cluster analysis reveals subclinical subgroups with shared autistic and schizotypal traits

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ABSTRACT

Autism and schizophrenia spectrum research is typically based on coarse diagnostic classification, which overlooks individual variation within clinical groups. This method limits the identification of underlying cognitive, genetic and neural correlates of specific symptom dimensions. This study, therefore, aimed to identify homogenous subclinical subgroups of specific autistic and schizotypal traits dimensions, that may be utilised to establish more effective diagnostic and treatment practices. Latent profile analysis of subscale scores derived from an autism-schizotypy questionnaire, completed by 1678 subclinical adults aged 18–40 years (1250 females), identified a local optimum of eight population clusters: *High, Moderate* and *Low Psychosocial Difficulties; High, Moderate* and *Low Autism-Schizotypy; High Psychosis-Proneness*; and *Moderate Schizotypy*. These subgroups represent the convergent and discriminant dimensions of autism and schizotypy in the subclinical population, and highlight the importance of examining subgroups of specific symptom characteristics across these spectra in order to identify the underlying genetic and neural correlates that can be utilised to advance diagnostic and treatment practices.

1. Introduction

Autism (ASC) and schizophrenia (SSC) spectrum conditions are heterogeneous psychiatric conditions with multiple etiologies. These conditions are diagnosed based on a non-specific set of symptoms in order to prescribe whole-disorder treatments, however, this approach is suboptimal given the substantial heterogeneity within the conditions. Furthermore, there are several symptom similarities between ASC and SSC, particularly in the psychosocial domain, that may or may not represent true comorbidity. Cluster analysis has previously identified two subgroups of high functioning ASC using clinical diagnostic tools (Klopper et al., 2017): moderate social impairment with higher restricted/repetitive behaviours, and severe social impairment. Fonseca-Pedrero et al. (2017) identified four subclinical subgroups of schizotypy: low, average and high schizotypy overall, and high interpersonal schizotypy. The identification these subgroups may be useful in the identification of at-risk groups, and in the development of more targeted interventions for specific symptom domains (Fonseca-Pedrero et al., 2017; Insel, 2010; Klopper et al., 2017). However, given the relationship between the spectra, investigating homogenous subgroups within autistic and schizotypal features combined may provide a more comprehensive picture of subgroups with specific psychiatric symptoms.

Emerging lines of evidence suggest that observable characteristics of ASC and psychosis may have diametric roots. For example, diametric abilities in social cognition (hypo- versus hyper-mentalising) (Abu-Akel and Bailey, 2000; Crespi and Badcock, 2008), local versus global visual processing (Russell-Smith et al., 2010), processing speed (de Boer et al., 2014), perspective taking (Abu-Akel et al., 2015) and set-shifting (intra- versus extra-dimensional) (Abu-Akel et al., 2017) are evident. Diametric cortical characteristics have also been reported, with abnormally high grey matter and low white matter in ASC, and vis-à-vis SSC (Mitelman et al., 2016), and reduced BOLD in the temporal-parietal junction during a social task associated with higher autistic traits, while the opposite was identified with higher psychosis-proneness (Abu-Akel et al., 2016).

In contrast, and more frequently, ASC and SSC have been shown to converge on negative symptom features and interpersonal deficits (Abu-Akel et al., 2017; Dinsdale et al., 2013; Ford et al., 2017a; Ford and Crewther, 2014; Russell-Smith et al., 2011; Spek and Wouters, 2010). Similar cognitive functioning profiles have also been identified, in terms of spatial working memory, short-term memory, response

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inhibition, perspective taking (Abu-Akel et al., 2015), visuo-spatial ability, working memory, and verbal comprehension (de Boer et al., 2014; Goldstein et al., 2002). Furthermore, neuroimaging studies suggest similar neural correlates between the conditions, particularly for cognitive deficits (Canitano and Pallagrosi, 2017; Ford et al., 2017b,2017c,2017d; Sugranyes et al., 2011). However, the clarity of this similarity is clouded by the heterogeneity of the samples examined in clinical studies (Canitano and Pallagrosi, 2017). These studies evidence cognitive and neural characteristics that overlap both ASC and SSC, thereby highlighting the limitations of current research methods that investigate clinical and subclinical characteristics of these conditions overall. In exploring emergent symptom domain subgroups of autism and schizophrenia spectrum symptoms and traits concurrently, meaningful subgroups of homogenous clinical features should emerge, which can be subsequently utilised in the investigation of underlying neural and genetic mechanisms (Insel, 2010).

Recently, confirmatory factor analysis demonstrated significant overlap within the autistic and schizotypal spectra across four psychosocial domains: Odd Behaviour, Relationship Disinterest, Cue Interpretation Difficulty, and Social and Communication Discomfort (Ford et al., 2017a). In addition, two schizotypy-specific factors emerged: Paranoia/Suspiciousness, and Hallucination/Delusional Experiences, as well as one ASD-specific factor: Fixation with Details. These factors were revealed through robust statistical dimension reduction, and already isolate specific autistic and schizotypal trait phenotypes, and demonstrate where the convergence and divergence of autistic and schizotypal traits occurs, and reveal the similarity between symptoms within the autistic and schizotypal spectra (Ford et al., 2017a). Although factor analysis quantifies the expression of individual factors, it does not group individuals according to similar characteristics. Considering the heterogeneity of ASC and SSC, and their symptom similarities, the identification of specific symptom subgroups within these two spectra may provide a helpful framework for investigating their neural and genetic correlates, and the development of more targeted interventions (Fonseca-Pedrero et al., 2017; Insel, 2010; Klopper et al., 2017).

