feel justified in relating brain 5-HT levels to the pathophysiology of depression, as they do.

I am also intrigued by their decision to examine the brain stem rather than the forebrain. Vascular stripping of the forebrain does take some little time, but the rate of disappearance of 5-HT from a pre-cooled brain in the 3 or 4 minutes needed would not be significant.

While Dr. Shaw and his colleagues are cautious (with good reason) in the discussion of their results, I am unable to accept their implication that a dubious "finding" in the hindbrain tissue may be causally related to limbic lobe function and affective disorder.

B. J. Carroll.

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Dear Sir,

The most suitable statistical test for our data was Student's t test, which showed that the difference between control and depressed groups was significant at the 5% level. The χ^2 test is certainly not appropriate in this situation. It is relatively insensitive and is wasting some of the available information.

There was little or no point in comparing the results in the depressed subjects with those of the alcoholic or schizophrenic individuals. The numbers in the subgroups were small and any comparisons would have been open to the criticism that any differences could have been due to alcohol or to long-term treatment with phenothiazines. No attempt was made to pool these data for the same reason, and we were also aware of the possibility that severe depressive illness could have been a secondary diagnosis in a proportion of the subjects suffering from alcoholism or schizophrenia. With these unknown variables in mind, the findings in the subgroup of Table II in the paper were published without comment.

The decision to use the brain stem was based on practical considerations. It is much easier to obtain a reproduceable piece of tissue by taking the brain stem than to dissect out the hypothalamus, and our technique was not sensitive enough to measure 5-HT in homogenate of whole brain.

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Francis E. Camps.
Eric Eccleston.

MRC Neuropsychiatric Research Unit,
Greenbank,
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THE LOGICAL REQUIREMENTS OF RESEARCH INTO SCHIZOPHRENIA

Dear Sir,

I am writing this letter in response to the stimulating article by D. Bannister (*Brit. J. Psychiat.*, **114** : *118*, 1968), in which he discusses, among other matters, new strategies for achieving a breakthrough in the study of schizophrenia and suggests that the field has thus far failed to advance. I feel that it may be of value to present a somewhat different point of view about the present status of schizophrenia research, since, in my estimation, research in this area is anything but static. In fact, I think that a remarkable number of fundamental discoveries have given great forward momentum to the field and that it should be necessary to detail only a few advances to demonstrate this point.

It may have been the re-introduction of the drug reserpine as an anti-psychotic agent that initiated this revolution in psychiatry. In any event, this was one of the first in a series of developments which have resulted in tremendous advances in our basic understanding of the biological substratum of mental processes. Among these accomplishments has been the elucidation of the metabolic pathways of enzymes involved in the metabolism of catecholamine neurohormones, resulting from studies carried out by Blashko, Armstrong, Axelrod, Von Euler and a large number of other investigators. Extremely important basic studies of tryptamine and serotonin metabolism have also been carried out by Page, Wooley, Udenfriend, Himwich and many others. A new science of psychopharmacology has been developed which has produced so many important works as to make it impossible to decide which are the most important. Among these must surely be included the dramatic improvement in the treatment of psychotic patients resulting from the use of new drugs. The clinical effects of hallucinogens have been very closely studied, and through the work of many investigators, including Daly, Shulgin, Zeller and Charalampous, to name a few, it is possible to design certain hallucinogenic molecules with some assurance about their potency and duration of action.

One of the most dramatic observations has been the finding that all effective anti-psychotic agents have the potential for producing parkinsonian symptoms. The elaboration of a possible metabolic disturbance in dopamine metabolism in parkinsonism by Hornykiewicz and Barbeau has also illuminated a possible mechanism of action of the anti-psychotic agents themselves. In another area, a great advance in epidemiological and genetic studies in mental illness has been generated by Kallmann, Slater, Gottesman