Brit. J. Psychiat. (1976), **129**, 191–2

Correspondence

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SERUM CREATINE KINASE IN ACUTE PSYCHOSIS

DEAR SIR,

In recent years there have been many published reports of increased levels of serum CPK during acute psychotic episodes. The interpretation of these findings is controversial. Meltzer (1976) thinks that the increased serum CPK values are caused by some as yet undefined processes which are also causative for the acute episode. Other authors (Cunningham *et al*, 1975; Harding, 1975) think that the rise in CPK values is due to factors which are not directly connected with the acute psychotic episode, and that therefore the serum CPK levels are of value neither diagnostically nor predictively. Soni (1976) very recently proposed that the increase in serum CPK in psychotic states is related to the increased psychomotor activity, but points out that the relationship is not a simple one and depends on the amount of muscular effort the subject is accustomed to make.

We have approached this problem from the observation of Meltzer that in the first-degree relatives of patients with acute psychotic disease one finds small but persisting elevations in serum CPK levels (75–140 IU/litre). Even though it is difficult to connect this finding with the return to normal levels in the psychotics after a few weeks and with the increased levels seen in chronic patients, the study of relatives rather than of patients offers the advantage of providing a correction factor for the non-psychiatric factors. It must also be remembered that there are genetic factors in psychosis. We have therefore measured the serum CPK levels, under standard conditions, in bloods taken over a period of two months from six patients with primary affective disorders—during a normothymic period—and in at least two of their first-degree healthy relatives. Our data do not agree quantitatively with those of Meltzer, since our values ranged between 20 and 85 IU/litre. Qualitatively they do agree with his findings in four of our six families, in which both relatives had values higher than their respective ill relatives. Of the two remaining families, in the first, one relative had a higher CPK level and one a lower level than the ill member, and in the second, both had lower levels than the ill member.

Obviously, these data indicate that further studies must be carried out with more sophisticated experimental designs taking into account the differing homogeneous diagnostic clusters among the acute psychotic subjects, at least differentiating between PAD subjects and those with the various types of schizophrenia. Undoubtedly it will be of value to study the first-degree relatives along with the subjects, but attention must also be paid to any non-psychiatric differences that may interfere with the interpretation of the results.

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MONOSYMPTOMATIC HYPOCHONDRIASIS

DEAR SIR,

Bebbington (1) has described the heterogeneous nature of conditions subsumed under this heading, and has stated the generally accepted view that such disorders have a uniformly poor prognosis. We believe that one important sub-group may be amenable to successful treatment. Riding and Munro (2) and Reilly (3) have found that mono-

delusional conditions with a hypochondriacal content may respond, often dramatically, to treatment with the diphenylbutylpiperidine agent pimozide in a dosage of 2–8 mgm daily, where a variety of treatment regimes has previously failed. It appears that this group is identified by the absence of a primary depressive illness, and that the delusional content is probably related to a paranoid-type process of a schizophrenic nature. We agree with Riding and Munro that dysmorphophobic (neurotic) conditions do not respond to this approach. Dermatological hypochondriasis, as described by Zaidens (4), is specifically mentioned by Bebbington and included in his poor-prognosis group. This is not an uncommon disorder, and where such conditions may be classified as non-dysthymic delusional parasitosis. Reilly, Jopling and Beard (5) and Riding and Munro (2) have demonstrated that remarkable improvement may be forthcoming following treatment with pimozide.

It is difficult to decide whether either of Bebbington's cases could be considered as properly delusional, though Case 2 sounds probable. We have noted that the personality in this case exhibited obsessional traits, and it is our impression that such traits are commonly present in patients who respond favourably to pimozide.

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CONTROLLED TRIALS OF IMIPRAMINE

DEAR SIR,

Drs Rogers and Clay (*Journal*, Dec. 1975, **127**, p 599) reviewed 30 studies comparing imipramine to placebo and noted that the great majority of them show imipramine to be significantly superior to placebo. Kerry and Orme (*Journal*, March 1976, **128**, p 310) have questioned this interpretation and say that it would be unfortunate if the results of this particular statistical review were accepted uncritically as evidence that imipramine is therapeutically effective. Rogers and Clay made no effort to test statistically the hypothesis that imipramine is more effective than placebo from the combined evidence of all 30 studies. Cochran (1954) provides a method for combining statistics from a number of independent trials so as to come out with an overall statement that the probability observed in the combined trials differs from that which would be expected by chance alone. Using the data provided by Rogers and Clay, the probability that the differences between imipramine and placebo could be observed by chance alone is less than 10^{-31}. This would seem to be sufficient evidence that tricyclics are really superior to placebo in treating depression, although, it is obvious to anyone in the field that much more needs to be learned about the clinical use of tricyclics.

Kerry and Orme assert that Rogers and Clay analysed only a small proportion of the published trials on antidepressants and that there are many trials in which a placebo has achieved a better result than an antidepressant, but that these trials were not included. We have reviewed the same studies on imipramine and our tally checks almost exactly with that of Rogers and Clay (Davis, 1970; Davis *et al*, 1969). In our analysis we did not uncover the 'many trials in which placebo has achieved a better result than an antidepressant' which Kerry and Orme claim were not included in the analysis of Rogers and Clay. In fact, we did not find that among studies which followed strict research design there were *any* that reported placebo significantly more effective than tricyclic antidepressants. There are, of course, many open trials of imipramine which report imipramine to be effective, and there are both open and placebo-controlled random assignment trials with other tricyclic antidepressants which also show that these tricyclics are effective agents in the treatment of depression. Both these sources of evidence would further support the efficacy of tricyclics.

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