April 27, 1965

Dr. John A. Stern
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Dear John:

Thank you very much for sending me a copy of your review, "Physiological Correlates of Mental Disease." I read it with great interest and found it stimulating. I found myself agreeing with many of the conclusions, especially those on pages 249-250 and again on 255. Your criticism that a most serious shortcoming is the problem of psychiatric diagnosis is, of course, correct, and this will confound all the studies of physiological correlates of mental disease. It has been a major problem for me, and in the days when I was at Hillside Hospital, I found the classifications so unreliable, so dependent on the vagaries and individual differences of the staff members, and subject even to political considerations (hospitalized teachers may not leave the institution with a diagnosis of schizophrenia for they would lose their job).

While the points in the article are well made, and the results logical, I think that certain studies have been omitted which would support the positions you have taken very well.

I believe you have underemphasized the role of functional electroencephalography as a classificatory device. The studies of Shagass, Goldman and Itil amply demonstrate that there are some differences in schizophrenic and depressive subjects in the amount of beta activity induced by barbiturates. Each of these authors has tended to use the EEG response merely to confirm the clinical diagnosis. As you suggest in your article, perhaps it is time to turn the tables, and if one would use the barbiturates response as a classificatory device and as a basis for the selection of treatment, would this not provide more uniform subpopulations? I do not know of any predictive study to date, and suspect that no one (including myself) has been brave enough to undertake such a predictive study. Perhaps, also, there is some doubt that we have a specific treatment for a subgroup of the severe mentally ill so that unless we wish to rely on convulsive therapy for depressive patients, the ultimate test of the theory would depend on a more specific therapy.

A second group of reports that would support your position are those relying on the response of subjects to somatic treatments as the classificatory device. In the electroshock studies by Kahn and myself, we described six patterns of behavioral response to induced convulsions, and indicated that those subjects who had a hypomanic response tended to be older, to have higher F scores, lower education, and be classified as involutional or psychotic depressive. In contrast, a group who developed paranoid responses tended to be younger, have lower F scores, higher education, and were chiefly schizophrenic of various types. That study was very gross and in subsequent years, when we were analyzing the data of the response of patients to phenothiazines and imipramine, we described similar patterns of response. Both the phenothiazine report and the imipramine report are general statements which can only be suggestive. However, we did find that imipramine induced a psychotic reaction in a small group of patients. When we analyzed their pre-treatment patterns, we found that they were chiefly classified as childhood schizophrenics, with onset about school age, and with a variety of other common characteristics. This has been published by my former associate, Max Pollack, in the latest volume of Biological Psychiatry. Similarly, my other former associate, Donald Klein, has written a report on a subgroup of phobic patients who had an unusually good response to imipramine. He has since gone on to use this treatment as a predictive device and has continued to collect data to show that there is a constellation of symptoms in young adults which is responsive to imipramine, and which then has some other common characteristics. It would be, perhaps, important, to identify these two subgroups, or any others that can be done with other simple means, and then carry out the neurophysiological analyses that you have recommended in your review.

Thank you very much for the opportunity to read your report, and please accept these comments as complementary to the fine job that you have done.

Sincerely,

Max Fink, M.D.
Professor of Psychiatry

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cc: Dr. D. G. McDonald