

# THE EFFECT OF ELECTRO-CONVULSIVE THERAPY ON SPINAL FLUID CONSTITUENTS

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DURING the course of an investigation of the effectiveness of various components of electric convulsive therapy in the treatment of hospitalized psychiatric patients (Brill *et al.*, 1957, 1959) observations were made on the spinal fluid concentrations of cations and total protein before and after treatment. The possibility existed that alterations in brain function and structure (which are believed by many to occur during a course of electro-convulsive treatment, and to be responsible for improvement in patients receiving such treatment) might be associated with, or reflected by measurable changes in the cerebral spinal fluid.

Although changes in blood serum following E.C.T. have been observed, there has been a surprising lack of studies on the cerebral spinal fluid. In a paper published in 1945, Spiegel-Adolf *et al.* (10), using dogs, measured the concentration of potassium, inorganic phosphorus, and total protein before and after electrically induced convulsions. The animals were given from two to fifteen shocks. Measurements were made from one-half hour to three days after the last seizure. The data obtained indicated that there was a significant rise in potassium and phosphorus values within one hour after the last seizure and a return toward pre-treatment levels in one to three hours. No change in the total protein concentration of the spinal fluid was observed. In an earlier study, Katzenelbogen (6), using metrazol-induced convulsions in a sample of psychiatric patients in St. Elizabeth's Hospital, measured a number of constituents in the spinal fluid and found no increase in  $\text{Na}^+$ ,  $\text{K}^+$ , or  $\text{Ca}^{++}$  following the treatment. However, the time of collection of samples following the treatment was not specifically given.

At the time both these studies were done, the methods available for the measurements of  $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Ca}^{++}$ , were time-consuming and difficult, possibly accounting for the small number of reports of such studies on the spinal fluid. The development of flame-photometric techniques has provided a convenient and accurate method for determining the concentration of these cations. In 1951, making use of this technique, Shaw and Holley (9) examined the cerebral spinal fluids of 100 hospitalized patients without any evidence of organic or functional disease of the nervous system for their levels of sodium

and potassium. The mean value obtained for sodium was 142 meq. with a range from 134 to 152 meq. The mean for potassium was 2.88 meq. with a range of 2.50 to 3.65 meq.

Katzenelbogen (5) summarized the earlier literature, and a recalculation of the data presented by him indicates that cerebral spinal fluid sodium levels in a population of 64 normals obtained by different investigators using different techniques ranged from 112 meq. to 166 meq. With respect to potassium, the summarized data, recalculated, show a range of 2.56 meq. to 4.32 meq. in 63 normal subjects. In his own study, Katzenelbogen found a range of 3.28 to 3.99 meq. of potassium in the spinal fluid of 12 psychotic patients. He also summarized the data on calcium levels in the cerebral spinal fluid. The values reported on subjects with no known functional or organic disease of the nervous system ranged from 4.1 to 6.1 mg. per cent., while the levels found by Katzenelbogen in 50 patients with schizophrenic and manic-depressive disorders ranged from 4.1 to 5.3 mg. per cent.

The range of total protein levels in the spinal fluid was found to be from 6 mg. per cent. to 100 mg. per cent., according to Neel (7) who summarized the data obtained from various workers from 1895 to 1938. Peterson (8) using a turbidimetric method on a general hospital patient population reports that on 257 spinal fluids examined which had essentially normal cell counts, normal globulin levels and normal colloidal gold curves, 94 patients had 40 mg. per cent. or less, 109 had 40–60 mg. per cent., 49 had 60–100 mg. per cent., and only 5 had over 100 mg. per cent. Katzenelbogen (5) in a study of the total protein levels in the spinal fluid of a mixed group of psychotic patients finds that 89 per cent. of his cases fell in the range of 16–45 mg. per cent., 4 per cent. in the 10–15 mg. per cent. range, and 7 per cent. in the 46–80 mg. per cent. range. In a study of 1,281 patients of the "dementia praecox group", Breutsch *et al.* (1) found that the range of total protein in the cerebral spinal fluid was 46–166 mg. per cent. with only four patients over 100 mg. per cent. The remaining patients varied between 46–99 mg. per cent.

In the present study the subjects were 96 male psychiatric patients from the Brentwood Veterans Administration Neuropsychiatric Hospital in Los Angeles, for whom shock treatment had been prescribed. None had had shock treatment in the preceding 9 months. All were male veterans. Sixty-six were suffering from chronic schizophrenic reactions and 30 from schizo-affective disorders or depressive reactions. The illness in a majority of the patients was characterized by exacerbations and remissions and many had received electroshock treatment previously with beneficial effect. The patients' ages ranged from 18 to 68 with a mean of 35. Patients with recognized organic disease of the central nervous system were excluded.

