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Brief report

Association study of schizophrenia spectrum disorders and dopamine D3 receptor gene: is schizoaffective disorder special?

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Abstract

Alterations in dopamine neurotransmission have been hypothesized to play a role in the etiology of schizophrenia. We considered the dopamine D3 receptor gene on chromosome 3 as a candidate gene for an association analysis. We compared PCR-based genotype markers for healthy controls ($n = 120$) and patients ($n = 95$) with schizophrenia and schizophrenia spectrum disorders as diagnosed by consensus according to DSM-III-R. Our results possibly indicate an association of schizoaffective disorder with DRD3 homozygosity ($P = 0.056$). © 2000 Elsevier Science Ireland Ltd. All rights reserved.

Keywords: D3 receptor gene; Schizophrenia; Schizoaffective disorder; Association

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1. Introduction

A genetic predisposition to schizophrenia has been demonstrated, but the mode of inheritance remains unknown (Gottesman, 1994). Based on investigations of the mechanisms of action of neuroleptics, alterations in dopamine neurotransmission have been implicated in the pathogenesis of schizophrenia (Seeman, 1987; Cloninger, 1988; Davis et al., 1991). We considered the DRD3 receptor gene as a candidate gene for an association analysis.

The DRD3 gene is located on the long arm of chromosome 3 (Le Coniat et al., 1991) and has been suggested as an important target for neuroleptics. An association between schizophrenia and the DRD3 receptor gene has been found for homozygous schizophrenic patients (Crocq et al., 1992). This finding has since proved controversial; e.g. it was confirmed by Nimgaonkar et al. (1996), but could not be replicated by Macciardi et al. (1994). Williams et al. (1998) have recently carried out a meta-analysis based on 29 independent samples from 24 different studies on the association of schizophrenia and the DRD3 gene published so far, allowing the examination of 2722 schizophrenic patients and 2629 controls. No significant differences of genotype counts were noted between patients and controls for the whole sample, considering frequency of any genotype. However, an excess of homozygosity and the 1,1 genotype could be found for Caucasians ($P < 0.05$), suggesting a small but significant effect of DRD3 in the susceptibility to schizophrenia, at least in Caucasians.

Results of schizophrenia studies have to be interpreted cautiously because of a possible misclassification of phenotypes at the diagnostic level (Meszaros et al., 1996a). Employing a 'narrow' or 'broad' (i.e. including schizophrenia spectrum disorders) notion of schizophrenia could strongly influence such results. In particular, both clinical experience and diagnostic systems (American Psychiatric Association, 1987) suggest that patients with schizoaffective disorder are different in psychopathological symptomatology, cause and outcome when compared to 'core' schizophrenics.

The aim of this study was to explore a possible involvement of DRD3 in the etiology of schizophrenia. We used patients with schizophrenia and schizoaffective disorder as diagnosed by consensus, and unrelated healthy controls to test the above association.

2. Methods

2.1. Sample

Ninety-five unrelated native Austrians with a DSM-III-R (American Psychiatric Association, 1987) consensus diagnosis of schizophrenia or schizophrenia spectrum disorder (uncoordinated type: 9, catatonic type: 1, paranoid type: 16, residual type: 35, schizoaffective bipolar type: 23, undifferentiated type: 11) were identified as probands. All individuals were recruited from inpatients and outpatients at the Department of General Psychiatry, University Hospital of Vienna. In addition, 120 unrelated healthy controls were examined in order to apply the association strategy. These were recruited from a larger pool of possible controls of native Austrians mainly from the area of Vienna (relatives of internal medicine patients in several Viennese hospitals) who had no history of psychiatric disorders themselves or among their first and second degree relatives. All participants gave written informed consent.

2.2. Diagnosis

The diagnostic process included a face-to-face interview with all patients using the Schedule for Affective Disorders and Schizophrenia, Lifetime version (Fyer et al., 1985, SADS-LA). In addition, parts of the International Personality Disorder Examination (Loranger et al., 1987, IPDE), an unstructured psychiatric interview, and a family history evaluation were completed for each individual. Clinical data were obtained from medical records as well as from the treating psychiatrists. After collection of all available clinical information, a DSM-III-R blind consensus diagnosis (axes I and II) was done by two independent psychiatrists (Aschauer et al., 1993; Meszaros et al., 1996b).

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