F. Letters

December 5, 1972

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Dear Jon:

I read the "Effects of Acute Administration of Papaverine HCL on the EEG and Behavior of the Normal Geriatric" with interest. The findings are consistent with the prevailing hypotheses relating EEG change and behavior.

The discussion focusses on the issues that I would raise: the selection of subjects and the drug dosage. The study should be continued in elderly subjects with EEG evidence of decompensation. The dosage issue is also critical, and a dose finding study would be useful, using progressively higher doses in pairs of subjects until EEG evidence of change is clearly evident or behavioral toxicity limits further trials. (Now that our EEG profiling methods, the recording and analyses, are standardized, the dose finding has become the most difficult part of our studies).

The text leaves a few questions unanswered. The battery of tests is large and must occupy a significant time span. When are the behavioral tests done, in relation to the EEG, and in relation to the drug ingestion? How long an EEG sample is taken?

The hypothesis anticipates a change in mean alpha frequency, not abundance (amount). It is possible for the amount of 8-9 cps to be reduced, and 10-11 cps to increase, and yet, the total alpha not exhibit much change. Indeed, this is not infrequent - we have reported this type of change with cannabis, and others have noted similar effects in cats with psychotropic drugs. It may be appropriate to undertake a "narrow band" analysis, i.e., reanalyze the records filtering first so that activity below 5 cps and above 13 (15) cps is suppressed, and then measure the changes in 1-cycle band widths from 6 to 13 cps.

Finally, since behavioral tasks were unaffected, it is consistent to find the EEG changes minimal. The task remains, to define the central effects of papaverine, and both dosage, time, and subjects may have to be varied to achieve the result, or to state that CNS effects are not significant.

George Gardos has sent us a restatement of the times and dosages of the subjects in the thiothixene study, requesting a reanalysis. We will rerun the analyses as soon as I am able - the equipment is moving this week and it may be some time until we are able to get to this work.

I look forward to seeing you in San Juan.

Sincerely yours,

Max Fink, M.D.
Professor of Psychiatry

MF:lg