

This item is the archived peer-reviewed author-version of:

How to talk about autism : reconciling genomics and neurodiversity

Reference:

Chiapperino Luca, Hens Kristien.- How to talk about autism : reconciling genomics and neurodiversity
Nature medicine - ISSN 1546-170X - Berlin, Nature portfolio, 29:7(2023), p. 1607-1608
Full text (Publisher's DOI): <https://doi.org/10.1038/S41591-023-02403-7>
To cite this reference: <https://hdl.handle.net/10067/1984930151162165141>

GENETICS

How to talk about autism: reconciling genomics and neurodiversity

Chiapperino, L., Hens, K. How to talk about autism: reconciling genomics and neurodiversity. *Nat Med* **29**, 1607–1608 (2023). <https://doi.org/10.1038/s41591-023-02403-7>

<https://www.nature.com/articles/s41591-023-02403-7>

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.

Luca Chiapperino¹ and Kristien Hens²

- 1) STS Lab, Institute of Social Sciences, Faculty of Social and Political Sciences, University of Lausanne, Switzerland.
- 2) Department of Philosophy, University of Antwerp, Belgium & Philosophy Institute, KU Leuven, Belgium

Corresponding author: kristien.hens@uantwerpen.be

Funding

LC's contribution to this work is part of the Swiss National Science Foundation (SNSF) Ambizione project "Constructing the Biosocial: an engaged inquiry into epigenetics and post-genomic biosciences" (Grant number 185822). KH is funded by a European Research Council (ERC) Starting Grant under the European Union's Horizon 2020 research and innovation programme (grant agreement No 804881)

Social understandings of autism have gone hand in hand with scientific ones since Leo Kanner characterised 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 individuals – was heavily criticized by the autism community for the lack of clarity around genetic sample handling, uncertainty about the potential benefits of the study and fears that the results could lead to harm¹. Into this turbulent context comes a paper in this issue of *Nature Medicine* from Rolland and colleagues, which describes the results of a population-based study on genes associated with autism²

Rolland et al. show that rare Loss of Function (LoF) variants previously associated with autism are also present in the general (undiagnosed) population and found that these variants are associated with a decrease in IQ scores and income among the carriers – what the authors call ‘sub-diagnostic effects’. Of note, the authors offer a complex and multifactorial explanation of the contribution (penetrance) of these LoF variants in the different populations of reference (13,091 individuals diagnosed with autism, 19,488 first-degree relatives of autistic individuals and 194,070 non-diagnosed individuals). 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 co-act 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 reminds us that the relationship between neurodiversity and genomics (its tools, concepts and study designs) can and should be complexified 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 deficit². However, the contention that autism might be genetic was not always a source of unease: parents of autistic children welcomed these findings as an alternative to psychoanalytical explanations that ‘blamed’ parents, and 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, upon receiving a diagnosis of autism, feel a sense of relief³. 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 be deemed crucial for individual and collective understandings of neurodiversity. The study by Rolland and colleagues breaks false dichotomies concerning 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 emphasise how speaking about autism through genomics is far from neutral, although Rolland et al. 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 pathology⁴. Bringing genomics close to the view of autism-as-difference

(rather than deficit) requires more than the careful discussion of genetic data. It raises the question: in what ways are the field's tools, concepts, and study designs skewed toward reifying and pathologising 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 and non-diagnosed individuals cannot be explicitly pinpointed to anything exclusively biological. 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 on social determinants of the phenotypic differences. But while they assign a central role to these social-biological transitions (e.g. life circumstances, developmental trajectories)⁶ in the modulation of risk and resilience to a diagnosis of autism, the discussion of factors beyond genomics remains speculative. Is a more refined knowledge about other factors besides genetics possible? We argue that such a biosocial perspective is necessary⁷ for population genetics to lay bare 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 function⁸. So what does this study mean for autistic identity? The undiagnosed individuals carrying 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 unfavourable life circumstances. Alternatively, they could be portrayed as something in between, such as autistics-in-waiting^{cf. 9} who have not (yet) found their way into proper diagnostic screening and support. 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, and yet a condition sometimes requiring 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 and colleagues suggests that such ideas may gain wider acceptance. Yet, for this to happen, a deeper conversation on the philosophies of diversity, normality and difference that populate critical studies of neurodiversity and postgenomics research may be in order.

<Stock image to be included>

Bibliography

1. Sanderson, K. High-profile autism genetics project paused amid backlash. *Nature* **598**, 17–18 (2021).
2. Rolland, Thomas & Cliquet, Freddy. Sub-diagnostic effects of genetic variants associated with autism. *Nature Medicine* (2023)
3. Navon, D. & Eyal, G. The trading zone of autism genetics: Examining the intersection of genomic and psychiatric classification. *BioSocieties* **9**, 329–352 (2014).
4. Hens, K. & Langenberg, R. *Experiences of adults following an autism diagnosis*. (Palgrave MacMillan, 2018).
5. Gerasimavicius, L., Livesey, B. J. & Marsh, J. A. Loss-of-function, gain-of-function and dominant-negative mutations have profoundly different effects on protein structure. *Nat Commun* **13**, 3895 (2022).
6. Silberman, S. *Neurotribes: The Legacy of Autism and the Future of Neurodiversity*. (Avery, 2016).
7. Blane, D., Kelly-Irving, M., D’Errico, A., Bartley, M. & Montgomery, S. Social-biological transitions: how does the social become biological? *Longitudinal and Life Course Studies* **4**, 136–146 (2013).
8. Chiapperino, L. & Paneni, F. Why epigenetics is (not) a biosocial science and why that matters. *Clinical Epigenetics* **14**, 6 (2022).
9. Hens, K. The many meanings of autism: conceptual and ethical reflections. *Dev Med Child Neurol* **61**, 1025–1029 (2019).
10. Timmermans, S. & Buchbinder, M. Patients-in-waiting: Living between sickness and health in the genomics era. *J Health Soc Behav* **51**, 408–423 (2010).