Identification of susceptibility genes for mental disorders based on structural chromosome aberrations

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ABSTRACT

The PhD study was carried out at the Centre for Basic Psychiatric Research, University Psychiatric Hospital in Aarhus and at the Institute for Medical Biochemistry and Genetics, Institute of Panum, Copenhagen.

The purpose was to identify genes implicated in the complex inherited mental disorders through analyses of structural chromosomal breakpoints. The strategy was to cross-link the Danish Cytogenetic Central Register with the Danish Psychiatric Case Register to identify cases with schizophrenia, bipolar affective disorder or depressive disorder co-occurring with a structural chromosome abnormality. The breakpoints were selected to be located within chromosome regions previously identified as susceptibility regions for these mental disorders by linkage analyses. Four individuals with translocations (t(1;16); t(4;12); t(16;17); t(9;17)) were selected for further analysis. The clinical assessment of the patients was done by trained psychiatrists. Three of the patients were diagnosed with bipolar affective disorder and one of the patients was diagnosed with recurrent depression. The breakpoint regions were identified with fluorescent in situ hybridisation, and one of the genes was further analysed with Southern blotting in order to determine if the breakpoint was located within this gene. The literature and available information about the genes located close to the delineated breakpoint regions were analysed in order to validate, which genes could be analysed further. The genes identified within or near the breakpoint regions comprise genes encoding proteins involved in regulation of transcription, synaptic formation, vesicle transport to the pre- and post- synaptic regions, targets of anti-depressants, detoxification of ester and amide compounds, and in the regulation of excitatoric glutamate receptors at post-synaptic regions. These gene products may be involved in the patophysiology of mental disorders, and should be analysed further in the future.