

May 26, 1969

Dr. Jerome Levine
Psychopharmacology Research Branch
NIMH
5454 Wisconsin Ave.
Chevy Chase, Maryland

Dear Jerry,

Since our discussion of the chlorpromazine blood levels and EEG measures, I have had an opportunity to discuss the proposal shortly with Sam Gershon and at greater length with Dr. Julius Korein. From both, I found the expectation that the blood levels should correlate with the EEG signals. This expectation may be unfounded.

NE:kb There have been many studies of blood levels and some measure of brain function, and in each the correlations are poor. This is usually "explained" by the problem of the 'blood-brain barrier'. In studies of pentothal anesthesia, for example, it is possible to maintain a steady blood level, and yet the EEG shows specific sequences of changes which are correlated with the subject's anesthetic state and not with the blood level (Faulconer, *Anesthesiology*, 13: 361, 1952). In a study of chloridiazepoxide, Whitman and Stern found no correlations between EEG and blood levels. In an unreported study, Dr. Hill and I found the EEG changes not to be linear with the blood levels for patients receiving butaperazine. In only one of our studies, that of cycloserine, was there a relation between blood level and EEG, and this was not linear. The EEG changes of slowing and burst activity appeared only after the cycloserine blood levels had risen above a limiting figure, and below that there were neither EEG nor behavioral changes. It is probable that the EEG relations for lithium will follow this model (cycloserine).

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I would be pleased to participate in another study relating blood levels with behavior and with other quantitative measures, and surely we can provide the EEG measures. I anticipate that the expectations may be unfulfilled for biological reasons (if past experience is sustained), and any relations will have to be teased out most carefully.

It would be most helpful if the EEG measures were provided on a consultation basis, and rather than answer technical questions (as to leads, tapes, etc), a more meaningful contribution could be made only if the design and intent of the study were explained in some detail, and the recording periods determined to maximize the probability of obtaining the requested answers to the implicit or explicit questions posed.

Enclosed is a copy of the one report handy to me. I look forward to seeing you at the ECDEU meetings next week.

Sincerely yours, 13: 301' 1969

Max Fink, M.D.
Professor of Psychiatry

MF:kp

cc: Dr. J. Korein

The blood levels should correlate with the EEG signals. This Dr. Julius Korein. From both I found the expectation that blood level should correlate with EEG measures. I have had an opportunity to discuss the since our discussion of the chlorpromazine blood levels

Dear Jerry

Cheryl Chase
2424 Wisconsin Ave.
NIH
Psychophysiology Research Branch
Dr. Jerome Levine

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