

A search for genes involved in bipolar affective disorder and schizophrenia

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This PhD dissertation was accepted by the Faculty of Health Sciences at the University of Southern Denmark, and defended on September 5, 2003.

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Dan Med Bull 2004;51:147.

ABSTRACT

The PhD dissertation was based on molecular-genetic analyses performed at the Department of Clinical Biochemistry and Genetics at Odense University Hospital. The aim was to identify regions in the genome harbouring risk genes for bipolar affective disorder and schizophrenia. The dissertation was based on four original research articles. Distantly related patients with bipolar affective disorder and schizophrenia from the Faroe Islands were analysed with genetic markers. A segment on chromosome 18p was found significantly more often in patients with bipolar affective disorder and schizophrenia compared to controls. This segment is likely to be inherited from a common founder and may harbour a common risk-gene for both disorders. Linkage and association studies have previously suggested the existence of one or more risk-genes for bipolar affective disorder and schizophrenia on chromosome 18. The present study has further supported these findings, suggested that a joint risk locus may be present and contributed to narrow down the region of interest.

The project also involved investigation of the *somatostatin receptor type 5* (SSTR5) gene and the *4-aminobutyrate aminotransferase* (ABAT) gene for association to bipolar affective disorder in Danish and British patients. Both genes are positioned in a candidate region for bipolar affective disorder on chromosome 16p13. The ABAT gene encodes an enzyme, which is directly responsible for the degradation of gamma-amino-butyric-acid (GABA) in the brain. SSTR5 mediates the effect of somatostatin, which is a neurotransmitter. Significant association was found between the SSTR5 gene and bipolar affective disorder, which suggests that this gene may be involved in the aetiology of this disease. Alternatively, the SSTR5 may be in linkage disequilibrium with a susceptibility gene close to SSTR5. The association study indicated that the ABAT gene is not a major susceptibility gene for bipolar affective disorder. Mapping of susceptibility regions and identification of risk genes for psychiatric disorders is potentially an important step toward unravelling the underlying genetic mechanisms of these diseases and facilitate the development of new drugs, which may lead to better treatment for many patients.