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.

Medical Research Fellow.
University of Melbourne Department of Psychiatry,
Clinical Sciences Block,
Royal Melbourne Hospital,
Parkville, N.2, Victoria, Australia

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.

David M. Shaw.
Francis E. Camps.
Eric Eccleston.

MRC Neuropsychiatric Research Unit,
Greenbank,
West Park Hospital, Epsom, Surrey.

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

and many others. Also the great strides in behavioural evaluation resulting from the work of Lorr, Wittenborn, Glueck, and Burdock cannot be overlooked. The model for a good number of basic studies, carried out in many laboratories, was set by the interdisciplinary laboratory at N.I.H. formerly headed by Seymour Kety. In this laboratory the application of basic science techniques to the study of brain behaviour relationships has reached a high level.

Perhaps more important than any single discovery has been a shift away from the breakthrough approach in the study of mental illness with the increasing maturity of the field of biological psychiatry. Frontal assaults on crucial disorders, such as schizophrenia, have been replaced by systematic and orderly basic studies of underlying biological systems. Unfortunately, the potential significance of these advances has not been widely discussed in the psychiatric press. This fault can, in large measure, be traced to the investigators themselves, some of whom do not work directly in the mental health areas. It seems to me unreasonable to expect a breakthrough from the spontaneous generation of brilliant light which will in one flash clarify the nature, the pathogenesis and the treatment of mental ills. No doubt an ultimate synthesis of many findings from various investigations will someday be made, but not until all of the essential groundwork has been completed.

ARNOLD J. FRIEDHOFF.

Department of Psychiatry and Neurology,
School of Medicine,
New York University, Medical Center,
550 First Avenue,
New York, N.Y. 10016, U.S.A.

THE LOGICAL REQUIREMENTS FOR WRITING A PAPER ON THE LOGICAL REQUIREMENTS OF RESEARCH INTO SCHIZOPHRENIA

DEAR SIR,

As one of the researchers felled by Bannister (*Journal*, February 1968, pp. 181-188), I wish to defend myself slightly and make some additional general comments. He used my report (Rubin, 1965) as an illustration of the failure to link conceptual and operational definitions ("... it is quite certain that the vast majority of studies in the biochemistry of schizophrenia do not attempt to explicate such relationships between the alleged causal agent and the omnibus abstraction of schizophrenia"). First, I did not study "schizophrenia", but acutely ill patients who were floridly psychotic on admission to the hospital, and all but one of whom manifested hallucinations, delusions, or extreme hyper-activity. Most were diagnosed as various subtypes of schizophrenic reaction, but the presence of acute psychosis, not the diagnosis of schizophrenia, was the criterion for inclusion in the study. Second, the linking of conceptual to operational definitions had been done primarily by other workers cited in the introduction of my report. Had Bannister familiarized himself with some this work published in other journals, he might have chosen to indict me for other (and perhaps more serious) methodologic crimes.

The most outstanding methodologic flaw in Bannister's paper is his restricting his literature survey to papers on schizophrenia published in the *British Journal of Psychiatry* since the beginning of 1964. Each paper cited is categorized as an example of failure to fulfil at least one of his five tenets for a valid research effort. Whether use was made of all papers appearing in the *Journal* in this time period or only of selected examples, and if the latter what percentage of the total they constitute, is not specified. At any rate, the conclusion is that "in a near literal sense a great deal of extant research in schizophrenia is half-baked".

In his tenets, Bannister carefully specifies the need for a clear definition of the population studied and inclusion of control groups to delineate population parameters. Since he surveyed no other psychiatric journal, the only logical conclusion he can offer is that a great deal of extant research in schizophrenia *published in the British Journal of Psychiatry* is half-baked. Perhaps Bannister is suggesting that the Editorial Board should use his five tenets as criteria for acceptance of manuscripts.

I would also like to comment on the wishful-thinking nature of his fifth tenet, the need for long-term research. If strictly adhered to, as Bannister suggests, all research into "schizophrenia" would be placed in the hands of the senior "grantsmen" for whom administrating long-term research is a full-time job. Those of us who remain the "littlest astronomers", whether by choice or because we are new to the game, would never be allowed near the telescope, even if only to quickly peek at the far-away stars.

ROBERT T. RUBIN.

Department of the Navy,
Navy Medical Neuropsychiatric Research Unit
San Diego,
California 95152, U.S.A.