Personality Neuroscience

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Editorial

Cite this article: Liu W, Pluta A, Charpentier CJ, and Rosenblau G. (2025) A computational cognitive neuroscience approach for characterizing individual differences in autism: Introduction to Special Issue. *Personality Neuroscience*. Vol **8**: e2, 1–7. doi: 10.1017/pen.2025.2

Received: 7 March 2025
Accepted: 8 March 2025

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CAMBRIDGE UNIVERSITY PRESS

A computational cognitive neuroscience approach for characterizing individual differences in autism: Introduction to Special Issue

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Abstract

Traditional psychological research has often treated inter-subject variability as statistical noise (even, *nuisance* variance), focusing instead on averages rather than individual differences. This approach has limited our understanding of the substantial heterogeneity observed in neuropsychiatric disorders, particularly autism spectrum disorder (ASD). In this introduction to a special issue on this theme, we discuss recent advances in cognitive computational neuroscience that can lead to a more systematic notion of core symptom dimensions that differentiate between ASD subtypes. These advances include large participant databases and data-sharing initiatives to increase sample sizes of autistic individuals across a wider range of cultural and socioeconomic backgrounds. Our perspective helps to build bridges between autism symptomatology and individual differences in autistic traits in the non-autistic population and introduces finer-grained dynamic methods to capture behavioral dynamics at the individual level. We specifically focus on how cognitive computational models have emerged as powerful tools to better characterize autistic traits in the general population and autistic population, particularly with respect to social decision-making. We finally outline how we can combine and harness these recent advances, on the one hand, big data initiatives, and on the other hand, cognitive computational models, to achieve a more systematic and nuanced understanding of autism that can lead to improved diagnostic accuracy and personalized interventions.

For most of the past century, psychological research has viewed inter-subject variability in behavior as mere statistical noise around a *true* value, focusing primarily on central tendencies like averages or medians of distributions (Molenaar, 2004; Nesselroade, 2004; Rozin, 2001) – highlighting its problematic status, sometimes this variation is termed a *nuisance*. Traditional statistical models aimed to predict differences in the average population based on specific experimental manipulations (Molenaar, 2004; Nesselroade, 2004; Rozin, 2001). While these experimental designs and methods have helped to develop important theories across psychological domains, they have significant drawbacks. As noted by Wundt much earlier, experimental manipulations typically explain only a small amount of variance in the data and, relatedly, often lack reproducibility, contributing to a replication crisis across the field (Hedge et al., 2018; Kravitz & Mitroff, 2023; Siritzky et al., 2023). This apparent crisis has led to calls for better characterization of behavior through larger sample sizes, robust measures guided by theoretical assumptions formulated as *a priori* hypotheses, and increased transparency in the design and conduct of studies. Open science initiatives have contributed to making these changes by supporting data sharing and study preregistration (Collaboration, 2012, 2015; Kravitz & Mitroff, 2023; Siritzky et al., 2023).

Individual differences research, on the other hand, relies on large sample sizes and data-driven analysis of variability. Its broad, unconstrained study design enhances our ability to capture behavioral diversity and can produce more replicable findings compared to experimental studies with constrained homogeneous samples. Along with advancements in data science, particularly the big data approach (Adjerid & Kelley, 2018; Gomez-Marin et al., 2014; Harlow & Oswald, 2016), there have been calls for better characterization of interindividual differences across cognitive domains (Adjerid & Kelley, 2018; Eisenberg et al., 2019; Gomez-Marin et al., 2014; Harlow & Oswald, 2016). Researchers have long suspected that deviations from the mean are not random noise but systematic variation. However, small sample sizes in most in-person psychological research have hindered the systematic investigation of these interindividual differences. Over the past couple of decades, individual differences have become a growing interest in psychological research. Personality psychology has spearheaded this movement, developing models of personality types (Ilmini & Fernando, 2017; Patzelt et al., 2018; Phan & Rauthmann, 2021), creativity (Lloyd-Cox et al., 2023; Mejia et al., 2021; Minai et al., 2021; Saunders & Bown, 2015), and cognitive styles (Riding & Rayner, 2013; Zhang, 2002) that could explain differences in perception (Haehner et al., 2023; Zhu et al., 2018), attention (Subramanian et al., 2013), and decision-making (Frolichs et al., 2022; King-Casas et al., 2008; Subramanian et al., 2013). While this field has provided evidence for interindividual variation in nonclinical groups, much less is known about the role of interindividual variability in neuropsychiatric disorders.

