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Correspondence

GLUCOSE TOLERANCE IN DEPRESSION

DEAR SIR,

Herzberg, Coppen and Marks have recently declared that the glucose tolerance in depressive patients does not deviate from the norm (*Journal*, May, 1968, p. 627). However, to my mind it would be premature to conclude from this that carbohydrate metabolism is unimpaired in depression. Van Praag and Leijnse (1, 2) made a longitudinal examination in depressive patients for the arterio-venous difference in glucose ($\triangle$ glucose) and non-esterified fatty acids ($\triangle$ NEFA) concentration: criteria of the extrahepatic uptake of glucose and NEFA respectively. It appeared that within a group of patients suffering from endogenous depression there is a subcategory with abnormally low $\triangle$ glucose values. Besides this, they found indications that the subnormal extrahepatic uptake of glucose is attended by an increased consumption of NEFA. It is not possible as yet to distinguish clinically between endogenous depressive patients with and without disordered energy metabolism.

The group of the endogenous depressions is fairly homogeneous as far as the psychic symptoms are concerned. Similarity in symptomatology does not, however, mean similarity in origin. Pathophysiological mechanisms of a different nature can draw forth the same clinical syndrome: of this somatic medicine supplies several examples. At any rate the above-mentioned observations make it probable that, in the field of depression, distinctions of a metabolic nature are possible that do not concur with the usual psychopathological distinctions. Averages can be deceptive in biological psychiatry.

It seems to me that this view is also, and indeed particularly, significant for clinical psychopharmacology (3, 4).

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DEAR SIR,

I was interested to read the paper by Drs. Herzberg, Coppen and Marks (*Journal*, May, 1968, pp. 627–630). After investigating 14 patients, only eight of whom were given intravenous glucose-tolerance tests, they conclude that "carbohydrate metabolism . . . is unimpaired in depression if the effects of previous undernutrition and inactivity are adequately controlled". They also state that: "No abnormality in glucose tolerance attributable to depression was observed. . . ."

I feel that these conclusions are an over-simplification of a complex problem and are not supported by the authors' data. Firstly, in my experience, the effects of undernutrition cannot be reversed as easily as the authors suggest. Reviewing data from three investigations of glucose utilization in depressions (Pryce, 1960) I found 11 cases (out of a total of 43) with an initial glucose utilization rate (K) of less than 1·30 per cent. per minute and an increase in K of 0·25 per cent. per minute or more on re-testing. This group had a low mean initial body-weight (53·4 kg.), a significant mean gain in weight (3·1 kg.) after treatment, and included the only episodes of illness (5 in 4 subjects) in which feeding difficulties were encountered before (initial) tests, which suggested that previous carbohydrate deficiency might have been responsible for the observed changes in glucose utilization. However, this association of marked weight-gain with a marked increase in K was observed not only in the five instances with feeding difficulties, but also in four others in whom an adequate hospital diet supplemented with 150 g. glucose daily was taken for four days before testing. Moreover, in four instances the increase in K was due not to expected low initial values but to abnormally high re-test values, suggesting that a phase of

increased glucose utilization (lasting up to three months) occurred during re-feeding. If this interpretation is correct, the effect of carbohydrate deficiency on glucose-tolerance depends not only on the severity of the deficiency and the measures taken to correct it, but also on the phase of the under-feeding–re-feeding cycle at which a test is carried out. This explanation would account for the remarkable doubling in the value of K on re-testing in Case 8 in Herzberg *et al.*'s paper. In this subject a weight-gain of 5·3 kg. is recorded, whereas the weight-changes in the other 7 subjects are under 1 kg.

Two other observations in their paper are worthy of comment. The first is the large range in the values of K in their eight subjects. As normals they quote ten subjects (aged 16–65) from a paper by Marks and Marrack (1962) who gave a mean K of 1·72, range 1·15–2·32 (S.D. 0·41). The subjects with depression (aged 26–76) gave a mean of 2·4, range 1·0–4·5 (S.D. 1·27), and seven of the sixteen values of K were well above the upper limit found in the normal group. The authors, however, seem to regard these as normal findings.

The second observation, ignored by the authors, is the large difference in K on re-testing in three of their subjects, although Marks and Marrack (1962), whom they quote, commend the use of K in studies of glucose tolerance precisely because "it is reproducible in an individual subject". I have suggested that the high values of K on re-testing in Case 8 may be of nutritional origin. The large differences in the two other cases (11 and 12), however, are difficult to explain. In my data differences of this order seemed invariably to be associated with dietary factors; but smaller differences (up to 0·3 per cent. per minute) were associated with another phenomenon, seldom mentioned in glucose tolerance studies. This is the large scatter of blood-glucose values around an ideal regression line which is sometimes found in intravenous glucose tolerance curves. In my subjects with depression this was greater than could be accounted for by experimental error in 40 per cent. of curves (and compared with smoother curves was associated with a significantly greater decrease in K). Herzberg *et al.* presumably obtained the value of K by fitting the best curve by eye through five values of blood-glucose on semi-logarithmic paper. This procedure can give varying results if there is much scatter of individual blood-glucose values, and may possibly account for some of the inconstancy in their values of K on re-testing.

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A CLINICAL INVESTIGATION OF PHOBIAS

Dear Sir,

I enjoyed reading the article by R. P. Snaith (*Journal*, June, 1968, p. 673), and should like to make the following two comments:

1. In my experience agoraphobia often has its origins in an episode of hyperventilation:

   " 'Typically, these patients noted the sudden onset of subjectively inexplicable panic attacks, accompanied by hot and cold flushes, rapid breathing, palpitations, weakness, unsteadiness and a feeling of impending death' " (p. 674).

   " . . . True vertigo was rare but a feeling of unsteadiness of the legs, an illusion of walking on shifting ground, or a lightness of the head was the usual pattern" (p. 675).

2. Four patients with symptoms of agoraphobia were given diphosphopyridine nucleotide (1 g. in 1,000 c.c. 5 per cent. dextrose by intravenous infusion). In three there was a lessening of anxiety and phobic symptoms; in two this change was marked.

   Two of these four patients are brothers. Both brothers were given 1,000 c.c. 5 per cent. dextrose by intravenous infusion, subsequent to the drip containing the D.P.N. One brother, who showed only slight improvement after his gramme of D.P.N., felt no change after the 5 per cent. dextrose infusion, nor after a subsequent 1 gramme of D.P.N.

   The other brother responded markedly to 1 gramme of D.P.N., equally dramatically to 1,000 c.c. of 5 per cent. dextrose in water some months later, but with only a slight change for the better to the second dextrose in water infusion. He responded more favourably again to a subsequent gramme of D.P.N.

B-blocking agents reduce to some extent the somatic symptoms of anxiety (1, 2), and often to a marked degree those, e.g. tachycardia and palpitations, related to respiratory alkalosis.

Perhaps there is "a neuro-physiological basis" (p. 676) for anxiety and phobic symptoms!

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