The 96 subjects were randomly assigned to one of the five treatment groups; regular E.C.T., E.C.T. plus anectine, E.C.T. plus pentothal, pentothal alone, and nitrous oxide alone. The present report is concerned with the spinal fluid concentration of cations and total protein in the entire sample rather than with the five sub-samples. A course of 20 treatments was administered to each patient, given at the rate of three times a week. Spinal fluid determinations were made on each subject prior to the beginning of treatment, two weeks following the last treatment, and again one month following the last treatment\*.

The results obtained in the present study for the pre- and 1 month post-

\* Because it was not possible to obtain every sample on every patient, the number of subjects in each category varied as indicated in the text.

treatment levels of sodium, potassium, calcium, and total protein in the cerebral spinal fluid are summarized in Table I. (The mean and range of these constituents measured 2 weeks after completion of treatment were substantially the same as those obtained after 5 weeks and are therefore not included in the table.)

TABLE I  
Concentration of Cations and Total Protein in C.S.F. of a Sample of Psychotic Patients

		Pre-Treatment			Post-Treatment		
		$\bar{X}$	Range of Values	S.D.	$\bar{X}$	Range of Values	S.D.
Meq. Na <sup>+</sup>	(a)	152	138-166	5.55	153	142-174	6.30
Meq. K <sup>+</sup>	(a)	3.1	2.6-3.8	.233	3.1	2.4-4.8	.389
Mg. % Ca <sup>++</sup>	(a)	5.4	3.8-8.6	1.14	5.2	2.0-9.0	1.22
Mg. % total protein	(b)	39	8-84	13.2	41	12-110	15.6

a=Method of Kingsley, G. R., and Schaffert, R. R., *Analytic Chem.*, 1953, 25, 1738.  
b=Method of Kingsley, G. R., and Getchell, G., *J. Biol. Chem.*, 1957, 225, 545.

(a) *Sodium and Potassium.* The data indicate that there is no change in the mean concentration of these ions between the pre-treatment levels and those observed one month following treatment. There appeared to be no shift in the range of values obtained before and after treatment in these patients. The range of values observed in the spinal fluid of these psychotic subjects is similar to that observed in the literature for "normal subjects" (5, 7, 8, 9).

The effect of convulsive or non-convulsive treatment upon the distributions of sodium and potassium levels as well as the relationship of these levels to the response to treatment (i.e. improvement or non-improvement) is shown in Figures 1 and 2. It can be clearly seen that there is no significant difference between the distributions of spinal fluid levels of sodium and

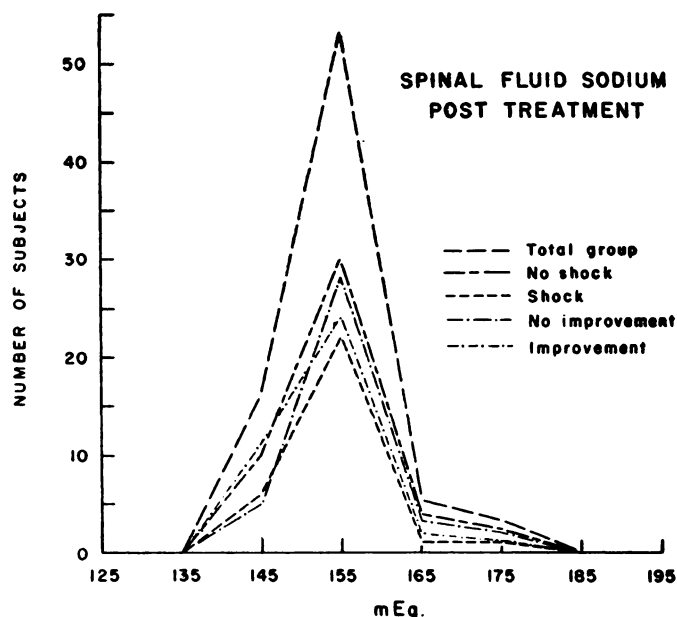


FIG. 1.—C.S.F. sodium levels in patients five weeks after termination of treatment.

