



Research Paper

A cluster analysis exploration of autism spectrum disorder subgroups in children without intellectual disability

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ABSTRACT

Background: The heterogeneity in autism spectrum disorder (ASD) remains poorly understood, particularly in individuals without intellectual disability (ID), where phenotypic variability can be most pronounced. The presence of phenotypic subgroups continues to be questioned. This study investigated whether children with ASD without ID are differentiable into clinically meaningful subgroups.

Method: Data from the 'gold standard' ASD diagnostic instruments for 61 children (5–14 years) with ASD without ID were subjected to exploratory cluster analysis. Cognition, language, pragmatic communication, and behaviour were used to explore subgroups.

Results: Children with ASD without ID could be differentiated into Moderate and Severe Social Impairment subgroups when core ASD symptoms were more closely examined. The Moderate Social Impairment subgroup showed less severe social interaction and communication impairments but *greater* lifetime severity of restricted/repetitive behaviours. In contrast, the Severe Social Impairment subgroup, with poorer social interaction and communication skills, had *lower* lifetime severity of restricted/repetitive behaviours. This subgroup also had greater cognitive and language difficulties, and poorer adaptive functioning. Importantly, however, these neurocognitive and functional differences showed only small to moderate associations with the differentiated ASD clinical profiles.

Conclusions: Evidence of dissociated levels of severity across core ASD dimensions supports the idea that clinically meaningful subgroups within ASD without ID can be identified. The dissociated profiles of ASD features could represent different underlying neurobiological

Abbreviations: ADI-R, Autism Diagnostic Interview - Revised; ADOS-2, Autism Diagnostic Observation Schedule - Second Edition; BASC-2 TRS, Behaviour Assessment System for Children - Second Edition, Teacher Rating Scales; CCC-2, Children's Communication Checklist - Second Edition; CELF-4, Clinical Evaluation of Language Fundamentals - Fourth Edition; CELF-P2, Clinical Evaluation of Language Fundamentals, Preschool - Second Edition; ELI, Expressive Language Index; IS, insistence on sameness factor; PRI, Perceptual Reasoning Index; RLI, Receptive Language Index; RRBI, restricted, repetitive behaviours, interests and activities; RSM, repetitive sensorimotor factor; VCI, Verbal Comprehension Index; WISC-IV, Wechsler Intelligence Scale for Children - Fourth Edition; WPPSI-III, Wechsler Preschool and Primary Scale of Intelligence - Third Edition; WRAML-2, Wide Range Assessment of Memory and Learning - Second Edition.

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mechanisms for each subgroup. Identifying such subgroups in practice can improve the clinical utility of diagnostic labels in this population. Thus, both categorical and dimensional approaches may be useful in classifying ASD, with neither alone being adequate.

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1. Introduction

Autism spectrum disorder (ASD) is defined by impaired social communication skills and restricted, repetitive patterns of behaviour, interests, and activities (RRBI) ([American Psychiatric Association, 2013](#)). There is, however, significant variability within the ASD phenotype across behavior, development, and neurocognition. This results in diagnostic inexactitude and the inability to identify potential biomarkers of the disorder.

DSM-IV-TR defined three subgroups of ASD, namely, autistic disorder (AD), Asperger's disorder (AS), and pervasive developmental disorder-not otherwise specified (PDD-NOS) ([American Psychiatric Association, 2000](#)). This led to diagnostic inconsistencies ([Lord, Petkova et al., 2012](#)), and the distinction between subtypes was unstable longitudinally ([Woolfenden, Sarkozy, Ridley, & Williams, 2012](#)). A further debate, not reflected in the DSM classification, has been a possible distinction between AD without intellectual disability (ID; often termed 'high-functioning autism' (HFA) in research literature), and AS based on differences in early language development ([Bennett et al., 2008](#); [Mayes et al., 2001](#)). In the clinical setting, reliably diagnosing HFA and AS was hampered by difficulties establishing early language development retrospectively ([American Psychiatric Association, 2010](#)). Early language developmental milestones were not a reliable differentiator of profiles of neuropsychological functioning ([Ghaziuddin & Mountain-Kimchi, 2004](#); [Miller & Ozonoff, 2000](#)), language ability ([Lewis, Murdoch, & Woodyatt, 2007](#); [Mayes & Calhoun, 2001](#)), or developmental trajectories ([Starr, Szatmari, Bryson, & Zwaigenbaum, 2003](#); [Szatmari et al., 2000](#)), questioning the clinical utility in differentiating HFA and AS based on the existing criteria.

