Brit. J. Psychiat. (1970), 117, 235–240

Correspondence

PSYCHOTHERAPY WITH FAILURES OF PSYCHOANALYSIS

DEAR SIR,

I wonder if it would contribute some perspective to the joustings of Melitta Schmideberg and Hilda Abraham (*Journal*, May 1970, p. 574) if, writing after 48 years on the sidelines, I confess that I am in hearty agreement with both parties to the controversy over the decaying standards (theoretical as well as therapeutic) of medical psychology and on possible measures whereby the therapeutic 'failures' consequent on this decay might be salvaged.

I am the more encouraged to make this confession since it is clear from the previous correspondence on these subjects that on most points of material difference Drs. Schmideberg and Abraham are in complete accord.

What delightful weather we are having these unexpected dog-days!

EDWARD GLOVER.

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TRYPTOPHAN PYRROLASE AND DEPRESSIVE ILLNESS

DEAR SIR,

I cannot let Dr. Curzon's reply (4) pass without drawing attention to some omissions which must lead to erroneous conclusions. Let me preface this by saying that we are substantially in agreement on points 2 and 3, and the main issue which divides us is the roles ascribed to tryptamine and 5HT. Dr. Curzon says in effect that because special means are required to detect tryptamine both its normal presence in brain and its physiological role are dubious. My own position is that as the mechanisms for its formation are clearly available its formation in brain is probable, although difficult to detect by current techniques. Dr. Curzon's argument presupposes that current measuring devices are adequate to detect the amounts of tryptamine capable of producing responses, but I do not think anyone has such knowledge at present. Further, he asserts a biological negative, and I have yet to meet an exception to the rule that this is impossible to prove. However, the issue will ultimately be resolved empirically and can be left there. On the other hand it is possible to be much more definite about the ancillary evidence and to rectify some omissions in Dr. Curzon's citations. On methysergide in mania, the dosage used in the controlled trial (2) was too low, as intimated (11), five months before publication of the trial as well as subsequently (12). Further, it is not true to say that the effects of methysergide could equally well be due to anti-serotonin activity. Animal experiments have shown that *in the brain* methysergide blocks the actions of amines such as tryptamine, phenylethylamine, amphetamine (in short the ones I have labelled Type A), but has no effect at all on the predominant depressant action of 5HT (6, 7). I do not deny that methysergide is a potent anti-serotonin agent in peripheral tissues, but to translate these findings to cerebral activity is a hazardous process and in the present case empirally unjustified.

Turning next to the patient with carcinoid tumour, Dr. Curzon says again that effects could be mediated by serotonin (as 5-hydroxytryptophan was raised) or to mental factors. Crawford *et al.* (3) published details on two patients with carcinoid tumours, and (like Dr. Curzon) I am grateful to Dr. George Ashcroft who gave me the clinical details. Patient 1 was definitely hypomanic; patient 2 was definitely depressed; in both patients the clinical notes said that it was impossible at the time to decide between biochemical disturbances and the stress of a severe illness as causative of the mental state. I think in the light of further knowledge a decision is now possible. In both cases the illness producing the stress was similar. In both cases elevated levels of 5-hydroxyindoles were found in the blood. But patient 1 was excreting a thousand times the normal quantity of tryptamine (84 mgm. per day in one twenty-four hour specimen!) and also had tryptamine in the blood, whereas patient 2 showed tryptamine excretion in the normal range (about 100 micrograms daily). I cannot share Dr. Curzon's conclusion that the hypomania could equally well have been due to 5-hydroxytryptamine or to mental factors. My view is supported by a previous study of carcinoid tumours which produced large amounts of 5HTP and in whom no mental illness attributable to 5HT was found (5). It is conceivable that a mild episode of depression may have been missed in this series, but I am confident that episodes of mania or hypomania would not have escaped notice. None of the patients showed such an illness at any time.

I should also point out that Dr. Curzon's apparent

quotation 'hypomanic patient (secreting) large amounts of tryp*tophan*' implies a verbatim report of my remarks. In fact the nearest it comes to anything I said is the reference to the case which 'secreted large amounts of tryp*tamine*, . . .' The distinction here between tryptamine and tryptophan is not without importance, for tryptophan is the precursor both of tryptamine and 5HT (via 5-hydroxytryptophan), whereas tryptamine is *not* converted to 5-hydroxyindoles (14) and consequently effects cannot be explained as due to 5HT.

The studies on cerebrospinal fluid 5HIAA (1) showed that eight depressives had a mean level of 34 ng/ml CSF and did not differ statistically from an age-matched control group. The mean figure for eight untreated manics was 32 ng/ml and again this did not differ from an age-matched control group. After treatment with amitriptyline the mean 5HIAA in the depressives dropped to 21·3 ng/ml (a change significant at the 0·02 level), whereas the mean for the manics after lithium was 30·7, which is not statistically significant. The correlations quoted by Dr. Curzon also do not reach the 5 per cent level of significance, and as only four manic patients were given the MMPI it is unwise to ignore the statistical test. This is further supported by the fact that all manic patients were given the Brief Psychiatric Rating Scale and in this larger sample no significant correlation was observed with 5HIAA.

Although only some of the evidence has been touched on, it will be apparent how selective one must be to sustain the role for 5HT which Dr. Curzon supports. I do not doubt that 5HT and catecholamines may play a part in the depressive syndrome (perhaps related to sleep or appetite), but the occurrence of disturbed sleep and appetite in the depressive syndrome does not thereby equate them with the symptom of depressed *mood*. There is a logical chain of evidence identifying the normal mechanisms of tryptamine action, its relation to elevation of mood and its relevance in affective illness; physiology has been used as a basis for investigation of pathology (8, 9). No comparable links exist, as far as I know, for 5HT and catecholamines, and their putative role in mood was derived from observations in affective illness. Further, the objections made to the catecholamine and serotonin hypotheses of affective illness (9, 13) have not yet received satisfactory answers. Conversely, the points raised by Dr. Curzon (who supports the role of 5HT in affective illness) and those made by Weil-Malherbe (15) (who is an advocate of the catecholamine hypothesis) have both received answers (10). Time, one trusts, will make us all wiser, but meanwhile it is hoped that the relatively simple chemistry involved will not deter more of your readers from appraising matters for themselves.

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Dear Sir,

I regret that there was an error in my letter to the *Journal*, May 1970, page 572. The second paragraph should read '. . . the hypomanic patient (secreting)