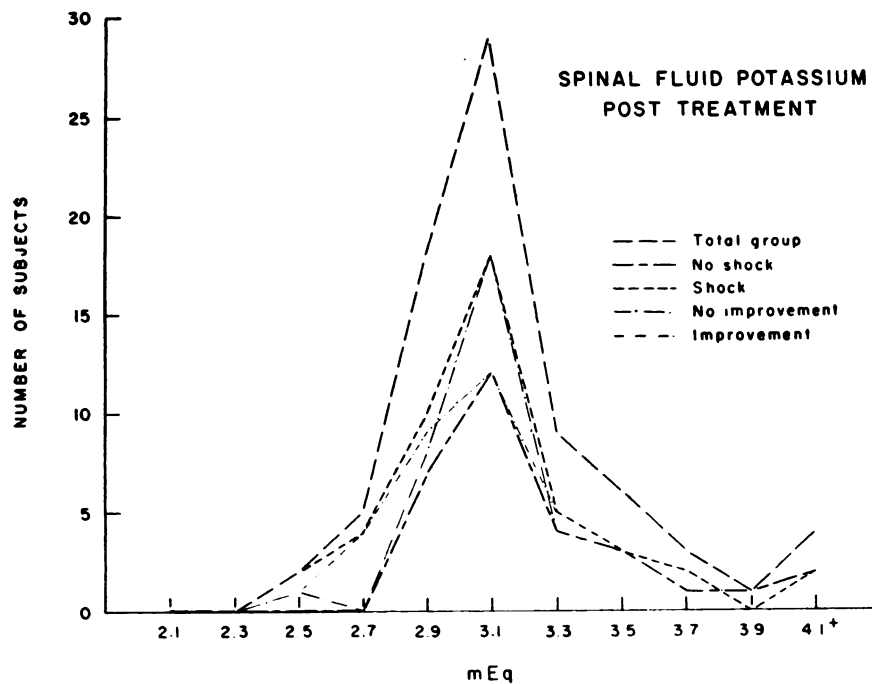


FIG. 2.—C.S.F. potassium levels in patients five weeks after termination of treatment.

potassium in those patients who received one of 3 types of electroshock treatment and those who received one of the other forms of treatment (i.e. repeated administration of pentothal or nitrous oxide). Furthermore, the similarity of the distribution curves of those patients who improved (irrespective of type of treatment) and of those showing no improvement strongly suggests that no relationship exists between spinal fluid sodium and potassium and the clinical state of the patient after treatment. It had been previously shown that clinical response to treatment was unrelated to the pre-treatment values of sodium and potassium in the spinal fluid (4).

(b) *Calcium*. Just as in the case of the other cations, the spinal fluid calcium levels do not show any significant change in their mean or range whether determined before treatment or 1 month after treatment. Among the pre-treatment values, only 4 patients of the 90 studied had calcium levels above 6.0 mg. per cent. With respect to the post-treatment data, again only 4 patients out of 73 had values greater than 6.0 mg. per cent. while only 3 patients, with previously higher levels, had levels less than 3.8 mg. per cent. The relationship of post-treatment calcium levels to improvement and to type of treatment is shown in Figure 3. When the pre-treatment spinal fluid calcium levels of patients who improved were compared with those who did not improve, it was found that the unimproved group tended to show higher initial levels.

(c) *Total Protein*. The data from Table I indicate the similarity of means and ranges of total protein levels in the spinal fluid when determined before treatment and 1 month after treatment. There was only one value (8 mg. per cent.) below 20 mg. per cent. in the 88 patients studied prior to treatment, and only 8 values that were over 55 mg. per cent. There was no relationship between age or EEG abnormality and level of spinal fluid protein. One month after treatment, out of a total of 74 determinations there were only two with

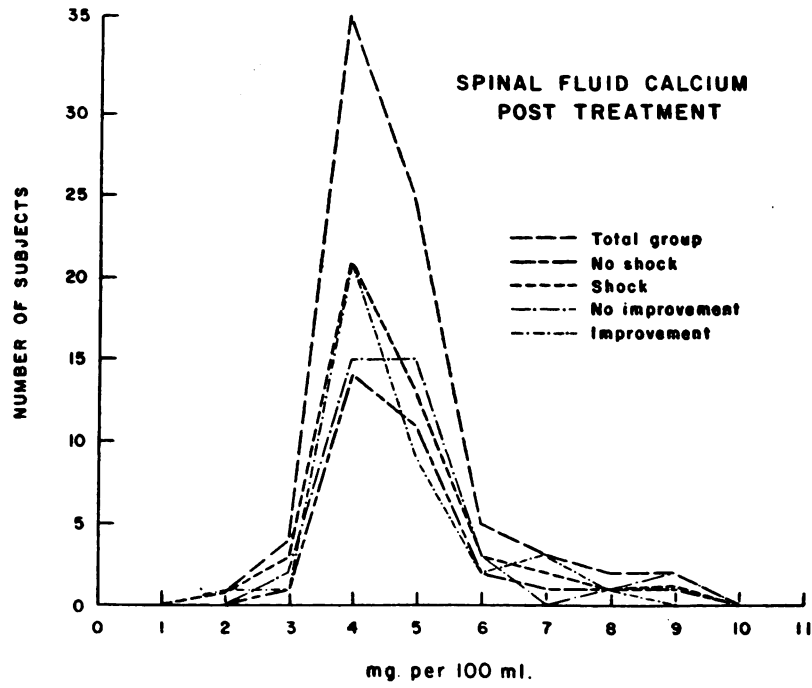


FIG. 3.—C.S.F. calcium levels in patients five weeks after termination of treatment.

