

Commentary – Autism Spectrum Disorder: Spectrum or Cluster?

John R. Pruett, Jr. and Daniel J. Povinelli

Autism is increasingly considered a *spectrum* disorder – autism spectrum disorder (ASD). However, considering ASD as a *cluster* in a feature space defined by variables related to aspects of dyadic interacting may explain the anecdotal rapidity of the casual “detection” of ASD, and refine our understanding of its phenomenology. Evidence suggests that dyadic interaction is one of the most important levels at which to consider ASD. Here, we propose that there may only be a few cardinal things that can go wrong in dyadic social interaction. Characterizing these aberrancies will aid our search for causal biomarkers, mechanisms, and more effective treatments for ASD.

The Spectrum?

Autism has been renamed *autism spectrum disorder* (ASD). DSM-5 (p. 53) explains the use of the term *spectrum*: “Core diagnostic features are evident in the developmental period, but intervention, compensation, and current supports may mask difficulties in at least some contexts. Manifestations of the disorder also vary greatly depending on the severity of the autistic condition, developmental level, and chronological age; hence, the term *spectrum*. Autism spectrum disorder encompasses disorders previously referred to as early infantile autism, childhood autism, Kanner’s autism, high-functioning autism, atypical autism, pervasive developmental disorder not otherwise specified, childhood disintegrative disorder, and Asperger’s disorder” [American Psychiatric Association, 2013]. These characterizations of the “spectrum” in ASD are compounded with etiological and phenotypic heterogeneity, and neurological, psychiatric, and medical co-morbidity. Despite the benefits of these various meanings for *spectrum*, we argue it is particularly advantageous to consider ways in which ASD is also a *cluster*.

Aspects of Dyadic Interacting Suggest Clustering

A formal and accurate DSM-V diagnosis of ASD requires a lengthy clinical evaluation and careful review and synthesis of detailed information from multiple sources. However, clinicians and non-clinicians often “detect” ASD on a playground, at dinner, or in a psychiatric clinic waiting room. By *detect*, we mean rapidly recognize a specific form of social atypicality which, though not isomorphic with a DSM diagnosis of ASD, strongly covaries with it.

We hypothesize that this rapid detection relates to our evolved sensitivity for species-typical ranges of key parameters of social relating. More precisely, we believe that such detections are made almost reflexively by the combined measurement of abnormalities along three axes of dyadic interaction. Considering the relative clustering of individuals in a space defined by these axes will provide utility beyond the varied ways *spectrum* is used above.

Humans are behaviorally complex. However, the list of essential components of *dyadic* interacting may be quite short. In particular, we propose that in the first few seconds of dyadic interaction, relevant behaviors position individuals along three dimensions: (1) social spacing [Lloyd, 2009], (2) the quality of eye contact and joint attention behavior [Emery, 2000], and (3) the timing of communicative exchange [Dunham & Dunham, 1995]. If distinct clusters of individuals emerge in this space, a dyadic interaction would quickly evoke either a typical sense of connection, or a social warning signal of disconnection (see Bargh, Schwader, Hailey, Dyer, & Boothby [2012] for discussion of automaticity in social cognition).

The DSM-5 offers support for our hypothesis. First, it includes “abnormal social approach” as part of criterion A1 for ASD [American Psychiatric Association, 2013]. Anecdotal clinical experience tells us that many

From the Department of Psychiatry, Washington University School of Medicine, St. Louis, Missouri (J.R.P.); Department of Biology, University of Louisiana at Lafayette, Lafayette, Louisiana (D.J.P.)