Cluster analysis groups individuals into homogenous clusters, according to their expression of certain traits, such as the above-mentioned factors. Numerous methods exist for detecting clusters in multivariate data (Arabie and Hubert, 1992), and cluster analysis strategies differ in how they define clusters. Critics suggest that the unknown number of clusters, a priori, and the relative lack of statistical sophistication of cluster analysis, warrants caution in its use (Morgan and Ray, 1995). Latent profile analysis, on the other hand, is a person-centered/data-driven clustering technique that provides an advantage over other methods as it groups individuals based on naturally-occurring patterns within the sample using continuous indicator variables (Scrucca et al., 2016; Vermunt and Magidson, 2002).

This study aimed to identify homogenous population subgroups of specific symptom domains through latent profile analysis of the autistic and schizotypal traits identified previously by Ford et al. (2017a). It was expected that latent profile analysis of a subclinical sample would reveal population subgroups of psychosocial difficulties, psychosis-proneness, and combined autism-schizotypy symptom domains.

2. Methods

Ethics approval was granted by the Swinburne University Human Research Ethics Committee. All participants provided informed consent to participate in the study.

2.1. Participants

Data collection methods for this study have been presented elsewhere (Ford et al., 2017a). Briefly, 1678 participants aged 18 to 40, 428 males (mean = 25.96, *SD* = 6.47) and 1250 females (mean = 26.49, *SD* = 6.79), completed a web version of the AQ and SPQ (using Opinio) (ObjectPlanet Inc., 1998-2013). Participants were recruited via social media, on-campus advertising, word of mouth, and an undergraduate research experience program. Only those outside the 18- to 40-year age range were excluded from the study, although first-degree family history of psychiatric conditions was recorded.

2.2. Materials

The AQ (Baron-Cohen et al., 2001) is a 50-item assessment of autistic tendency across five dimensions, with ten items representing each subscale: Social Skills, Communication, Attention Switching, Attention to Detail, and Imagination. Half the items are reverse-scored. The SPQ (Raine, 1991) has 74 items, with three superordinate dimensions encapsulating its nine subscales: Cognitive-Perceptual features (Ideas of Reference, Odd Beliefs, Unusual Perceptual Experiences, and Suspiciousness); Interpersonal features (Social Anxiety, No Close Friends, and Constricted Affect); Disorganised features (Odd Behaviour and Odd Speech). Responses to the AQ and SPQ (ASQ) were recorded on a 4-point Likert scale from 1(*strongly disagree*) to 4(*strongly agree*); with higher scores indicating greater autistic and schizotypal tendency, respectively. Scoring of ASQ items was based on the raw scores, i.e., they were not scaled as per the traditional scoring system, to provide higher item-item correlations and improve reliability (Austin, 2005; Ford and Crewther, 2014). Total AQ and SPQ scores were, therefore, out of 200 and 296, respectively.

ASQ items underwent confirmatory factor analysis using maximum likelihood estimation as described in Ford et al. (2017a), to reveal seven subscales that aligned with the three factors of Ford and Crewther (2014): Odd Behaviour, Relationship Disinterest, Cue Interpretation, Social and Communication Discomfort (Social Disorganisation), Fixation with Details (Social Rigidity), and Paranoia/Suspiciousness and Hallucination/Delusional Experiences (Perceptual Oddities). Internal reliabilities for the subscales were good (Cronbach's $\alpha = 0.67 - 0.91$). Participant scores on these subscales were used for the cluster analysis described below.

2.3. Statistical analysis

Participants were clustered based on the seven ASQ subscales derived from Ford et al. (2017a). The seven ASQ subscales were standardised so that all subscales had equal variance, which allows for the relative contribution of each subscale to the cluster analysis to be examined. Latent profile analysis was employed in order to recognize sets of mutually exclusive and exhaustive latent classes within the data. Models with the number of clusters ranging from two to nine were compared using the Bayesian Information Criterion (BIC), log-likelihood, and Integrated Complete-Data Likelihood (ICL), with lower values indicating better model fit for all indices. The optimum number of clusters for these data was selected using the BIC as recommended by Pastor et al. (2007), with the interpretability of cluster profiles, in terms of clinical application, taken into consideration.

Separate multivariate analysis of variances (MANOVA) were conducted to determine whether there were significant differences in the mean values for the seven subscales between the resultant clusters. The final clusters were then validated using the variables of sex, age, and the presence of a family history of psychiatric illness, with adjusted residuals used to isolate the significant cluster associations using chi squared tests of independence. It was expected that there would be a greater proportion of those with a family history of psychiatric illness in clusters with higher subscale scores overall, while a greater proportion of males was expected in higher psychosocial clusters and, consequently, a greater proportion of females was expected in the schizotypy specific clusters. Age was not expected to differ between the clusters.