

June 21st, 1973

George Gardos, M.D.,
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Dear George,

I have read your paper "Low Dose Thiothixene in Chronic Schizophrenia" with much interest, and have a few comments about the issues that most interest me.

The references to the EEG effects appear to be incomplete, and are put in a context which does not clarify what the study communicates to me. The record shows that the behavioral changes were small and that the dropout rate was high. There were few differences in clinical effects between the low and high dose thiothixene groups. In particular, this reflects a very high dropout rate. The significant changes were a reduction in uncooperativeness with high dose, and a decrease in depression with low dose.

It is important to note that concurrent with these limited differences in behavior, there were small but defined differences in EEG. Here, too, the level of significance was low, largely because of the small sample. But you could safely report that high dose thiothixene elicited a lower average frequency, reflecting an increase in theta and alpha activity, and a decrease in beta activity (Table 8, EEG report revised 2/12/73).

Should you consider the behavioral data of significance, then I believe you ought to report the EEG data of equal significance, for the high doses did elicit EEG changes of the antipsychotic class, according to my classification (and that of Itil). Low doses did not produce any evidence of stimulation (defined as increased beta, increased variability and decreased amplitude). To the extent that you wish to use these observations, I would conclude that the hypothesis that low doses produce stimulation is not supported.

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For many years I have been seeking to understand the relationship between EEG changes and behavioral changes with psychoactive drugs. These observations with high dose thiothixene showing small changes - increases in theta and alpha activity, which accompanied behavioral improvement in some patients and a reduction in uncooperativeness - is consistent with our general hypothesis of the association of EEG and behavior in man.

Among the questions that we tried to answer was whether the two groups differed in their initial EEG characteristics. When we assessed the EEG characteristics of the subjects at the end of placebo with those at the end of low dose, we found no significant differences, which led us to conclude that the samples were homogeneous at the outset. In your analysis of the behavioral data, I miss this analysis. It is not clear whether covariance was a technique applied to your data, which would answer my question; or whether some other tests for homogeneity prior to treatment were introduced. I mention this because you present the behavioral data (your Table 2) in terms of post scores only, and I believe the reader is entitled to know whether these differences are related to initial position.

Since you sent me the original, I am returning it to you. It is an interesting report and with the small amendments which I suggest, I would encourage its publication.

My best regards.

Sincerely yours,

Max Fink, M.D.
Professor of Psychiatry

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