Received March 03, 2016; accepted for publication May 14, 2016

Address for correspondence and reprints: John R. Pruett, Jr., Department of Psychiatry, Washington University School of Medicine, 660 S. Euclid Ave, Campus Box 8134, St. Louis, MO, 63110. E-mail: pruetjtj@psychiatry.wustl.edu

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made. Published online 22 June 2016 in Wiley Online Library (wileyonlinelibrary.com)

DOI: 10.1002/aur.1650

Copyright © 2016 The Authors Autism Research published by Wiley Periodicals, Inc. on behalf of International Society for Autism Research

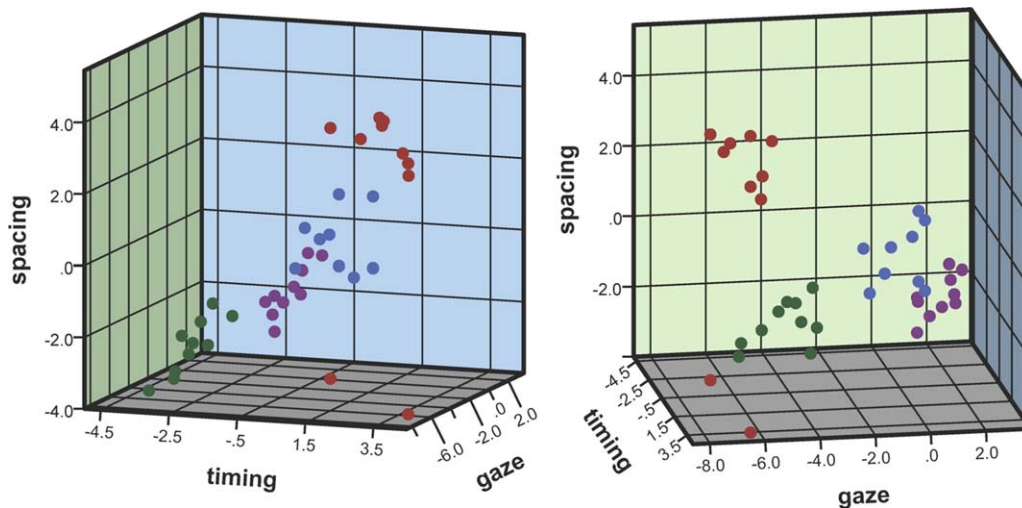


Figure 1. A schematic illustration of our hypothesis. Hypothetical data are plotted for 40 individuals from four different groups. Individuals with ASD (red), ADHD (green), typical development (blue), and Williams syndrome (purple) are represented in a space defined by dimensional measures of interpersonal spacing, gaze behavior, and the timing of contingent exchange in dyadic interaction.

individuals with ASD remain abnormally distant, while others intrude too close, or exhibit behaviors inappropriate for the current interpersonal distance. There are reports about interpersonal space perception in a few clinical conditions. Remarkably, however, there is little published scientific information about this topic for ASD. Second, cardinal social-communicative impairments in ASD include reduced viewing of eyes, gaze following, and joint attention. These behaviors contribute to the DSM-5 criteria and important screening instruments, correlate with measures of impairment, and may appear early in infants subsequently diagnosed with ASD [Jones & Klin, 2013]. Third, DSM-5 also includes “failure of normal back-and-forth conversation” and “failure to initiate or respond to social interactions” as part of criterion A1. *Contingent* behaviors related to the timing of interaction in dyadic social contexts are believed to scaffold aspects of social, emotional, and cognitive development. Contingency has been explored to a limited degree in the parent-child interaction literature in ASD [Apicella et al., 2013]. However, there is a surprising paucity of hypothesis-testing experimental cognitive psychological research on contingency in ASD [Gergely, 2001].

If we could quantify dyadic behavior along these three dimensions, we predict distinct clusters of points would form (Fig. 1). Typically developing children would (1) have a centered range of interpersonal spacing values, (2) make good eye contact and follow others’ gaze, and (3) demonstrate a centered range of values reflecting the timing of contingent responses in dyadic interaction (cluster 1). After norming the typical expression of these variables to zero, atypical cases

could be compared to these zero-centered values. Cases falling inside the typical, zero-centered cluster would evoke a rapid sense of social connectedness. Hypothetical cases falling at marginally long, versus extremely long, Euclidean distances from the typical, zero-centered cluster would generate weak, versus strong, social warning signals, as described above.

Individuals with ASD would separate both from clusters formed by typical and other atypical groups in the following ways.

Children with ASD would generally remain too distant (though, occasionally, too close); demonstrate greatly reduced eye contact, gaze following, and use of gaze to initiate joint attention (lower gaze numbers¹ compared to typically developing children); and show greatly delayed responses during dyadic interpersonal exchange (positive contingent timing numbers) (cluster 2).

