

S20-03 - SEARCHING FOR COGNITIVE ENDOPHENOTYPES IN BIPOLAR DISORDER: WHY AND HOW?

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Findings from family, adoption and twin studies suggest that vulnerability to bipolar disorder follows a polygenic mode of inheritance with multiple genes, each of small effect, combining and contributing to the risk and the clinical expression of the disorder. The endophenotype approach has been proposed as a way to identify susceptibility genes in disorders with complex underpinnings. Endophenotypes are supposed to bridge the genotype to the clinical syndrome and to have a simpler genetic architecture than clinical diagnoses.

Our first aim is to confirm if cognitive measures are good potential endophenotypes. Therefore, we will examine the reliability and frequency of cognitive impairments in individuals with bipolar disorder and their biological relatives. The study of healthy relatives avoids confounding factors and should help identify potential endophenotypes.

We will also look for evidence linking particular cognitive impairments to specific genes on one hand and to the risk for bipolar disorder, on the other.

A literature review of articles published in 2008-2009 suggests that the genetic architecture of cognitive endophenotypes is more complex than initially predicted. In many published studies, no genetic association was found between cognitive deficits in bipolar disorder. We will try to understand the reasons and consequences of those disappointing results by analysing some methodological limitations, in particular regarding the statistical treatment of confounding factors.

We will also discuss theoretical considerations pointing out the fact that we may have been expecting too much and oversimplifying when supporting the idea that cognition is a less complex entity than bipolar disorder.