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Studies on sodium transfer and 5-hydroxyindoles in depressive illness

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Coppen (1960) has claimed that the rate of transfer of ^{24}Na from blood to cerebrospinal fluid was lower in patients with a depressive illness than in schizophrenic patients and that the rate of transfer returned to normal as the patients improved clinically. The present communication describes an investigation of this claim and compares the ^{24}Na transfer rates in groups of patients with depressive illness and schizophrenia. Data on the levels of 5-hydroxyindoles in blood and cerebrospinal fluid of these patients are also presented.

SUBJECTS AND METHODS

Specimens of blood and cerebrospinal fluid were obtained from 28 suitable patients who agreed to cooperate in the investigation. A psychiatric evaluation of the patients was made by two of the authors. For the depressive patients the interview technique described by Affleck, Forrest, and Martin (1961) was employed in which 17 items were assessed on a three-point scale. This resulted in a symptom scattergram and on the basis of this a second rating on a five-point scale was made (1 = symptom free, 5 = severely disturbed). For the schizophrenic patients a list of 18 items covering affect, ideation, feelings of passivity, and perceptual disturbance was used and a rating made on a five-point scale (1 = symptom free, 5 = severely disturbed). Only patients whose illness was of at least moderate severity were included and 50% of the patients were rated as severely or very severely disturbed, *i.e.*, rating 4 or 5. None of the patients had received electro-convulsive treatment in the three months before the study.

The rate of entry of ^{24}Na into cerebrospinal fluid was determined in a manner similar to that described by Coppen (1960). On the morning of the investigation the patients were confined to bed. One hundred microcuries of ^{24}Na in the form of an isotonic solution of sodium chloride was injected intravenously and 30 minutes later each patient received morphine ($\frac{1}{6}$ grain) and hyoscine ($\frac{1}{100}$ grain) by injection as premedication to produce relaxation during the lumbar puncture. Approximately one hour after injection of ^{24}Na, 10 ml. of cerebrospinal fluid was obtained by lumbar puncture with the patient in the horizontal position. At the time of lumbar puncture two samples of blood were taken, one of 10 ml. into a tube containing heparin for the estimation of radioactivity, and a second one of 2·5 ml. taken with a Steriseal disposable plastic syringe into a plastic tube containing heparin for the estimation of 5-hydroxyindoles.

The radioactivity in the cerebrospinal fluid (2 ml.) and plasma (2 ml.) was estimated in a well-type scintillation counter, a total of 10,000 counts being recorded. Although it was not possible to perform the lumbar puncture exactly one hour after the injection of ^{24}Na, most of the punctures were done between 60 and 75 minutes. The values for the rate of entry of ^{24}Na in Table 1 are the one-hour ratios

$$\left(\frac{\text{Cerebrospinal fluid concentration of } ^{24}Na}{\text{Plasma concentration of } ^{24}Na} \times 100 \text{ at one hour.}\right)$$

In those cases where more than one hour elapsed between injection of ^{24}Na and obtaining cerebrospinal fluid the one-hour ratios were calculated from the observed values by assuming that the rate of increase of lumbar ^{24}Na concentration was linear and that the change in plasma ^{24}Na concentration between one hour and two hours after injection was negligible (Coppen, 1960; Selverstone, 1958).

Total 5-hydroxyindoles were estimated by a modification of the method of Weissbach, Waalkes, and Udenfriend (1958).

RESULTS

Table I shows the results obtained for the groups of patients with depressive illness and schizophrenia. There was no significant difference between these diagnostic groups in the ^{24}Na transfer rate or the levels of 5-hydroxyindoles in blood and cerebrospinal fluid. The levels of sodium and potassium in plasma and in cerebrospinal fluid were determined in most of the patients and were within the normal range.

