Genetics

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How to talk about autism: reconciling genomics and neurodiversity

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A new study showing that genetic and non-genetic factors contribute to autistic traits calls for a fundamental realignment of the concepts and methods of genomics, with a critical understanding of the biosocial complexity of autism.

Social understandings of autism have gone hand in hand with scientific ones since Leo Kanner characterized early infantile autism as a neurodevelopmental disorder in the mid-twentieth century. Historically, this relationship has been adversarial, to put it mildly. Even recently, the Spectrum 10K project – which examined the DNA of a large sample of autistic people – was heavily criticized by the autism community for the lack of clarity on the handling of genetic samples, uncertainty about the potential benefits of the study and fears that the results could lead to harm[1]. Into this turbulent context comes a paper in this issue of *Nature Medicine* from Rolland et al. that describes the results of a population-based study on genes associated with autism[2].

Rolland et al. found that rare loss-of-function (LoF) variants previously associated with autism are also present in the general (undiagnosed) population and that these variants are associated with a decrease in IQ scores and income among the carriers – what the authors call 'sub-diagnostic effects'[2]. Of note, the authors offer a complex and multifactorial explanation of the contribution (penetrance) of these LoF variants in the various populations of reference (13,091 people diagnosed with autism, 19,488 first-degree relatives of autistic people, and 194,070 undiagnosed people). One could easily conclude that people carrying these biological characteristics achieve less in society because of these LoF variants. However, the authors carefully postulate that there are unknown social–biological processes that make some people with a genetic predisposition to autism resilient to the manifestation of the condition. Therefore, specific social environments might act together with biological predispositions to produce both risk and resilience. Given the sensitivity of genetic findings related to IQ and autism, the authors should be commended for their careful interpretation and presentation of their results. At the same time, the study provides a reminder that the relationship between neurodiversity and genomics (its tools, concepts and study designs) can and should be made more complex in the post-genomic age.

In the past, genetics and genomics have contributed to a controversial image of autism as a distinguishable, often heritable, biological deficit[2]. However, the contention that autism might be a genetic condition was not always a source of unease: parents of autistic children welcomed these findings as an alternative to psychoanalytical explanations that 'blamed' parents – specifically, the mother. Also, the idea that autism is firmly linked to one's biology is often welcomed by autistic people themselves. A qualitative study found that many adults, after receiving a diagnosis of autism, feel a sense of relief[3]. The diagnosis is a moment of identity-making; genes and biology make phenomena real. In a deeply fractured public debate on these matters, genes can seem to offer biological mechanisms of autism as a disorder, and also can be deemed crucial for individual and collective understandings of neurodiversity. The study by Rolland et al.[2] breaks false dichotomies about biological and social differences related to autism, and is also aligned to the idea of autism as a neurodiversity. Indeed, characteristics of genes or DNA do not support the idea that autism is a deficit; instead, they align with an understanding that celebrates difference and neurodiversity.

It is essential to emphasize how speaking about autism through genomics is far from neutral, although Rolland et al.[2] have skillfully managed the difficult task of navigating language issues. Take, for instance, the centrality of the term 'loss of function'. Such language is a relic of a theoretical and methodological tradition in genetics that considers distinct DNA-based alterations that affect gene products as being more relevant than other kinds of alterations for understanding phenotypic differences – including those associated with autism. This assumption has been so powerful that even computational predictors of variant effects privilege LoF variants and therefore lack an appreciation of the heterogeneity of pathways that link mutations to pathology[4]. Bringing genomics close to the view of autism as a difference (rather than a deficit) requires more than the careful discussion of genetic data. It raises the following question: in what ways are the field's tools, concepts and study designs skewed toward reifying and pathologizing these differences? Should the field also consider the intimate relationship between 'diversity' and 'dysfunction' or 'deficit' baked into genomic methods?

Rolland et al. specify that the difference between diagnosed people and undiagnosed people cannot be explicitly pinpointed to

anything exclusively biological[2]. Instead, autism merely associates with certain difficulties that merit psychiatric assessment in a particular social, material and educational environment. These unsupportive environments challenge people with autistic traits — what in popular writing is known as the 'tyranny of the neurotypicals'[5]. Of note, the authors carefully avoid any firm commitment to the causal hierarchies among these factors, and they note the dearth of knowledge about social determinants of the phenotypic differences. But while they assign a central role to these social–biological transitions (for example, life circumstances and developmental trajectories)[6] in the modulation of risk of and resilience to a diagnosis of autism, the discussion of factors beyond genomics remains speculative. Is a more refined knowledge about other factors beyond genetics possible? We argue that such a biosocial perspective is necessary[7] for population genetics to lay bare the complexities, uncertainties and unknowns of the multiple contributors to autism.

Making sense of neurodiversity and the conditions for autistic flourishing will require interdisciplinary collaboration between researchers and autistic people. The term 'autism' can refer to a psychiatric diagnosis, which implies that people struggle. But for many autistic people, it is also a way of being that is not intrinsically linked with dysfunction — let alone loss of genetic function[8]. So what does this study mean for autistic identity? The undiagnosed people who carry autism-associated variants could be seen as unaware autistic people whose life circumstances made a diagnosis unnecessary. Or they could be recast as disadvantaged people who faced unfavorable life circumstances. Alternatively, they could be portrayed as something in between, such as 'autistics-in-waiting'[9] who have not (yet) found their way into proper diagnostic screening and support[10]. In the past, it has been suggested that if proper genetic markers for autism could be found, genetic testing would confirm or replace psychiatric assessments. We are wary of this suggestion, as it introduces genomics as the gatekeeper of autistic identity. We argue for an approach that holds seemingly incompatible truths: autism as a unique, situated experience, yet a condition that sometimes requires support; autism as a way of relating to oneself and one's diversity, and nonetheless a difference that has biological underpinnings. The study from Rolland et al.[2] suggests that such ideas may gain wider acceptance. However, for this to happen, a deeper conversation about the philosophies of diversity, normality and difference that populate critical studies of neurodiversity and post-genomics research may be in order.

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Competing interests

The authors declare no competing interests.