

**Shared and differentiating genetics  
characterizing autism spectrum disorder  
and major depressive disorder**

**Max Gubert Olivé**

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Supervisors:

Jakob Grove, Anders Børglum, Thomas Bataillon

Bioinformatics Research Center

Aarhus University

Denmark

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## Abstract

Autism spectrum disorder (ASD) and major depressive disorder (MDD) are two polygenic psychiatric disorders with high prevalence in children and adults. Numerous genome-wide association studies (GWAS) have identified risk loci associated with each disorder and, although distinct symptomatology characterizes ASD and MDD, a significant shared genetic structure has been demonstrated. In this project, we analysed genome-wide single nucleotide polymorphism data of ASD and MDD cases from the Lundbeck Foundation Initiative for Integrative Psychiatric Research and worked both at the level of individual loci and at the polygenic level to identify genetic components that are either common or distinct between ASD and MDD. We identified four genome-wide significant loci shared by the two disorders in a combined ASD-MDD GWAS and two risk loci differentiating ASD and MDD in a case-only GWAS. The strongest genetic correlations for the ASD-MDD phenotype were mostly found with other psychiatric phenotypes, while the differentiating ASD vs MDD liability correlated additionally with cognitive and educational traits. Genetic correlations of ASD and MDD with other traits revealed that most phenotypes are correlated in the same direction, with opposite effects only shown in educational traits. The analysis of polygenic risk scores (PRS) showed that comorbid ASD-MDD cases have a double polygenic load with genetic risk for both diseases, and revealed differences across ASD-only, MDD-only and comorbid subgroups when examining the relative burden of PRS for other phenotypes. Overall, the results add new biological insights to the intricate genetic architecture of ASD and MDD and contribute to a better understanding of the genetic similarities and differences between the two disorders.

## Note

This study investigates the genetic similarities and differences between what in medical research is labelled as autism spectrum disorder and major depression disorder. It will include terminology such as 'cases', 'risk' and 'disorder' in order to clarify the argument as accurately as possible and be concordant with other medical literature.

It should be acknowledged that a diagnosis such as autism is indeed a spectrum. Thus the experiences of autism can range from severe incapacitated functioning to inherently positive experiences such as creative thinking, attention to detail and deep focus<sup>1</sup>. Terminology utilized in this study should thus be understood as a means of communication in the medical research field even though it does not accurately depict the complexities of the lived experiences of the people described here.

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<sup>1</sup>Cooper, R., Cooper, K., Russell, A. J., Smith, L. (2021). "I'm Proud to be a Little Bit Different": The Effects of Autistic Individuals' Perceptions of Autism and Autism Social Identity on Their Collective Self-esteem. *Journal of autism and developmental disorders*, 51(2), 704–714

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