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Reduction of Cerebrospinal Fluid Glutamic Acid in Huntington's Chorea and in Schizophrenic Patients*

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Summary. Glutamic acid levels were investigated in the cerebrospinal fluid and blood serum of patients with schizophrenia, Huntington's chorea, and sciatic nerve compression by lumbar disc protrusion. In the serum the glutamic acid levels were equal in all three groups; in the cerebrospinal fluid (CSF) of schizophrenic and Huntington's patients, however, the glutamic acid was decreased to almost half that of the lumbar disc group which served as control. Most of the patients were treated with neuroleptic drugs. However, since in one case (the daughter of a Huntington's patient) the CSF glutamic acid was decreased although this woman had had no neuroleptic treatment, it seems more likely that the glutamic acid decrease is due to the disease rather than to the neuroleptic treatment.

Key words: Huntington's chorea – Schizophrenia – Glutamic acid – Cerebrospinal fluid – Neuroleptic therapy.

Zusammenfassung. Im Liquor von drei Patienten-Gruppen mit Huntington-Chorea, Schizophrenie und Bandscheibenvorfällen wurde der Glutaminsäuregehalt bestimmt. Im Liquor der Huntington-Patienten und der Schizophrenen war die Glutaminsäure fast auf die Hälfte erniedrigt im Vergleich zu den Kontrollen mit Bandscheibenvorfällen. Der Glutaminsäuregehalt des Blutserums war bei allen drei Gruppen gleich hoch. Die meisten Huntington- und Schizophrenie-Patienten standen unter neuroleptischer Behandlung, nur eine Tochter eines Huntington-Patienten, bei der die Krankheit noch nicht manifest war, zeigte ebenfalls eine Glutaminsäureverminderung im Liquor. Da diese Patientin keine neuroleptischen Medikamente erhielt, ist es wahr-

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scheinlicher, daß die Glutaminsäureverminderung durch die Erkrankung und nicht durch die neuroleptische Behandlung verursacht ist.

Schlüsselwörter: Huntington-Chorea – Schizophrenie – Glutaminsäure – Liquor – Neuroleptische Behandlung.

Introduction

It has been known since the early descriptions in the nineteenth century that schizophrenia-like symptoms occur in Huntington's chorea (for review, see Bruyn, 1968). Usually, the initial stage of Huntington's psychosis is schizophreniform, whereas in the later stages organic dementia is mixed with delusions and hallucinations (Streletzki, 1961). In schizophrenia, the dopamine hypothesis prevailed for some time. Today, however, it is no longer considered likely that the cause of the disease is located in a dopaminergic mechanism only, although the neuroleptic treatment acts via dopaminergic pathways. Therefore, we decided to investigate other transmitters, starting with glutamic acid. Since cerebrospinal fluid (CSF) from patients with Huntington's chorea is more easily obtained by neurologists, we started with chorea. After getting positive results in chorea, we turned to schizophrenia and found the same diminution of glutamic acid in the CSF of schizophrenic patients. Glutamic acid is a transmitter of corticostriate neurons (Kim et al., 1977) and of hippocamposeptal projections (Zaczek et al., 1979).

Methods

Six cases of Huntington's chorea were investigated; in addition, CSF from the 35-year-old daughter of one of these patients was investigated. This daughter did not show any neurologic or psychiatric symptoms and did not receive neuroleptic treatment, while the other six patients were treated with neuroleptic drugs. Furthermore, the CSF of seven schizophrenic patients was investigated, all of whom received neuroleptic drugs. As a control, CSF from ten cases of radicular nerve compression by lumbar intervertebral disk protrusion were investigated. There was no sex difference in the CSF glutamic acid levels.

In all cases the CSF was taken by lumbal puncture at 10 a.m. The patients had no breakfast to avoid nutritional influences on glutamate serum levels. The CSF was taken in sitting position, collected in a glass tube, immediately frozen at −80° C with a mixture of dry ice and acetone, and then stored in a refrigerator at −80° C until analysis.

