

Parental psychiatric diagnoses as predictive factors for autism spectrum disorder in the child: confluence of genetics and environment

Zoe B. Kaplan^{a,*} and Rebecca J. Schmidt^{a,b}

^aDepartment of Public Health Sciences, School of Medicine, University of California Davis, Davis, CA, USA

^bThe MIND Institute, School of Medicine, University of California Davis, Sacramento, CA, USA

Autism spectrum disorder (autism) is a neurodevelopmental condition that affects over 28 million people globally.¹ With age-adjusted prevalence estimates ranging from 429 cases per 100,000 in Denmark to 707 cases per 100,000 in Sweden,¹ Nordic countries are among those with the highest prevalence of autism,¹ though this could reflect the use of more comprehensive detection methods rather than an underlying increased autism susceptibility. Currently, the etiology of autism is understood as multifactorial and driven by genetic, epigenetic, and environmental (non-genetic) influences.² Parental mental health conditions are hypothesized to increase the likelihood of autism in the child, in part through shared genetic pathways. Mental health conditions, including autism, likely have poly-genetic origins, meaning the accumulation of many common genetic variants may augment the chances of developing the condition.^{3,4} Autism may share underlying genetic contributions with other mental health conditions.³ Two population-based studies found positive associations between maternal psychiatric conditions diagnosed before birth and child autism, with less consistent positive associations between paternal psychiatric conditions and child autism.^{5,6} The mechanisms by which parental mental health conditions could contribute to autism may include inherited genetic factors, environmental exposures, timing of exposures, and interactions between environmental exposures and genetics.

In this issue of the Lancet Regional Health–Europe, Yin et al. contributed to this field by investigating the relationship between autism in the child and 16 parental psychiatric diagnoses.⁷ This population-based cohort study followed 1,488,920 children born in Sweden between 1997 and 2016 until autism diagnosis or the end of the study period in 2017. Child autism diagnoses and psychiatric diagnoses of their biological parents were based on ICD codes from Swedish National Registers. Parental diagnoses were made prior to the birth of the child.⁷

Overall, findings indicated that parental psychiatric diagnoses increase the likelihood of autism in the child.⁷ Yin et al. found that child autism diagnosis had the highest likelihood when psychiatric diagnoses occurred in both parents (aHR = 3.76, 95% CI = 3.48–4.07), followed by the mother only (aHR = 2.34, 95% CI = 2.24–2.43), and then the father only (aHR = 2.02, 95% CI = 1.92–2.12), compared to children whose parents had no psychiatric diagnosis. The likelihood of autism in the child increased as the number of parental psychiatric diagnoses increased. All psychiatric disorders were associated with increased likelihood of autism in the child compared to no parental diagnosis. Autism in both parents was associated with the highest likelihood of autism in the child (aHR = 10.29, 95% CI = 3.86–27.42), reflecting previous findings on familial occurrence of autism.³ To demonstrate reliability, the main findings of the study were replicated using a Finish cohort.⁷

Additional questions remain that were beyond the scope of this study. The finding that all parental psychiatric diagnoses were associated with autism in the child suggests that there may be commonalities in mechanisms driving autism across different parental diagnoses. Psychiatric diagnoses likely do not represent discrete exposure liability categories and research that delves beyond diagnoses could reveal common etiologic threads across disorders that drive autism development.⁸ For example, stress is associated with mental health conditions as a result of psychiatric symptoms or social stigma.⁹ Maternal stress during pregnancy has been associated with an increased likelihood of child autism, potentially via dysregulation of the maternal immune system.² Future studies should consider measuring maternal stress during pregnancy, and analyzing it in conjunction with genetic and epigenetic markers of autism to understand the interplay between parental physiological states like stress and genetic load in autism development.

Timing of related exposures should be investigated further. The nature of symptoms and treatments associated with a psychiatric diagnosis can vary throughout the life course.⁸ Most environmental exposures associated with autism occur during the prenatal and early postnatal period, when most neuronal growth and organization occurs.² Children whose mothers experienced acute



The Lancet Regional Health - Europe
2024;40: 100919

Published Online xxx
<https://doi.org/10.1016/j.lanepe.2024.100919>

DOI of original article: <https://doi.org/10.1016/j.lanepe.2024.100902>

*Corresponding author.

