effective treatments are applied. There is no paradox in this statement. Coppen and Metcalfe's own data give some demonstration that the M.P.I. has both properties.

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TRIAL OF OXYPERTINE FOR ANXIETY NEUROSIS

DEAR SIR,

In the October issue of this *Journal*, McAllister takes us to task for concluding on the basis of intercorrelations of approximately 0·20 or less between scores on Cattell's I.P.A.T. Anxiety Scale and independent clinical ratings of anxiety that "The I.P.A.T. Anxiety Scale does not appear to be a valid technique for the assessment of anxiety states". He does so on the grounds that the I.P.A.T. Anxiety Scale is mainly a measure of anxiety as a personality trait and that it may be valid for this purpose without necessarily having any significant correlation with ratings of anxiety as a state. We wish to make four points in reply.

First, we doubt whether it was improper of us to assess the validity of the scale by comparing test scores and clinical ratings of anxiety. Indeed, this procedure is explicitly recognized by Cattell, who on p. 9 of the *Manual* describes the intercorrelation between test scores and psychiatric assessments of anxiety as being one of the three "most conclusive ways possible" of determining the scale's external validity. It would thus appear that McAllister's views are at variance with those of the author of the scale.

Secondly, while agreeing that in general it is quite legitimate to draw a conceptual distinction between measures of personality traits and of clinical states, we doubt whether such a distinction can be applied unambiguously in the present case. In particular, it is difficult to reconcile McAllister's views with Cattell's description of the "overt symptomatic" score which is distinguished precisely to provide "*a record of actual symptoms*" (p. 6, our italics).

Thirdly, even if McAllister were right to draw this distinction with respect to the I.P.A.T. Anxiety Scale, this has no relevance to our conclusion, since at no time did we question the scale's validity as a *personality* measure.

Fourthly, we question McAllister's interpretation of the scale's purpose, which he maintains is to measure predisposition to anxiety. We, on the basis of the evidence cited in our article, suggest that the scale measures neuroticism. Since our study was not specifically designed to adjudicate between these rival interpretations, we do not wish to be dogmatic on this point. We may note, however, that our interpretation is consistent with the findings of Bendig (1960), who on the basis of an extensive factor-analytic study of anxiety and neuroticism inventories (which included the Cattell Scale) suggested that "Anxiety and Neuroticism are both manifestations of a more general emotionality factor and are not separate dimensions within commonly used inventories . . ." (p. 167).

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PHENOTHIAZINE TREATMENT IN SCHIZOPHRENIA

DEAR SIR,

To test the hypothesis that phenothiazine treatment in schizophrenia loses much of its effectiveness if its initiation is delayed, we recently studied the records of 109 schizophrenic patients.

All these patients had a well-confirmed diagnosis of schizophrenia (made independently by at least two psychiatrists), were less than 45 years old, had graduated high school, and had been in-patients in this hospital at some time more than three years prior to the study.

Our basic assumptions were that all these patients must have begun their schizophrenic illness at around the same age, and that those who had first received phenothiazines at early ages would, therefore, tend to have received them at an earlier stage in their illness than those who first received them at later ages.

As an index of how well or badly the patients did, we used the percentage of lifetime after the first psychiatric consultation spent in mental hospitals.

A Pearson correlation coefficient was calculated between the ages at which phenothiazines were first given, and the following index:

total time in mental hospitals × 100
(age on 30 January, 1965) minus (age at first psychiatric consultation)

This correlation coefficient came to −0·11.

We concluded from this that the patients who first received phenothiazines at early ages did not do significantly better or worse than those who first received them at later ages.

Since our basic assumptions may have been incorrect, we cannot regard these negative findings as disproving the hypothesis stated.

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GENETIC POLYMORPHISM IN METABOLISM OF PHENELZINE

DEAR SIR,

A current problem in clinical psychiatry is to account for the variability in the response of patients to individual antidepressant drugs. One factor which has so far not received much attention is the possibility of individual or group variations in the rate of metabolism of the drug within the body. We should therefore be grateful for the hospitality of your columns to bring briefly to the attention of your readers our recently published observations on the influence of a genetic enzyme polymorphism on the treatment of depression with phenelzine (Nardil) (1).

Our hypothesis derives from the observation that the anti-tuberculous drug, isoniazid, is metabolized at two different rates, so that human beings are clearly divisible into either slow or rapid inactivators, slow inactivation being a Mendelian recessive factor. This polymorphism depends on the activity of liver acetyl transferase and is also shown by sulphamethazine and hydrallazine. As phenelzine possesses a mono-substituted hydrazine chain similar to isoniazid (Fig. 1) we suggest that it may be subject to the same acetylator polymorphism. Technical considerations made direct testing of this hypothesis impossible, but instead observations were made on depressed patients receiving phenelzine therapy who were previously phenotyped as slow or rapid acetylators using isoniazid.

Forty-seven previously untreated out-patients with a diagnosis of neurotic (24) or endogenous (23) depression were rated on the Hamilton and Hildreth scales before and after 4 weeks' treatment with

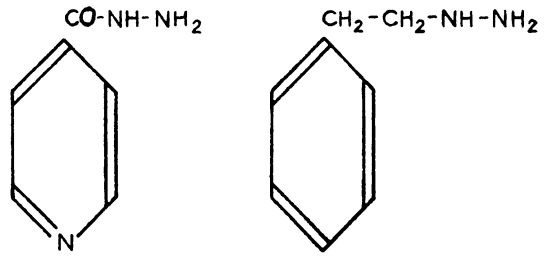

FIG. 1.—The structural formulae of isoniazid and phenelzine.

phenelzine 15 mg. t.i.d. In addition, the day on which subjective improvement was first noticed and the occurrence of side-effects, rated as mild or severe, were noted. The phenotyping procedure was carried out before the commencement of treatment, but the results were concealed from the clinicians until the end of the experiment. There were 30 slow (15 neurotic, 15 endogenous) and 17 rapid (9 neurotic, 8 endogenous) acetylators.

The only statistically significant finding was the occurrence of "severe" side effects in nine patients, all of whom were slow acetylators ($p < 0.05$). Other trends which did not reach the 5 per cent. level of statistical significance were a tendency for slow acetylators to respond to phenelzine better, and, for endogenous depression, more quickly, than rapid acetylators.

The results observed, although not conclusive, are in keeping with the hypothesis that phenelzine is subject to polymorphic acetylation in human populations and this has therapeutic relevance.

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