The glutamic acid was determined by the fluorometric method originally described by Graham and Aprison (1966). From each patient the fluorometric determination was done three times, and the mean was used for further statistical calculations. Furthermore, the blood serum glutamic acid levels were determined using the same method.

Results

The glutamic acid data in CSF and serum are shown in Tables 1 and 2. The diminution of CSF glutamic acid in schizophrenia as compared to lumbar disc patients was significant at the 0.001 level. The diminution of CSF glutamic acid in

Table 1. Glutamic acid levels in CSF

	No. of patients	Mean glutamic acid (nM/ml)	SEM
Schizophrenia	7	26.90	±1.46
Huntington's chorea	7	28.79	±1.98
Lumbar disc patients	10	46.25	±2.28

$P\ (1/3) < 0.001$
$P\ (2/3) < 0.001$

Table 2. Glutamic acid levels in serum

	No. of patients	Mean glutamic acid (nM/ml)	SEM
Schizophrenia	4	188.53	± 3.71
Huntington's chorea	7	183.60	±13.88
Lumbar disc patients	11	203.15	± 9.07

$P > 0.1$
$P > 0.1$

Huntington's chorea as compared to lumbar disc patients was significant at the 0.001 level. In the blood serum, there was no significant difference among schizophrenia, Huntington's chorea, and lumbar disc patients. The daughter of the Huntington's patient had the same CSF glutamic acid reduction as the mother and was, therefore, included in the patient group.

Discussion

The normal CSF glutamic acid levels differ widely in the literature, depending on the methods. However, the small variations within our groups and the highly significant differences among our groups leave little doubt that those differences are real. At first glance one could perhaps suspect that the reduction of CSF glutamic acid to almost half the normal level might be due to the neuroleptic treatment of the schizophrenic and choreic patients. However, the one case of the daughter who had reduced CSF glutamic acid, although she was not treated with neuroleptic drugs, makes it more likely that the decrease of glutamic acid is due to the disease and not to the treatment.

There are two ways to clarify this point: we shall investigate patients not treated with neuroleptic drugs, although it is increasingly difficult to find such cases, and we shall also investigate the effect of neuroleptic drugs on CSF glutamic acid levels in animal experiments.

One might suspect that an elevation of CSF protein in lumbar disc patients may be the cause of the difference. The CSF protein was normal in six of ten disc patients and only slightly elevated (to about 60 mg%, the normal range being up to 50) in the other four. CSF glutamic acid, however, did not differ in these two subgroups of disc patients. Furthermore, we investigated four patients with headache or temporal lobe epilepsy; in all of them CSF glutamic acid was in the same range as in the disc patients.

Perry et al. (1973) found a reduction of seven animo acids (α-amino-n-butyric acid, alanine, valine, isoleucine, leucine, tyrosine, phenylalanine) in the CSF of Huntington's patients, but not of glutamic acid. This was probably due to the method: they used an autoanalyzer while we used a spectrofluorometric method with a specific enzyme. In contrast to Perry's 31 choreics who also showed a reduction of six amino acids in the blood plasma, his schizophrenic contrasts had no reduction of these amino acids in the fasting plasma.

If the measurement of CSF glutamic acid should turn out to be a reliable indicator of Huntington's chorea and their offspring before manifestation, this would be an important early sign for the risk of illness in this dominant hereditary disease and for genetic counseling. Should glutamic acid reduction be confirmed in schizophrenic disease, it might also be used for early diagnosis in suspected or borderline cases. Thus it could help prevent personality breakdown and disruption of social and occupational relations. It might also be an indication that some other way of somatic (biological) diagnosis of mental disease without lumbar puncture is needed. It remains to be seen whether a long-term, double-blind study on the effects of glutamate treatment in early cases of Huntington's chorea and schizophrenia could be carried out despite the fact that glutamic acid is believed not to penetrate the blood brain barrier.

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