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Failure to detect dopamine receptor IgG autoantibodies in sera of schizophrenic patients

Short Note

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Summary

Autoantibodies against dopamine receptors in schizophrenic patients have been postulated. IgG was fractionated from sera of 15 schizophrenic patients (DSM III) in an acute episode. However, 3H-spiperone binding to dopamine receptors was not inhibited by this fraction.

Key words: Dopamine, autoantibodies, schizophrenia.

Introduction

The cause of schizophrenia is still unknown. Recently again, an immunological disorder has been postulated (de Lisi and Crow, 1986; Kornhuber and Kornhuber, 1987). Already in 1939 Lehmann-Facius described anti-brain antibodies in sera and cerebrospinal fluid (CSF) of psychotic (obviously schizophrenic) patients. Several other groups found antibodies against brain tissue and thymus in schizophrenic patients (Heath and Krupp, 1967; Baron et al., 1977; Koliaskina et al., 1980; Pandey et al., 1981; Watanabe et al., 1982; de Lisi et al., 1985). Genetic studies as well as the finding of a disturbed blood brain barrier in schizophrenia (Torrey et al., 1985; Kornhuber and Bauer, 1986) are compatible with the autoimmune hypothesis.

The dopamine hypothesis of schizophrenia, based on the findings of Carlsson and Linqvist (1963) that neuroleptics bind to a dop-

amine receptor, is supported by the fact that the D2-receptor binding is quantitatively related to the clinical neuroleptic potency of various neuroleptic drugs (Creese et al., 1976). Furthermore, direct and indirect dopamine agonists were shown to produce schizophrenia-like symptoms.

Abramsky and Litvin (1978) and again Knight (1982) postulated that antidopamine receptor antibodies might be the cause of schizophrenia. Several other studies reported changes in blood and CSF immunoglobulin levels of schizophrenic patients (Solomon et al., 1969; Strahilevitz et al., 1970, 1976; Pulkkinen, 1977; de Lisi et al., 1981; Ahokas et al., 1985; Legros et al., 1985).

Therefore we looked for autoantibodies against dopamine receptors in sera from schizophrenic patients. First we studied the IgG fraction; this study is described here.

Material and methods

The sera of 15 patients with the DSM III diagnosis of schizophrenia were investigated. The disease showed a relapsing-remitting course in all cases and the patients were tested, while they were in an acute episode of at least 3 weeks durance. All patients received neuroleptics, mainly haloperidol and/or fluphenazine. Fifteen neurological patients served as controls. Heparinized sera were taken between 9 a.m. and 11 a.m., centrifuged at $300 \times g$ for 15 minutes and stored at $-20°C$ in plastic vials.

IgG (1, 2 and 4) fractions were isolated by affinity chromatography using Protein A sepharose (Pharmacia, Stockholm), eluted at pH 3.0, lyophilized and stored at $-20°C$.

Dopamine receptor binding assays were performed using a commercial test system in a slightly modificated manner (RP 84; Wellcome, Dartford; usually used to determine haloperidol levels in blood). One milliliter of the samples resolved in phosphate buffer (0.05 M) were added to the original mixture of dopamine receptors (calf striatum) and 3H-spiperone only. Competitive binding was standardized using haloperidol dilution series (15–1000 nM) in phosphate buffer. All samples were done in duplicate.

Results

None of the IgG fractions neither of schizophrenic patients nor of the controls showed any competition in the test system (Fig. 1). The diluted haloperidol standards showed linear competitive binding to dopamine receptors in the Lineweaver-Burk plot ($p < 0.001$).

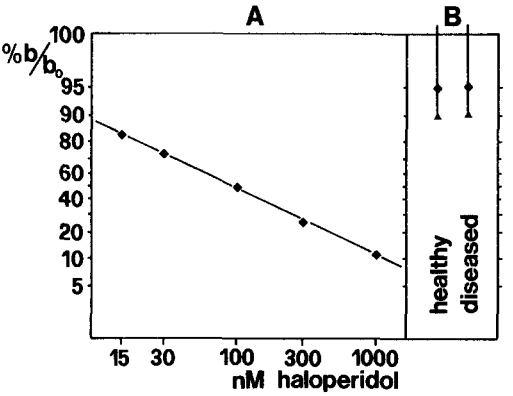

Fig. 1. A Competition of specific 3H-spiperone binding to dopamine receptors by haloperidol (standard curve, log-logit graph, b specific binding, b_0 zero standard). B Control donors' respective schizophrenic patients' IgG-fractions did not show any competition of binding

Discussion

In 15 patient sera we failed to detect any autoantibodies against dopamine receptors in the IgG fraction while spiperone binding to dopamine receptors could be inhibited by haloperidol. IgG-autoantibodies seem not to play a major role in acute episodes of schizophrenia. However, the study would not record seldom cases, or minor levels of antidopamine receptor antibodies (e.g. caused by neuroleptic treatment), or the occurrence of IgG3-subtype only.

In several autoimmune diseases the chronic inflammatory state is represented by IgM autoantibodies. A study for antidopamine receptor antibodies in the IgM fraction is in progress.

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