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Histocompatibility Antigens in Primary Affective Disorders

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Summary. We determined 27 histocompatibility antigens of A, B, and C locus with a standard lymphocyte cytotoxicity test in 125 patients suffering from primary affective disorders, 77 of bipolar type, 24 of unipolar type, and 24 with schizo-affective psychosis. Comparison with a normal control group showed significant increases in the frequencies of antigens Bw40 and Cw4 in unipolar patients and a significantly decreased frequency of antigen Cw3 in bipolar patients. The statistical significances, which were at the 5% level, disappeared when the *P* values were corrected for the number of antigens investigated. Our results failed to confirm previous findings of significantly altered antigen frequencies among patients with primary affective disorders.

Key words: HLA antigens – Primary affective disorders – Unipolar type – Bipolar type – Schizo-affective psychosis.

Introduction

The demonstration of significant associations between different histocompatibility antigens (HLA) with diseases of unknown etiology (Bechtěrev's disease, psoriasis) has attracted attention among psychiatrists, particularly because the important question of the etiology of endogenous psychoses has not been answered. Several papers have already been published which deal with the association of HLA antigens with endogenous psychoses, both schizophrenia and primary affective disorders.

Shapiro et al. (1976) published the first study that was extensive and methodologically careful. They found in manic-depressive patients significant increases of HLA-A3, HLA-B7, and HLA-Bw16, and a significant decrease of HLA-B8 in comparison with a normal population. The increased frequency of HLA-Bw16 was particularly conspicuous; this antigen was found in all eight bipolar patients in the sample and in none of the unipolar patients. The authors subjected their results to critical examination. When their *P* values were corrected

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by being multiplied by the number of antigens investigated, the only difference that remained significant was that between bipolar patients and controls.

Stember and Fieve (1977) also compared patients suffering from primary affective disorders with a control group and found in the patients increased frequencies of HLA-B13, HLA-B5, and HLA-Bw35, and a decreased frequency of HLA-B12. They presented their results only as percentages and did not carry out further statistical calculations.

Govaerts et al. (1977) determined HLA-A and B antigens in 118 manic-depressive patients, 68 of the unipolar and 50 of the bipolar type. Both types showed the same antigen frequencies, with the exception of a slight increase of HLA-B15 in the bipolar patients. The frequency of HLA-Bw15 was reduced in the manic-depressive patients as compared with the control population.

In a preliminary study, our group found an increased frequency of HLA-B5 in manic-depressive patients (Zemek et al., 1977) and increased frequency of HLA-B7 in manic-depressive patients with mentally ill first-degree relatives (Zvolský et al., 1977).

In this report we present the results of examination of a larger group of patients.

Material and Methods

We examined 125 patients suffering from primary affective disorders, 77 being manic-depressive (bipolar), 24 suffering from endogenous depressions (unipolar), and 24 patients with schizo-affective psychosis. Patients were only included when the diagnosis had been verified through agreement between three psychiatrists. The patients were subjected to psychiatric interview and detailed genealogical examination. Histocompatibility antigens (HLA) were determined by a standard lymphocyte cytotoxic test. If the results of this test seemed doubtful, the test was repeated.

The frequencies of HLA antigens were compared with the frequencies in a normal population (Májský, 1977). For antigens Cw2, Cw3, and Cw4 the control group comprised 261 persons, for the remaining antigens 301 persons. Comparison with the normal population was carried out for the whole group of patients, for each of the diagnostic subgroups, for groups of patients with mentally ill first-degree relatives, for groups of patients with mentally ill first- and second-degree relatives, and for patients without mentally ill relatives. Male and female bipolar patients were compared with the corresponding normal controls.

Statistical calculations were carried out with the use of Minsk and Hewlett Packard computers, and the results were assessed using the χ^2 test and, when necessary, Fisher's test. P values were corrected by being multiplied by the number (27) of antigens investigated.

Results

Table 1 shows the frequencies of HLA antigens in the various groups of patients and in the group of normal controls. The frequencies of antigens Bw40 and Cw4 were significantly increased in the unipolar patients and the frequency of antigen Cw3 was significantly decreased in the bipolar patients. The significances were at the 5% level; they all disappeared after correction for the number of antigens investigated. All other comparisons failed to reveal significant differences.

Table 1. Frequencies of HLA antigens in patients suffering from primary affective disorders and in a normal control group

HLA	All patients ($n=125$)	Bipolar ($n=77$)	Unipolar ($n=24$)	Schizo-affective ($n=24$)	Normal controls
					($n=301$)
A1	38	21	9	8	85
A2	51	32	11	8	146
A3	33	21	8	4	76
A9	28	18	5	5	58
A10	21	16	2	3	46
A11	14	6	3	5	29
A28	9	6	0	3	13
A29	5	3	1	1	7
A30+31	5	1	2	2	20
Aw32	3	1	1	1	2
B5	12	8	2	2	46
B7	37	24	6	7	81
B8	25	11	7	7	51
B12	27	15	5	7	79
B13	15	8	5	2	27
B14	4	3	0	1	18
B18	8	5	3	0	14
B27	8	5	1	2	20
Bw15	9	6	1	2	40
Bw17	8	5	0	3	26
Bw21	9	7	2	0	14
Bw22	7	5	0	2	8
Bw35	23	16	3	4	43
Bw40	16	9	5*	2	23
					($n=261$)
Cw2	5	2	1	2	13
Cw3	17	9*	4	4	57
Cw4	20	12	6*	2	25

* $P<0.05$

Discussion

In the present study the patients were selected according to the same criteria as the patients in our earlier studies. Nevertheless we were unable to confirm the results of those studies and of the studies reported by others. Our present examination did not reveal any significant differences between the psychiatric patients and the normal controls. For technical reasons we were unable to determine, like Shapiro et al. (1976), HLA-Bw16 in our patients.

Our results do not exclude the possibility that examination of HLA antigens is relevant to the study of primary affective disorders, but they do seem to weaken it. Taken together with the previous positive findings, the present negative findings indicate that antigen data from small groups of patients should be interpreted with caution.

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