BIAL'S REACTION FOR NEURAMINIC ACID IN CEREBROSPINAL FLUID FROM SCHIZOPHRENICS

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THE possibility that schizophrenia is associated with a relative deficiency of neuraminic acid in the cerebrospinal fluid has been suggested by Bogoch (1) and confirmed by Chistoni and Zappoli (5).

The original studies depended on the relatively simple colorimetric reaction of fresh cerebrospinal fluid with Bial's reagent. Klenk and Langerheins (6) had shown that neuraminic acid reacts with orcinol to give a colour which can be related linearly to the original neuraminic acid concentration. Further work, Bogoch (2), Svennerholm (9) and Papadoulos *et al.* (8) has shown that the method is not specific for cerebrospinal fluid neuraminic acid. It is affected in particular by fructose and glucose, and more elaborate techniques have been developed.

This paper is concerned only with the question of whether the original simple chemical work can be repeated. Despite the subtleties of the possible chemical basis for the reaction it might still be used to demonstrate a difference between the "apparent neuraminic acid" content of schizophrenic and other cerebrospinal fluids. If the results of Bogoch (1) could be repeated this test alone could be expected to establish the diagnosis in the majority of cases of schizophrenia. Further, it was by using this technique that interest was aroused in neuraminic acid and schizophrenia.

METHODS

(*a*) *Clinical*

Bleuler's (4) concept of schizophrenia has been used. Only typical cases were included in this study. All of them were in-patients and the diagnosis had been made by three psychiatrists. They were not selected for age, sex or duration of illness, but the majority were chronic cases. No cases of paraphrenia have been included. Eighty-four cases were included in this study.

The controls are from forty-six cases who were lumbar-punctured to exclude neurological disease, but who gave no reason to suspect schizophrenia and in whom the cerebrospinal fluid proteins, cells and sugar were normal. Eleven physically healthy controls are also included. They gave no reason to suspect neurological nor schizophrenic illness.

The lumbar punctures were performed in a standard fashion, between 5 ml. and 6 ml. of fluid being collected into specially cleaned containers. When possible, estimations were performed in duplicate immediately after the fluid was withdrawn. In a few cases this was not possible and the cerebrospinal fluid was then immediately frozen and kept at −20°C until it could be studied.

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(*b*) *Laboratory*

Cerebrospinal fluid was microscoped and if cell counts in excess of 3 cells/c.mm. were found the cerebrospinal fluid was discarded.

The estimations of apparent neuraminic acid were performed in two separate laboratories. In one, in Derby, the technique of Bogoch (1) was used, in the other, in Sheffield, the Uzman and Rumley (10) method was used to produce intenser colours. The results from the two methods are identical, the only difference being that in the latter method all the volumes of test materials and reagents are trebled. The standard used was a sample of methoxy-neuraminic acid prepared by Professor E. Klenk. Nelson's (7) technique was used for estimation of glucose.

Results

It was not possible to detect any reduction in the apparent neuraminic acid content of schizophrenic patients' cerebrospinal fluid. In fact, the mean value for schizophrenia in this study, 40·4 μg./ml., is higher than for the controls, 38·8 μg./ml. Fig. 1 shows all the results plotted according to age and diagnosis.

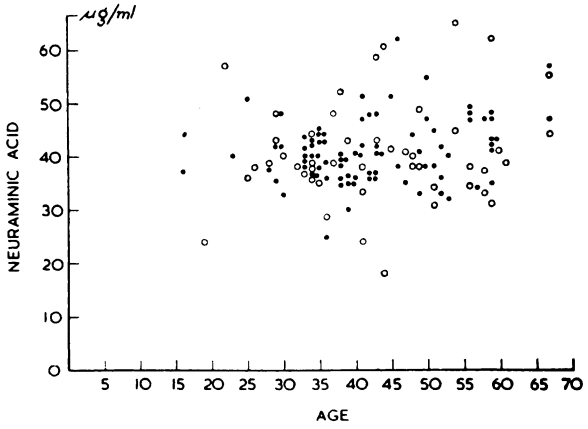

FIG. 1.
Apparent neuraminic acid in the cerebrospinal fluids of schizophrenic patients (●) and other persons (○) plotted against their age in years.

The majority of the controls (38 cases) were derived from lumbar punctures designed to diagnose or help to exclude neurological diseases. The eleven neurotic cases who gave no reason to suspect schizophrenia, nor a neurological condition, had a mean apparent neuraminic acid content of 37·1 μg./ml. with a standard deviation of 6·2. They are not significantly different from the rest of the material.

Most of the schizophrenic patients were receiving phenothiazines. Twelve patients were not receiving treatment and their mean apparent neuraminic acid content was 40·2 μg./ml. with a standard deviation of 7·4. This group was younger and included more acute cases, but is not distinguishable by the cerebrospinal fluid's reaction with orcinol.

In our hands 50 mg./100 ml. of glucose gives an apparent extra neuraminic acid content of 7·4 μg./ml. The interference of glucose is essentially linear. The effects of fructose have not been studied. Our results, with Bial's reagent and any one cerebrospinal fluid, are repeatable with less than 3% error.

Discussion

The results indicate that we have been unable to confirm Bogoch's (1) original findings, that Bial's reaction in the cerebrospinal fluid of schizophrenics produces a less intense colour than in non-schizophrenics. We have not been concerned with the significance of the changes in macromolecules (glycoproteins) more recently reported by Bogoch *et al.* (3). Also the possibility that more specific techniques for estimating neuraminic acid in cerebrospinal fluid would show it to be reduced in schizophrenia, e.g., Chistoni and Zappoli (5) cannot be excluded. It does however seem relevant to state that the chemical technique used in this study is the one which stimulated interest in the subject of neuraminic acid in schizophrenia.

Summary

Using Bial's reaction the apparent neuraminic acid concentrations in the cerebrospinal fluids of 84 schizophrenics and 46 non-schizophrenics were not found to be significantly different.

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