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Dear John:

Thanks for your many comments on our amobarbital - SKF study. You are quite correct, and I will take this opportunity to reply to some of the questions now; and reserve some for the end of our present study.

(1) A literature review of amobarbital effects is no problem, for the EEG data on acute and chronic administration is detailed and quite good (e.g., see my bibliography (1964) and Brazier's (1952)). The zero cross analysis literature is sparse, however, and despite the availability of the technique for 12-13 years, I know of no good analysis of any drug effect by this method.

"Why were the analyses comparing placebo with drug effects so barren...?" We are puzzled also, and in our critique suggest our lack of control of sleep, sampling problems and the small, nonhomogeneous, sample. Of course, our dosages are very low also, and this is the focus of the present study. Despite low dosage, I believe we can demonstrate drug effects. It is no problem to demonstrate the effect of 100 mg amobarbital IV in 4-5 minutes. It is a problem to discriminate the same dose orally.

(2) N = 20, d.f. = 18. Our error.

(3) The shifts in the patterns of the remaining variables in discriminant function analysis is a problem. Apparently, different measures show greater degrees of change with some conditions. This may reflect our small sample and be a statistical artefact; or, it may represent drug effect differences. Further studies must be done to answer this criticism.

(4) Incidentally, the direction of drug changes are indicated in Appendices 2 and 3 by the signs. For example, in Appendix II, baseline cross average at 60' was much higher (increased beta activity) for 300 mg than 50 or 100 mg. (+2.67**, i.e., 4 is greater than 2). Similarly, 50 mg (2) showed a slower baseline cross than placebo (-1.96) but not significantly so.

(5) Your comment about the Drohocki integrator and "frequency analyzer" output is technically correct, but in operation the curves are different. Drohocki uses a wide band-width filter denying thereby that any information resides in shifts in frequency. Our data suggests that frequency is an important aspect of EEG signals, and while power spectral frequency analyzers can be tuned to narrow bands, and thereby show shifts in frequencies - these data are confounded by amplitude changes. The merit - if any - of period analysis is that it reflects frequency information independent of amplitude.

(6) A hope or a prediction - note the word "potentially."

The remainder of your comments are equally cogent, and I will incorporate them in the next draft. I am grateful for your time and consideration in reviewing this progress report. We are replicating the study, correcting as many of the flaws in the first study as we can.

George has mentioned your consideration of another laboratory in Cincinnati. I hope the opportunity will meet your expectations. You must know that I have been puzzled, and somewhat chagrined that the opportunities in this center did not stimulate your interest. Our political problems were great, and perhaps may still be overwhelming - but I am confident that George would be most enthusiastic to have you join Missouri University, if you wish.

Have a pleasant summer, and many thanks for your review of our progress report.

Sincerely yours,

Max Fink, M.D.
Professor of Psychiatry

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P.S. While this report is not ready for publication, I am submitting it as an abstract to Neil for the next SPR meeting. Perhaps the Program Committee would like to include such a report of an application as a follow-up of last year's methodology papers.