Quantitative immunoelectrophoresis of serum from hospitalized chronic schizophrenic and epileptic patients

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SUMMARY Ten serum proteins are measured by quantitative immunoelectrophoresis in 20 chronic schizophrenic and nine epileptic patients. Results from each group are compared with each other and with normal values and significant differences noted. Schizophrenic patients had higher haemopexin levels and epileptic patients had higher α_2 group component levels, both compared with normal subjects. Also schizophrenics had higher α_1 PG_p and α_1 AT levels compared with epileptics.

There exist numerous reports of alterations in biochemical parameters among groups of hospitalized schizophrenic patients. Such parameters have included protein levels determined in various ways and probably among differing types of patients, the diagnosis of schizophrenia being an individual decision which is hard to define and which is not always even described. The conflicting reports of abnormalities have not allowed any firmer hypothesis about the pathogenesis of the schizophrenias than existed before investigations into the protein changes in schizophrenia were begun. The controlled study reported here seeks to take into account some of the variables often ignored by other workers, and thus to place on a firmer basis the minor alterations in serum protein levels which have been described.

MATERIALS AND METHODS

PATIENT SELECTION

Two groups of patients were selected on the following criteria.

1. **GENERAL** All patients were Europeans aged between 20 and 60 years; they had no past history of jaundice or of general organic disease, and showed no evidence of current organic disease. They were fit for occupational or work therapy. Every patient was able to eat the full ward diet; no food supplements were given.

2. **DIAGNOSTIC CRITERIA** a. *Schizophrenia* Schizophrenic symptoms of the first rank (Schneider, 1959) had been detected on admission and could still be elicited when examined by one of us during the selection interview. Evidence of passivity experiences, primary delusions or thought resonance, withdrawal, sharing, or broadcasting were thus required. Selection was made initially from patients already diagnosed independently by other physicians as having paranoid schizophrenia. Symptoms of the second rank, including hallucinations, motor and volitional symptoms, and emotional disturbances with other forms of thought disorder were also recorded in all patients. Those with signs of organic dementia or with affective illness were excluded. Treatment with drugs (apart from monoamine oxidase inhibitors) was not a selection factor.

b. *Epilepsy* All patients had had grand mal attacks or focal seizures including lapses of consciousness, but not true petit mal. All were exhibiting symptoms and signs of the schizophrenia-like psychoses of epilepsy as described by Slater, Beard, and Gilthero (1963). Thus a schizophrenia-like picture, usually without gross affective blunting and with or without signs of organic brain disease, was necessary for inclusion in this group.

3. **DATA COLLECTION** The patients studied included all those conforming to the selection criteria in a large English mental hospital and in four long-stay wards in a second similar institution. All patients were seen by one of us and information about the past history was recorded from the clinical records onto standard proformas. There followed a diagnostic interview in which the clinical features required for selection were elicited. After selection, an afternoon venous blood sample was collected without stasis and was separated within four hours of collection.

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4 METHODS Sera were stored at -20°C until analysis by the quantitative immunoelectrophoretic technique described by Laurell (1965) and modified by Clarke and Freeman (1968). Figure 1 shows the type of plate produced by this method; each protein produces a precipitation curve, the area under which is proportional to the quantity of that protein in serum, and inversely proportional to concentration of antibody to that protein. Ten proteins were selected for estimation, and compared with a reference serum. The range for each of these proteins found in a normal European population, using this technique, has been published (Clarke and Freeman, 1968). Clinical information, together with protein concentration was coded and transferred to IBM 80 column punched cards for statistical treatment.

RESULTS

PERSONAL DATA In Table 1 the average age, weight, age at onset of disease, duration of illness, duration of in-patient care on admission, drug regimes, and fit frequency are presented. The epileptic patients tended to have had an earlier age of onset (of the epilepsy) than the schizophrenics, and thus the duration of their disease was greater, both as in-patients and altogether. Of the 20 schizophrenic patients, 15 had chronic paranoid psychoses, two were undergoing their first attack of acute schizophrenia (with paranoid ideation), and three had other schizophrenic (hebephrenic, catatonic) illnesses. None of these ever had epileptic fits, but one had had an ECT convulsion the previous week. In the nine epileptic patients no fits had been recorded within the four weeks before interview.

PROTEIN VALUES These are presented in Table 2, all

TABLE 1
PERSONAL DATA ON THE PATIENTS STUDIED

	Schizophrenics	Epileptics
Number	19	9
Number (male)	5	7
Mean weight (kg)	64.7	73.2
Average age (yr)	37.4	39.4
(range—yr)	22-57	29-49
Average age at onset (yr)	26.8	17.1
Mean duration of illness (yr)	8.8	22.3
Mean duration of current in-patient admission (yr)	1.6	4.9
Mean fit frequency		
> 1/month, patients	Nil	4
< 1/month, patients	Nil	5
Drug therapy	Patients (no.)	
Phenothiazines	9	3
3 months or more		
Phenothiazines	6	1
3 months or less		
Nil or minor tranquillizer only	5	5
Anti-epileptic drugs	Nil	8
		(phenytoin)
		9
		(mysoline or barbiturates)

figures being given as percentages of a standard normal serum. It will be seen that the schizophrenic patients studied here have significantly higher haemopexin values than the normal series; while the patients with epilepsy had significantly higher α_2 group component levels than the normal subjects and the schizophrenics. The schizophrenic patients also had higher $\alpha_1\text{PGp}$ and $\alpha_1\text{AT}$ levels than the epileptics. Apart from these no other characteristics could be defined.