Across neuropsychiatric disorders, there is larger variability or greater interindividual differences in self-reported or observed behaviors such as personality traits and social skills (Jauk & Kanske, 2019) compared to control groups (Lochner & Stein, 2003; Steinhausen, 2009; Wolfers et al., 2019). These differences, combined (almost inevitably) with smaller sample sizes in clinical studies, present significant hurdles for improving diagnosis and treatment decisions (Beauchaine & Cicchetti, 2016; Jacob et al., 2019; Wolff et al., 2018). This issue is particularly pronounced in autism spectrum disorder (ASD), where formalizing heterogeneity is seen as critical for linking genetic profiles to neural and behavioral phenotypes (Pelphrey et al., 2011; Wolfers et al., 2019). Autism is marked by significant challenges in social interaction and communication, linked to differences in social perceptual and cognitive abilities across the diagnostic spectrum. The complex and diverse neurodevelopmental characteristics of autism are further compounded by interindividual variability observed in many other neuropsychiatric disorders (Jacob et al., 2019). This has led to a shift from viewing autism as unidimensional to one seeing it as an overall term including multiple syndromes, each resulting from different etiological pathways (Amaral et al., 2008; Geschwind & Levitt, 2007; Insel et al., 2010).

Addressing the heterogeneity in autism is imperative for two reasons. First, it can enhance diagnostic accuracy, which currently relies heavily on clinical observations only (Geschwind & Levitt, 2007; Insel et al., 2010; Wolff et al., 2018). Second, it can facilitate the development of more targeted cognitive-behavioral interventions for core autism symptoms, which remain elusive and rarely based on individual symptoms. However, in order to characterize and formalize the heterogeneity within ASD, several significant obstacles must be overcome. These include (1) increasing sample sizes of autistic individuals from a wider range of cultural and socioeconomic backgrounds, (2) building bridges between autism symptomatology and individual differences in autistic traits in the non-autistic population, and (3) introducing finer-grained dynamic methods to capture behavioral dynamics at the individual level. Here, we briefly describe emerging literature on the first two obstacles, before providing our perspective on how to overcome the third and more challenging one of developing finer-grained assessments and cognitive models of autism symptoms.

With respect to increasing sample sizes of autism research, there have been several initiatives spearheaded by the National Institute of Mental Health to support interdisciplinary research aimed at advancing the understanding of ASD and developing new interventions. The Autism Cluster of Excellence (ACE) initiative brings multiple research sites together jointly to investigate the underlying causes of ASD, including genetic, environmental, and developmental factors. ACE centers foster collaboration among researchers from diverse disciplines, including neuroscience, genetics, psychology, and education. The commitment to data sharing in the ACE program has led to large databases of behavioral and neural data such as the National Database for Autism Research and the Autism Brain Imaging Data Exchange. These data-sharing efforts encompass various types of data, including genetics, genomics, brain imaging, and behavioral assessments. This rich and diverse dataset is invaluable for testing the replicability of findings from smaller, single-site studies, enhancing the robustness and generalizability of research findings in the field of autism (Heinsfeld et al., 2018; Nielsen et al., 2013; Payakachat et al., 2016).

To address the second point, building bridges between autism symptomatology in individuals diagnosed with autism and autistic traits in the non-autistic population, there is a need to investigate autistic traits in larger and more diverse samples of individuals with an autism diagnosis alongside individuals without a diagnosis. Measuring self-reported autistic traits alongside objective measures of autistic symptom domains across diagnosed and undiagnosed individuals would shed light on the convergence of autism symptomatology and autistic traits in the general population. Initiatives like the Simons Foundation Autism Research Initiative provide an important resource for recruiting larger and heterogeneous groups of individuals with an autism diagnosis for behavioral studies. This initiative provides a valuable resource for researchers aiming to investigate ASD across different stages of life, from infancy through adulthood. The Simons Foundation Powering Autism Research for Knowledge (SPARK) initiative has aggregated a cohort of over 50,000 individuals with ASD and their families, who are interested in contributing to research. Researchers can access this large and diverse pool of participants nationwide for online behavioral studies. They can additionally apply to utilize existing phenotypic and genetic data on their recruited participants. SPARK has become increasingly popular for recruiting participants across developmental stages and levels of functioning, allowing studies to investigate variability in autism symptoms, including the co-occurrence of certain autism risk genes in phenotypes (Gaugler et al., 2014; Grove et al., 2019; Matoba et al., 2020; Myers et al., 2020; Wilfert et al., 2021), as well as a more thorough investigation of the influence of sex and gender differences in autism (Dillon et al., 2023; Fombonne et al., 2020; Saré & Smith, 2020). Large online studies leveraging such databases are beginning to shed light on the similarities and differences in autistic traits between people with autism or their family members and those without a close relative diagnosed with autism (Bora et al., 2017; Ruzich et al., 2016).