E-mail address: zbkaplan@ucdavis.edu (Z.B. Kaplan).

© 2024 The Author(s). Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

psychiatric problems or used psychiatric medications during pregnancy could experience a higher burden of exposures during a sensitive developmental period compared to children whose mothers have a psychiatric diagnosis but did not have symptoms or use medications during pregnancy. Studies on parental mental health conditions and autism that document the mother's symptoms and psychiatric medication use during pregnancy could enhance understanding of their contributions.

Lastly, more research is needed on how to better support parents with mental health conditions in raising their children. Family-based interventions that focus on the emotional health of parents and children could provide a strong foundation for the child's social and emotional development, even when parents have existing mental health conditions.¹⁰ Future research should take a holistic approach to identify potentially modifiable factors playing a role during and after pregnancy. Prenatal psychosocial interventions could help pregnant people reduce stress and manage symptoms during a critical period for child neurodevelopment.

Contributors

ZBK: conceptualisation, writing—original draft, and writing-review & editing. RJS: writing—review & editing.

Declaration of interests

ZBK: No declarations of interest. RJS has received funding to support the MARBLES Study from the Simons Foundation. RJS consulted for the Beasley Law Firm and Linus Technology, Inc. RJS has received travel support to present at the 35th Annual Meeting of the Organization of Teratology Information Specialists (OTIS) and to serve on the

Observational Study Monitoring Board (OSMB) for HEALThy Brain and Child Development (HBCD) Study, and has received compensation to serve on NIH Reviews.

References

- 1 Solmi M, Song M, Yon DK, et al. Incidence, prevalence, and global burden of autism spectrum disorder from 1990 to 2019 across 204 countries. *Mol Psychiatry*. 2022;27(10):4172–4180.
- 2 Saxena R, Babadi M, Namvarhaghghi H, Rouillet FI. Role of environmental factors and epigenetics in autism spectrum disorders. *Prog Mol Biol Transl Sci*. 2020;173:35–60.
- 3 Havdahl A, Niarchou M, Starnawska A, Uddin M, van der Merwe C, Warrier V. Genetic contributions to autism spectrum disorder. *Psychol Med*. 2021;51(13):2260–2273.
- 4 Visscher PM, Wray NR, Zhang Q, et al. 10 years of GWAS discovery: biology, function, and translation. *Am J Hum Genet*. 2017;101(1):5–22.
- 5 Chien Y, Wu C, Chang Y, Cheong M, Yao T, Tsai H. Associations between parental psychiatric disorders and autism spectrum disorder in the offspring. *Autism Res*. 2022;15(12):2409–2419.
- 6 Jokiranta E, Brown AS, Heinimaa M, Cheslack-Postava K, Suominen A, Sourander A. Parental psychiatric disorders and autism spectrum disorders. *Psychiatry Res*. 2013;207(3):203–211.
- 7 Yin Weiyao, Anna Pulakka, Reichenberg A, et al. A comprehensive assessment of parental psychiatric disorders and risk of offspring autism: Swedish-Finnish register based study. *Lancet Reg Health Eur*. 2024. <https://doi.org/10.1016/j.lanepe.2024.100902>.
- 8 Pacheco J, Garvey MA, Sarampote CS, Cohen ED, Murphy ER, Friedman-Hill SR. Annual Research Review: the contributions of the RDoC research framework on understanding the neurodevelopmental origins, progression and treatment of mental illnesses. *J Child Psychol Psychiatry*. 2022;63(4):360–376.
- 9 Dubreucq J, Plasse J, Franck N. Self-stigma in serious mental illness: a systematic review of frequency, correlates, and consequences. *Schizophr Bull*. 2021;47(5):1261–1287.
- 10 Havighurst SS, Radovini A, Hao B, Kehoe CE. Emotion-focused parenting interventions for prevention and treatment of child and adolescent mental health problems: a review of recent literature. *Curr Opin Psychiatry*. 2020;33(6):586–601.