In DSM-5 ([American Psychiatric Association, 2013](#)), ASD classification moved from subtypes to the notion of a spectrum disorder. The proposal is of two core dimensions that characterise ASD, which vary in composite symptoms and severity across individuals. In contrast to the DSM-IV-TR categorical system, all individuals are classified within a single diagnostic group. While this approach eliminates the previous confusion in diagnosing subtypes, there is concern that it minimises the phenotypic heterogeneity in ASD, particularly with individuals without ID ('ASD without ID'). Distinguishable phenotypes within ASD without ID may exist, but it is likely that the previous diagnostic criteria did not adequately delineate the defined subtypes ([Ghaziuddin, 2010](#)). Moving forward using a more dimensional approach, individual differences can be determined by characterising symptom profiles. Data that examine such differences in an objective manner is a potential way forward to assess the utility of subtypes.

Cluster analysis provides an objective method of exploring the way that phenotypic characteristics group together. Increasingly, such exploratory techniques are being employed to reduce the phenotypic heterogeneity of ASD into more cohesive subgroups based on selected clinical features. Surprisingly, few cluster analytic studies have explored the variability in ASD symptomatology in children or adolescents with ASD without ID ([Beckett, 2005](#); [Bitsika, Sharpley, & Orapeleng, 2008](#); [Prior et al., 1998](#); [Verte et al., 2006](#)).

In two cluster analytic studies of individuals with ASD without ID, three-cluster solutions were identified that loosely aligned with DSM-IV-TR classifications ([Prior et al., 1998](#); [Verte et al., 2006](#)). On closer examination, however, the subgroups were primarily differentiated by the severity of ASD symptoms ([Verte et al., 2006](#)), or by variability in cognitive, communicative, and behavioural difficulties ([Prior et al., 1998](#)). Thus, the subgroups showed a similar profile differentiated by severity of impairment, not quality or type of ASD symptomatology. These authors interpreted the findings as supporting the spectrum approach of ASD, as per DSM-5. When employing a data driven approach to explore potential subgroups, however, clusters will differ according to the variables analysed. Both [Prior et al. \(1998\)](#) and [Verte et al. \(2006\)](#) only sampled ASD symptomatology via parent report, which may have provided a biased perspective. Further, the ability to capture the heterogeneity of this population was limited by only analysing the presence or absence of symptoms ([Prior et al., 1998](#)), or by solely examining symptom domain scores ([Verte et al., 2006](#)). The sample of clinical variables may therefore have been limited and impacted the ability to reveal clinically meaningful subgroups.

[Bitsika et al. \(2008\)](#) did not limit their analysis to ASD symptoms; rather, they examined ASD severity, together with other functional indices, including cognition and adaptive functioning. In doing so, three clusters that differed significantly in reciprocal social interaction, communication, and adaptive functioning were described. The subgroups differed significantly in both the severity and profile of symptoms across core domains, supporting the potential to differentiate qualitatively distinct clusters. Thus, characterisation of core symptomatology together with associated clinical features may help to capture the phenotypic heterogeneity in ASD.

More recently, latent profile analysis has been used to examine the dimensional profile of ASD features. In a childhood ASD study including individuals both with and without ID, [Greaves-Lord et al. \(2013\)](#) identified six phenotypic classes when parent reported ASD symptomatology was examined. Classes 1–3 were reported to align with the DSM-5 conceptualisation of ASD and were characterised by different degrees of impairment within both social communication and RRBI domains. In

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