The third and most challenging obstacle is developing finer-grained assessments and cognitive models of autism symptoms that can help bridge the gap to animal models and genetics, on the one hand, and to real-world behavioral outcomes, on the other hand. This need is not unique to studying autism but is much needed across neuropsychiatric domains. Indeed, researchers have acknowledged the need for a computational psychiatry approach to precision phenotyping, increasing the precision with which we characterize certain sub-phenotypes of the autism spectrum (Tiego et al., 2023). A more nuanced approach to characterizing and quantifying the observed behavioral differences and their biological correlates can deepen our understanding of neuropsychiatric disorders and their symptoms (Friston et al., 2014; Hitchcock et al., 2022; Huys et al., 2016; Montague et al., 2012; Wang & Krystal, 2014). In this respect, computational psychiatry describes mathematical approaches to quantitatively analyze the complex interactions across biobehavioral system levels within and between neuropsychiatric disorders (Frässle et al., 2018; Karvelis et al., 2023; Petzschner et al., 2017; Stephan & Mathys, 2014; Wiecki et al., 2015). The hope of computational psychiatry is to identify nuanced patterns of behavior as well as their underlying cognitive mechanisms and neural implementation. This latter goal can be achieved through cognitive computational modeling.

Computational modeling can reveal clinically meaningful individual differences

Cognitive computational models have been widely used in the field of cognitive neuroscience (Castelfranchi & Falcone, 2010; Farrell & Lewandowsky, 2018; Kriegeskorte & Douglas, 2018; Lewandowsky & Farrell, 2010; Pitt et al., 2002; Sun, 2008). These models can be conceptualized as formal mathematical translations of theoretical assumptions. These mathematical models can reveal internal, unobservable states that govern behavioral output (Baker et al., 2009; Baker & Tenenbaum, 2014; Gluck et al., 2010; Just et al., 1999; Wolpert et al., 2003). By translating cognitive processes into mathematical terms and testing them on an individual level, cognitive computational models have revealed individual differences in a wide array of decision-making contexts. Previous studies have differentiated decision-making of more risk averse and risk seeking individuals (Daw et al., 2011; Jacob et al., 2019; Levy, 2017; Pushkarskaya et al., 2017, 2018), impulsive versus more deliberate individuals who plan ahead (Blankenstein et al., 2017; Kable & Glimcher, 2007, 2010; Kurzban et al., 2013), or those that learn from environmental feedback itself or through imitation of others, versus individuals that are more likely to engage in metacognition and represent the task structure (Charpentier et al., 2016, 2017, 2020; Feher da Silva et al., 2023; Ramsey et al., 2021; Vélez & Gweon, 2021). Cognitive computational models can enhance our understanding of behavioral dynamics over time, enabling a more nuanced characterization of individual differences and providing a fundamentally dynamic perspective on cognitive variability within individuals (Schurr et al., 2024).

Computational modeling can inform the links between autistic traits and social functioning

With respect to autism specifically, recent research has highlighted the utility of computational modeling in studying autistic traits within the general population. This is especially important because autistic traits are known to exist on a continuum within the general population (Robinson et al., 2011). Some studies suggest that clinically relevant autistic traits are an extension (or end point) of that continuum (Constantino & Todd, 2003; Ronald & Hoekstra, 2011; Skuse et al., 2005), while other studies suggest a discontinuity between autistic traits in the general population and those of individuals with an autism diagnosis (Abu-Akel et al., 2019; Frazier et al., 2009; Peralta & Cuesta, 2007). Irrespective of these two opposing positions, exploring autistic traits in the general population provides several advantages and can critically inform research on ASD. This claim is warranted by the observation that nonclinical groups with high autistic traits exhibit a higher degree of social functioning (De Groot & Van Strien, 2017) than individuals with ASD. It is, therefore, possible to examine the cognitive profiles or behavioral strategies that contribute to greater social functioning despite high autistic traits. Exploring autistic traits in neurotypical individuals also makes it possible to avoid the confounding effects of comorbid conditions that co-occur with ASD. Furthermore, it enables researchers to study larger cohorts (De Groot & Van Strien, 2017), making it possible to control confounding effects or specifically examine their interaction with autistic traits as a question of interest. The Broad Autism Phenotype questionnaire (Hurley et al., 2007), for instance, describes behavioral and cognitive tendencies that are less severe but rather stable characteristics, similar in nature to those found in individuals with an ASD. Importantly, autistic traits seem to scale with the genetic risk for ASD. Relatives of individuals with ASD without a diagnosis have been shown to exhibit more autistic traits than those without a close relative with an ASD diagnosis (Piven et al., 1997).

