October 10th, 1972

Allen Raskin, Ph.D.,
Research Psychologist,
Psychopharmacology Research Branch,
National Institute of Mental Health,
5600 Fishers Lane,
Rockville, Maryland 20852.

Dear Allen,

I have read the application, "Hyper- and Normobaric Oxygen in Senility", with interest. As I understand the proposal, 80 patients will be assigned in 4 cohorts of 20 each to hyper- and normobaric oxygen and air; with four days pre-treatment, 15 days of treatment with 2 sessions a day, and evaluations on day 16 (and ? ?). The principal test instruments are the Wechsler memory scale, Bender Gestalt, and Stockton geriatric scale. These instruments are selected as reflecting, in part, the integrity of the central nervous system.

Since the study attempts to replicate earlier studies in which EEG variable were measured, this measure could be included. As part of our review, we read the report by Talton et al. and noted that they carried out careful EEG analyses without finding changes. Unfortunately, they did not describe the size of sample nor the temporal relation of the EEG measures to other tasks.

In reviewing this proposal with my co-workers, we believe that it should be practical to record EEG samples from these patients; to provide quantitative measures of frequency, amplitude, and variability changes; and to relate these to such measures of behavior, particularly of cognitive performance, as may be available. A suggested protocol, based on our understanding of the project from the documents provided, is appended.

Our suggestions are based on an awareness that recording during the actual sessions would be too costly and controls too difficult to make such recording an inherent part of the study. Rather, we see the EEG measures providing independent indices of changes in brain function, their extent and duration, in parallel to the measures of cognitive performance.

We are suggesting that two EEG records be obtained during the placebo period - one for acclimatization, and one as the baseline analysis.

We are concerned that these patients may be receiving various psychotropic and sedative medications during the course of the study. The record does not specify the manner in which concurrent drugs will be treated. Since the EEG is highly sensitive to psychotropic drugs, either all drugs should be withdrawn (in which case a long wash-out period, greater than 3 weeks, would be necessary) or, care should be taken that the patient's usual medications be continued throughout the study in the same amounts and the same schedule as during the pre-evaluation period.

Because we have found that inter-institutional projects require additional care, we suggest a pilot study for the recording methods, training of personnel in the special requirements of the tests, and feasibility of the various procedures at the times specified.

A useful element would be the visual analysis of the paper records. A limitation of quantitative EEG analysis is an insensitivity to transient events, such as short seizure bursts. A visual analysis of the records, using one of the more elaborate recording systems, may provide these data. While these readings need not be done by the same team doing the quantitative analyses, it may be helpful.

In addition to the protocol, I have submitted a list of the equipment which would be required for such a study, and estimated the costs for the assays involved. If the suggestions meet with your approval, I believe I can assure the participation of some members of the staff at SUNY-Stony Brook and New York Medical College.

We also became interested that the reports suggest changes in vascular flow, and while we have no direct experience with the procedures, we think that rheoencephalography may contribute to the questions posed. The techniques have been under study for many years at Rockland State Hospital by Kenneth Lifshitz.

I am sending a copy of these remarks to Sam Gershon. Should the probability of inclusion in the study be high, we can prepare a more formal review of the literature of EEG

effects of hyperbaric and normobaric oxygen and the methods we employ; modify the protocol to meet the needs of an integrated study; and apply for the necessary institutional approvals.

My best regards.

Sincerely yours,

Max Fink, M.D.

MF/ij
cc. S. Gershon, M.D.