Children with attention-deficit/hyperactivity disorder (ADHD) would invade one’s personal space (less-than-zero spacing numbers), demonstrate relative deficits in use of gaze (relatively lower numbers compared to typically developing children, but higher than those for children with ASD), and respond too quickly (less-than-zero contingent timing numbers) (cluster 3).

Finally, children with Williams syndrome would also invade one’s personal space (also negative spacing

¹For simplicity, we treat gaze as a unitary construct. Developing a dimensional measure of gaze would involve consideration of different gaze behaviors (e.g., initiation, maintenance, and use of eye contact). Children from different groups might vary differently on these behaviors. A derived gaze measure would generate gaze values as a weighted sum of such items.

numbers) and respond too quickly (negative timing numbers), but they might fixate others' eyes even more intensely (greater-than-zero gaze numbers) (cluster 4).

If the hypothesized clustering proves robust, the developmental etiology of variance in these three variables could be examined in ASD.

Low-Level Behaviors and Cluster Separation

Behavioral variation driven by sensory and/or motor functioning could produce the hypothesized separations, in our space defined by interpersonal distance, gaze, and timing, without need for appeal to higher-level cognitive differences detectable later in development (e.g., theory of mind). In this way, our scheme would capture behavioral variation present in infancy and potentially maintained throughout life, even in the face of co-occurring differences in other aspects of phenotype. Considering ASD as a cluster defined by interpersonal spacing, gaze behavior, and dyadic interactional timing would, therefore, help mitigate many of the challenges posed by heterogeneity [Pelphrey, Shultz, Hudac, & Vander Wyk, 2011] and complement recent explorations of *measurement equivalence/invariance* [Duku et al., 2013] (across groups varying in age, sex, IQ, etc.).

For example, motor problems are prevalent in ASD, early-appearing, and some are potentially ASD-specific [MacNeil & Mostofsky, 2012]. Atypical motor behavior could affect interpersonal spacing and contingency, contributing to ASD-specific clustering, as above. Reduced salience for eyes and impaired biological motion processing (likely) contribute to ASD by impairing social gaze. Such effects would move individuals along the gaze dimension of our hypothesized feature space into the ASD cluster. At a general level, then, the observed ASD cluster in Figure 1 would reflect canalized outcomes [Waddington, 1942] determined by initial differences in sensory and/or motor functioning.

A Cluster May Have More Explanatory Power

We have highlighted parts of existing DSM-5 criteria that pertain to aspects of dyadic interaction which, if properly quantified, we think will separate ASD from other groups. We do not propose, at this time, that new signs and symptoms be added to the DSM.

ASD remains a *spectrum* according to others' definitions alluded to above. And, the DSM-5 criteria are, of course, a *cluster* of signs and symptoms with dimensional consideration to severity. The cluster we hypothesize, however, forms from consideration of variance along three critical dimensions of dyadic interaction.

Though our hypothesis pertains to social-communicative aspects of ASD, we are not diminishing

the significance of restricted and repetitive behaviors. It would be interesting to study correlations between these and our proposed key variables of dyadic interacting.

Testing our hypothesis would involve developing measures for quantifying variation in spacing, gaze, and timing, and norms facilitating cross-age comparisons to account for ways that variance along our key behavioral dimensions might change over time. Raters could score subjects from different populations on these measures and provide group-based classifications. Their results could be compared against categorizations from gold-standard ASD assessments. We predict that speed, certainty, and accuracy of the raters' assignments would reflect the separation of points in cluster space. A recent study of gaze congruency and latency effects on others' sense of relatedness during interactions provides just one concrete example of an approach for testing aspects of our hypothesis [Pfeiffer et al., 2012]. Atypical scores on one, versus multiple, measure(s) could be evaluated to assess for primacy (e.g., of timing over gaze and spacing), or for which combinations of impairments (e.g., timing plus gaze) prove most important for ASD. Interventions targeting these behaviors could move points closer to the zero-center in cluster space, reduce scores on clinical assessments, and slow the speed of "detection." The depth of canalization associated with each variable could be assessed by studying whether lay observers or young children (and, conceivably, even non-human animals) can detect variation in spacing, gaze, and timing. If our hypothesis holds, investigators could follow the emergence of low-level ASD-specific sensory and/or motor behaviors earlier into infancy with high-risk sibling designs [Jones, Glia, Bedford, Charman, & Johnson, 2014]. Findings would inform early ASD risk assessment, afford a more mechanistic understanding of causal variables, and provide new ways to define subgroups [Campbell, Shic, Macari, & Chawarska, 2014].