Table I also shows the results obtained in a group of patients who were exercised by walking around

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TABLE I

^{24}NA TRANSFER RATE AND 5-HYDROXYINDOLE LEVELS IN PATIENTS WITH DEPRESSION AND SCHIZOPHRENIA[1]

	Patients		*^{24}Na Transfer Rate (%)*	*5-Hydroxyindoles (mμg./ml.)*	
	No.	*Age (yr.)*		*Cerebrospinal Fluid*	*Blood*
Depression	11	53±12	3·48±1·9	12·2±8·2	114±80
Schizophrenia	11	42±15	3·16±0·7	11·5±4·1	82±56
Exercised patients	6	56±15	4·71±1·4	16·6±9·4	82±34

[1]Table shows mean value ± standard deviation.

the wards, with assistance from nurses if necessary, for the period between the injection of the ^{24}Na and the lumbar puncture. The ^{24}Na transfer rate in the exercised patients was higher than in those not exercised ($t = 2·1$, $p = 0·05$) and the level of 5-hydroxyindoles in cerebrospinal fluid tended to be higher in the exercised patients than in those not exercised.

From the depressive patients it was possible to select a small group of four patients who had severe depression without paranoid symptoms. The mean value for the ^{24}Na transfer rate (2·4 ± 0·8) for these four patients was much lower than for the whole group of depressives.

DISCUSSION

The mean one-hour ratio for ^{24}Na transfer in the depressed patients (3·5%) and the schizophrenics (3·2%) in the present investigation was similar to that obtained by Coppen for his control group (3·9%) but lower than that (6%) obtained by Benda, Planiol, Tubiana, and Constans (1954). Various possibilities exist which may explain the apparent discrepancy between our results and the results obtained by Coppen who found a lower value in patients with depression. First, if from the patients in the depressive group a subgroup of patients with severe endogenous depressive illness was selected, the transfer rate for this subgroup was lower (2·4%) than in the whole group of depressive patients. Secondly, all the patients received premedication with morphine and hyoscine. This procedure is open to the criticism of introducing further variables but it ensured that the patients were relaxed at the time of lumbar puncture and maintained them at a uniform level of reduced activity. Thirdly, most of the patients had been receiving phenothiazine drugs which may have caused a reduction of the ^{24}Na transfer rate, since Christensen, Feng, Polley, and Wase (1958) and Quadbeck and Sachsse (1961) have shown that chlorpromazine decreases the permeability of the blood-brain barrier for sodium in rats.

At the beginning of the investigation it was assumed from the work of Selverstone (1958) and Tubiana, Benda, and Constans (1951) that under the conditions of sampling the cerebrospinal fluid ^{24}Na appearing in lumbar fluid did so by direct transfer in the lumbar region and that passage of sodium from ventricular fluid to the lumbar region was unimportant. The possibility of a variable amount of mixing of cerebrospinal fluid from higher levels with lumbar cerebrospinal fluid during the studies by Coppen was thought to have been eliminated by standardizing the procedure for obtaining cerebrospinal fluid and by the finding in two patients that exercise failed to increase the transfer rate. Since the effect of exercise was studied in only two of Coppen's patients it was considered advisable to reinvestigate this aspect using walking exercise for the one hour between injection of ^{24}Na and lumbar puncture. The ^{24}Na transfer rate for the exercised patients was higher than that for those not so exercised although the values for sodium concentration in the cerebrospinal fluid of these patients were not outside the normal range. This apparent increase in the ^{24}Na transfer rate in the exercised patients may have been due to an increased transfer of ^{24}Na from blood to cerebrospinal fluid in the lumbar region or, more likely, due to a more efficient mixing of ventricular with lumbar fluid.

In support of the possibility that the increased values for the ^{24}Na transfer rate in the exercised patients were due to a mixing of ventricular with lumbar fluid was the finding that the level of 5-hydroxyindoles in cerebrospinal fluid also tended to rise after exercise.

SUMMARY

The rate of transfer of ^{24}Na from blood to cerebrospinal fluid was compared in groups of patients with depressive illness and schizophrenia. There was no significant difference between these two groups in the rate of transfer of ^{24}Na.

The ^{24}Na transfer rate of a small group of the depressive patients who showed severe depression without paranoid symptoms was lower than that of the whole group of depressives.

Exercise appeared to increase the transfer rate and

this increase may have been due to more rapid mixing of ventricular fluid with cerebrospinal fluid.

There were no significant differences between the two groups of patients in the levels of 5-hydroxyindoles in blood or cerebrospinal fluid. The levels of 5-hydroxyindoles in cerebrospinal fluid tended to rise after exercise.

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