Recent studies that have leveraged computational modeling better to define cognitive mechanisms that co-occur with high autistic traits have produced promising avenues for autism research. For example, one study used a hierarchical Bayesian modeling framework to examine the integration of nonsocial and social cues through a reward-based learning task. They found that more pronounced autistic traits in a group of healthy control subjects were related to less integration of social cues in decision-making. Computational modeling further demonstrated that performance differences between individuals with low versus high autistic traits were not due to an inability to process the social stimuli (gaze direction) and their causes, but rather to the extent to which participants relied on social information to infer the nonsocial cue (Sevgi et al., 2020). Another recent large-scale study found that high autistic traits were associated with reduced goal emulation during observational learning. This means that participants with higher autistic traits were more prone to imitate the observer but showed a reduced tendency to represent the overall goal of the observed person, which corresponded to the reward structure of the task (Wu et al., 2024). This emerging literature on social decision-making and autistic traits suggests that high autistic traits do not amount to a general inability to process social cues (Sevgi et al., 2020). They do, however, have a nuanced influence on the extent to which different types of social information are used, which may result in less adaptive outcomes.

Computational modeling can help to specify differences in the cognitive mechanisms underlying behavioral phenotypes

Cognitive computational models have also revealed differences in the cognitive mechanisms of individuals with an ASD diagnosis. In line with previous theories (Baron-Cohen et al., 1985), some studies have shown that individuals with ASD have difficulties in representing their partners' intentions. Yoshida and colleagues (Yoshida et al., 2010), for instance, employed a stag-hunt game to characterize unobservable computational processes implicit in social interactions and to measure whether individuals prefer smaller individual versus larger joint rewards. They found that the decisions of autistic individuals were less guided by inferring their partners' beliefs and instead were guided by a fixed strategy compared to non-autistic control participants. Autistic individuals who showed less mental state inference had greater symptom load. Similarly, a study on social learning showed that autistic adolescents relied less on social knowledge and feedback to learn about peers' preferences (Rosenblau et al., 2021). However, this study specifically tested whether autistic teens could learn about the preferences of non-autistic peers. Given that autistic and non-autistic adolescents may have differing preferences, these disparities could contribute to the "double empathy problem" – a phenomenon where misunderstandings between autistic and non-autistic individuals arise from mutual challenges in understanding each other's perspectives (Milton, 2012).

Other studies using economic exchange tasks have shown more nuanced differences in autistic individuals, which result in more adaptive behavior. For instance, autistic individuals have been shown to assess their partner's cooperation history more accurately and reciprocate less when partners are untrustworthy (Maurer et al., 2018). In accordance with this finding, a study on information sampling for cooperation showed that autistic adolescents had lower overall expectations (i.e., priors) about their partner's reciprocation tendencies (Liu et al., 2024). Given the range of trustworthy and untrustworthy agents, the autistic priors more accurately reflected the overall trustworthiness distribution of their potential partners. Moreover, autistic adolescents shared less often with untrustworthy agents than the non-autistic sample, which suggests that they are less prosocial than non-autistic adolescents. Moreover, this type of strategic interaction was less related to social skills in the autism group. Participants' task behaviors were less strongly associated with social skills as measured by the social responsiveness scale (SRS) compared to the non-autistic group, in which the SRS was the strongest predictor of cooperation tendencies. These findings suggest differences between strategic decision-making in economic exchange and non-economic social interactions in autistic individuals. In non-autistic groups, individuals' strategic choices may be more reflective of their mentalizing abilities and prosocial tendencies.

In conclusion, computational approaches offer a promising way to identify nuanced behavioral patterns and their underlying cognitive mechanisms. Studies leveraging both advances in building big data platforms and computational modeling hold promise for better characterizing autism phenotypes. This could pave the way for defining autism subtypes more clearly and examining their etiology, developmental trajectories, and comorbidities. Moreover, these advances can predict responses to therapeutic interventions, leading to more personalized and effective treatment plans (Collin et al., 2022; Johnson et al., 2021). Finally, we can combine insights from larger studies on autistic traits in the general population and those that investigate variability in symptoms in individuals diagnosed with ASD to inform commonalities and differences between populations with high autistic traits and no ASD diagnosis and those with a diagnosis. It could also help to systematically investigate the roles of sex, gender, and gender diversity in populations with high autistic traits and ASD diagnoses, given emerging evidence of the importance of examining sex differences in autism (Bölte et al., 2023; Loomes et al., 2017). This special issue focuses on how an individual differences approach, rather than the focus on central tendencies, can deepen our understanding of autistic traits and symptoms. It emphasizes the importance of investigating variability in autistic traits and phenotypes to refine autism classification. The issue highlights cutting-edge methods suited to capturing heterogeneity in behavioral and brain function and showcases big data approaches for analyzing large samples as well as computational modeling approaches that can expose how differences in cognitive mechanisms underlie meaningful behavioral variability.

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