Acknowledgments

This work was supported by R01 MH093510 and the McDonnell Center for Systems Neuroscience. The authors would like to thank Susan Culican, Angela Reiersen, and Joseph Piven for comments on the manuscript and helpful suggestions and discussions along the way. We would also like to thank Teddi Gray for help with manuscript preparation.

References

- American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders (DSM-5). Washington, DC: American Psychiatric Association.
- Apicella, F., Chericoni, N., Costanzo, V., Baldini, S., Billeci, L., Cohen, D., & Muratori, F. (2013). Reciprocity in interaction: A

- window on the first year of life in autism. *Autism Research and Treatment*, 2013, Article ID 705895.
- Bargh, J.A., Schwader, K.L., Hailey, S.E., Dyer, R.L., & Boothby, E.J. (2012). Automaticity in social-cognitive processes. *Trends Cognitive Sciences* 16, 593–605.
- Campbell, D.J., Shic, F., Macari, S., & Chawarska, K. (2014). Gaze response to dyadic bids at 2 years related to outcomes at 3 years in autism spectrum disorders: A subtyping analysis. *Journal of Autism and Developmental Disorders*, 44, 431–442.
- Duku, E., Szatmari, P., Vaillancourt, T., Georgiades, S., Thompson, A., Liu, X.Q., Paterson, A.D., & Bennett, T. (2013). Measurement equivalence of the autism symptom phenotype in children and youth. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, 54, 1346–1355.
- Dunham, P.J., & Dunham, F. (1995). Optimal social structures and adaptive infant development. In: C. Moore & P.J. Dunham (Eds.), *Joint attention: Its origins and role in development* (pp. 159–188). Mahwah, NJ: Lawrence Erlbaum Associates, Inc.
- Emery, N.J. (2000). The eyes have it: The neuroethology, function and evolution of social gaze. *Neuroscience and Biobehavioral Reviews*, 24, 581–604.
- Gergely, G. (2001). The obscure object of desire: Nearly, but clearly not, like me: Contingency preference in normal children versus children with autism. *Bulletin of the Menninger Clinic*, 65, 411–426.
- Jones, E.J.H., Glin, T., Bedford, R., Charman, T., & Johnson, M.H. (2014). Developmental pathways to autism: A review of prospective studies of infants at risk. *Neuroscience and Biobehavioral Reviews*, 39, 1–33.
- Jones, W. & Klin, A. (2013). Attention to eyes is present but in decline in 2-6-month-old infants later diagnosed with autism. *Nature*, 504, 427–431.
- Lloyd, D.M. (2009). The space between us: A neurophilosophical framework for the investigation of human interpersonal space. *Neuroscience and Biobehavioral Reviews*, 33, 297–304.
- MacNeil, L.K. & Mostofsky, S.H. (2012). Specificity of dyspraxia in children with autism. *Neuropsychology*, 26, 165–171.
- Pelphrey, K.A., Shultz, S., Hudac, C.M., & Vander Wyk, B.C. (2011). Research review: Constraining heterogeneity: The social brain and its development in autism spectrum disorder. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, 52, 631–644.
- Pfeiffer, U.J., Schilbach, L., Jording, M., Timmermans, B., Bente, G., & Vogeley, K. (2012). Eyes on the mind: Investigating the influence of gaze dynamics on the perception of others in real-time social interaction. *Frontiers in Psychology*, 3, 537.
- Waddington, C.H. (1942). Canalization of development and the inheritance of acquired characters. *Nature*, 150, 563–565.