

May 9, 1964

Dr. John Farquhar  
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Philadelphia, Pennsylvania

Dear John:

I have just returned from California, and should like to answer your inquiry as to the possibility of using changes in the electroencephalogram as an index of the effects of barbiturates. The history of the measurement of changes in brain function with barbiturates is a long one and it is quite clear that most barbiturates enhance the amount of fast wave activity appearing in the electroencephalogram. The time of the appearance of this activity depends very much on the type of pretreatment record, and the ability to measure these changes depends largely on the techniques of quantification.

The studies by Charles Shagass, Douglas Goldman and Turan Itil have shown that the amount of fast activity can be enhanced if the pre-existing record is one with considerable low voltage fast to begin with. It is also clear that if one wishes to bring out the fast activity following an oral dose of a drug, this can be done by the subsequent administration of a specified amount of pentothal, and under this pentothal activation the appearance of barbiturate spindles can be seen earlier than by the naked eye.

After discussion with Dr. Itil, I believe that we can carry out the measurements to determine the time at which a barbiturate response appears and perhaps, its duration by repeating the measurements at subsequent occasions in other subjects.

With regard to quantification, I believe that both the frequency analyzer methods available at this hospital and the newly developed computer techniques provide us with measurements which are as delicate and as well defined as anywhere in the country. In addition, if the computer techniques are utilized, we are able to carry out certain statistical approaches which have been described by Murphree, who was also interested in determining the time of on-set of pentothal effect.

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As for the details of the study, I believe it would be necessary to obtain the services of volunteers, requesting that they come to the laboratory late in the afternoon. It would be advisable that they come for a number of sittings in which EEG recording would be taken on each occasion. During the first two recordings, they should be given a placebo; on the second or third, a non-barbiturate in an amount to be specified and this to be repeated in a subsequent sitting. I would hope that the examinations would be taken as a minimum one week apart, and that the subjects not be under any other drug effects. The recordings should go on for a minimum of three to four hours to obtain the on-set of the drug effect and in some subjects, for many hours to determine when the record has returned to the base-line level. I believe it would be necessary to undertake at least ten subjects and preferably closer to twenty to complete the project.

The original question, whether there would be differences in effect for amobarbital in 50 mg. doses either in a standard preparation or in delayed action form - after discussing the problem with Dr. Itil, I am not confident that we could pick up 50 mg. and would suggest that if the design is proper, a dose closer to 200 mg. would be more easily measurable. However, we will be pleased to try a 50 mg. dose.

We should like to undertake this study during the summer and can do so, since I will then have the assistance of a number of medical students who can participate in the program.

I trust that this answers your inquiry, and I look forward to undertaking such a study.

Sincerely yours,

Max Fink, M. D.  
Director

MF/jb