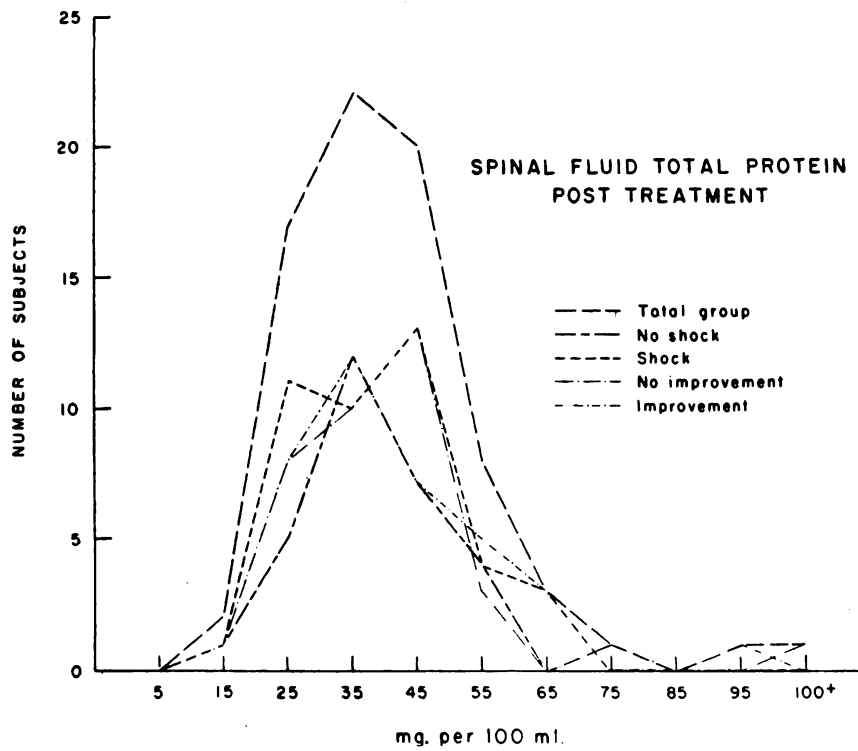


FIG. 4.—C.S.F. protein levels in patients five weeks after termination of treatment.

values (12 and 19 mg. per cent.) under 20 mg. per cent., and eight with values over 55 mg. per cent. The relationship of spinal fluid total protein to improvement and to type of treatment is illustrated in Figure 4. The coincidence of the distribution curves clearly indicates that neither the type of treatment, nor the response to it, is reflected in the level of spinal fluid total protein.

#### DISCUSSION

Although changes taking place in the concentration of these and other substances in the spinal fluid *immediately* following an electrically induced convulsion have been described in animals and in humans (Spiegel-Adolf, 1948) the above data would indicate that by the end of the 5th week following cessation of treatment, the concentrations of these substances apparently have returned to pre-treatment levels.

Statistical analysis of the concentrations of sodium, potassium, calcium and total protein in the spinal fluid as related to improvement of the patient or to the mode of treatment of the patient revealed that only the pre-treatment level of spinal fluid calcium showed a relationship with improvement of the patient (4). A total of twenty biochemical variables in serum and the spinal fluid were statistically analysed, and since only this one parameter of the spinal fluid constituents was found to have a relationship, it is possible that this finding could appear by chance alone. Of course, it is possible that the overall determination of these ions and protein in spinal fluid may not reflect transient or permanent localized changes in particular areas of the brain which could influence the activity of neural nets and secondarily the clinical condition of the patients.

Our data cannot answer the question concerning the production of any persistent physical alteration in the brains of these patients whether treated by shock or non-shock methods. What is clear however, is that if changes did occur they were not reflected in changes in sodium, potassium, calcium, or total protein levels in the spinal fluid.

The rather broad ranges of values for calcium and total protein found in this patient sample are not appreciably different from those which have previously been described for normal subjects. The fact that such broad ranges occur is in itself of interest and as yet without adequate explanation.

#### SUMMARY AND CONCLUSION

1. The distributions of values of sodium, potassium, calcium, and total protein in a sample of 96 psychotic patients are not different from reported distributions found in non-psychotic populations.
2. The response to treatment seems unrelated to the pre-treatment values of these elements of the spinal fluid.
3. Electro-convulsive treatment does not result in any significant change in these components of the spinal fluid when measured 1 month after completion of a course of treatment.
4. Change in clinical condition does not appear to be associated with any change in these constituents of the spinal fluid.

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