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Improved detection of common variants associated with schizophrenia by leveraging pleiotropy with cardiovascular disease risk factors/lipids

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Several lines of evidence suggest that genome-wide association studies (GWAS) have the potential to explain more of the 'missing heritability' of common complex phenotypes. However, reliable methods to identify a larger proportion of single nucleotide polymorphisms (SNPs) are currently lacking. Here, we present a genetic pleiotropy-informed method to improve gene discovery using GWAS summary statistics data. We apply this methodology to identify new loci associated with schizophrenia (SCZ), a highly heritable disorder with significant missing heritability. Epidemiological and clinical studies suggest co-morbidity between SCZ and cardiovascular disease (CVD) risk factors, including systolic blood pressure, triglycerides, low and high-density lipoprotein, body mass index, waist-hip-ratio, immunological parameters, and type 2 diabetes. We validate this 'pleiotropic enrichment' by demonstrating increased replication rate across independent SCZ sub-studies. We have recently replicated these findings in larger sample. The majority of the loci are associated with both SCZ and CVD risk factors, mainly triglycerides, low and high-density lipoproteins. Together, these findings suggest the feasibility of using genetic pleiotropy-informed methods to improve gene discovery in SCZ and identify potential mechanistic relationships with various CVD risk factors. The larger part of the pleiotropic signal was found with lipid levels, suggesting that lipid biology may be involved in schizophrenia pathophysiology. As such, genetically determined dyslipidemia in schizophrenia is in line with evidence for white matter abnormalities and myelin dysfunction and supports the neurodevelopmental hypothesis of schizophrenia.

Biography

Srdjan Djurovic obtained his Dr. Sci. Med. (PhD) from University of Zagreb, Croatia and University of Graz, Austria. He is a Group leader/Professor at the Department of Medical Genetics, and NORMENT Center of Excellence, University of Bergen and Oslo University Hospital – Ullevål, Oslo, Norway. He has published more than 170 papers in reputed journals and has been serving as a reviewer and Guest Professor of repute.

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