FIG. 1. Characteristic protein patterns in (a) epilepsy; (b) pooled adult serum, and (c) schizophrenia. Only the following proteins were estimated: α_1 lipoprotein ($\alpha_1\text{LP}$), α_1 easily precipitable glycoprotein ($\alpha_1\text{PGp}$), α_1 antitrypsin ($\alpha_1\text{AT}$), α_2 group specific component ($\alpha_2\text{GC}$), α_2 HS ($\alpha_2\text{HS}$), α_2 macroglobulin ($\alpha_2\text{M}$), caeruloplasmin (Caer), haptoglobin (Hpt), haemopexin (Hpx), transferrin (Trf), beta lipoprotein (βLP), β_{1A-C} (third component of complement).

TABLE 2
MEANS AND STANDARD DEVIATIONS FOR EPILEPTIC AND SCHIZOPHRENIC PATIENTS

Protein	Epileptic		<i>P</i> <	Normals		<i>P</i> <	Schizophrenia		<i>P</i>	
	Mean	SD		Mean	SD		Mean	SD	Schiz.	v. ep.
α_1 Lp	134	26	—	127	20	—	145	27	—	—
α_1 PGp	108	26	—	115	19	0.05	134	28	—	—
α_1 AT	152	11	—	114	18	0.05	141	48	—	—
α_2 GC	145	25	0.01	117	15	—	131	19	0.01	—
α_2 HS	93	9	—	—	—	—	100	15	—	—
α_3 M	105	31	—	122	25	—	115	33	—	—
Caer	171	32	—	137	25	—	143	27	—	—
Hpt	104	85	—	103	44	—	113	50	—	—
Hpx	117	15	—	107	13	0.001	132	26	—	—
Trf	98	23	—	110	15	—	115	27	—	—
β Lp	119	38	—	177	43	—	148	52	—	—
β_{1A-C}	99	18	—	107	24	—	109	33	—	—
n	9		—	100		—	19		—	—

DISCUSSION

Fessell (1961) reviewed the reports of altered serum protein levels in the functional psychoses—that is, non-organic—listing 128 references to relevant work; further studies have subsequently been reported. No protein alteration of diagnostic or prognostic value was found; this may be due to the varying criteria employed in selection of patients, and to differing analytical methods. Alterations in plasma protein concentration may be expected in the presence of undetected liver, kidney, circulatory, neoplastic, or inflammatory disease, and as a result of hormonal drug treatment or a deficit in endogenous hormone production. The influence of race, exercise, and diet is uncertain. Thus it is difficult to compare one previous study with another, or with this one.

The protein alterations reported by previous workers and surveyed by Fessell (1961) and by Seal and Eist (1966) include: (1) increased levels of haptoglobin, orosomucoid, C-reactive protein, rheumatoid factor, combined α_1 and α_2 globulins, β globulin, and caeruloplasmin; (2) decreased albumin and transferrin; (3) unaltered caeruloplasmin and α and β lipoproteins.

Some previous findings have been confirmed by our study. The levels of caeruloplasmin detected were reviewed by Fessell (1961) and by Sandor (1966); both pointed out that initial findings of a raised caeruloplasmin level in schizophrenia (Abood, Gibbs, and Gibbs, 1957; and Scheinberg, Morel, Harris, and Berger, 1957; Martens, Vallbo, and Melander, 1959; and Saunders and Chipkiewicz, 1959) have not been confirmed more recently. We report normal caeruloplasmin levels in schizophrenic patients. Among females, especially those taking oestrogens, caeruloplasmin levels are higher than in males. The only two females among our nine epi-

leptic subjects had markedly raised caeruloplasmin levels (250% and 172% reference serum): they were not pregnant, not taking a contraceptive pill, and the changes characteristic of the 'acute phase reaction' were not present.

Abood, Gibbs, and Gibbs (1957) claimed that caeruloplasmin levels were raised within minutes as a response to disturbed behaviour, and among their epileptic patients an abnormally high mean level was detected. Vuyze and Visser (1966) also detected a raised caeruloplasmin level in serum pooled from 10 epileptic patients, while the serum from 10 schizophrenics contained normal amounts. The mean level in our nine epileptic patients was higher than that found either among our normal subjects (though not significant, $P = > 0.05$) or among the schizophrenic patients studied ($P = > 0.05$). We have no evidence that recent epileptic attacks, degree of hydration, dietary or hormonal influences, liver disease, or current emotional crises had any influence in either of our groups.

Unlike Strisower, DeLalla, Gofman, and Strisower (1957) we found lower levels of β lipoprotein ($P = > 0.05$) in both the schizophrenics and the epileptics than in the normal subjects. We regard this as an artefact, probably due to storage of serum. Seal and Eist (1966) detected raised haptoglobin levels among 60 male schizophrenics, which they suggest might represent a long-term concomitant of the disease. We were not able to confirm these findings.

The raised α_1 PGp in schizophrenics ($P = < 0.05$) compared with the normal series, is difficult to explain. α_1 AT values were also higher ($P = < 0.05$) among the schizophrenics than among the normal series. While the raised haemopexin values ($P = < 0.001$) in schizophrenia might be evidence of tissue destruction, haptoglobin values were normal and no

clinical evidence would support such a hypothesis. The schizophrenics' raised haemopexin level was significantly above that of the epileptics, which in turn were similarly, but less markedly, raised above normal. Why a heme-binding protein should be elevated is not clear.

In conclusion, there were raised mean values for α_1 PGp and α_1 AT ($P = < 0.05$) and haemopexin ($P = < 0.001$) among our 19 schizophrenics, but the control group of epileptics had normal mean values apart from a high α GC ($P = < 0.01$). We regard these abnormalities as valid, although unexplained, characteristics of our chronic paranoid schizophrenic population.

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