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BDNF AND DISC1 ARE ASSOCIATED WITH COGNITIVE DYSFUNCTION BUT NOT WITH SCHIZOPHRENIA IN A HUNGARIAN SAMPLE

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Introduction: Previous studies have found association between several schizophrenia candidate genes and neurocognition in schizophrenia patients and healthy individuals. Both brain-derived neurotrophic factor (BDNF) and disrupted in schizophrenia 1 (DISC1) are important for neurodevelopmental processes and have been implicated as schizophrenia candidate genes, as well as genes influencing neurocognition.
Objectives and aims: To test for the previously described association of these genes with schizophrenia and neurocognition.
Methods: DNA samples from a homogeneous sample of 280 schizophrenia patients and 230 healthy controls were genotyped for polymorphisms in schizophrenia candidate genes DISC1 (rs821597 and rs821616) and BDNF (rs6265). Clinical assessment was performed using the Schedule for Deficit Syndrome and the Positive and Negative Symptom Scale. Neurocognitive functioning was assessed in a subsample of 263 patients and 135 healthy controls by a comprehensive neuropsychological test-battery. Based on the raw neuropsychological measures we calculated a global index of cognitive impairment and domain-specific composite z-scores. Association between the above composite scores and the SNPs was examined using GLM and GENMOD analysis.
Results: The investigated SNPs were not associated with schizophrenia, nor with the deficit or non-deficit subgroups. However we found significant association between global cognitive impairment and rs821616 in DISC1 ($F=3.02$, $p=0.05$) and rs6265 in BDNF ($F=4.47$, $p=0.01$); moreover rs6265 was associated with working memory ($F=6.22$, $p=0.002$) and attention ($F=7.27$, $p=0.0074$)
Conclusion: Using neurocognition as an endophenotype for psychotic disorders in genetic studies has the potential to determine common and separate genetic factors influencing disease risk and neurocognition.

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