Cole - EEG

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Jonathan O. Cole, M.D.
Director, McLean Affective Disorders Program
McLean Hospital
115 Mill Street
Belmont MA 02178-9106

Dear Jon,

We seem to have gotten the same bug -- pharmaco-EEG -- at the same time and we seem not to be able to get over it. I, too, believe that pharmaco-EEG methods have not had the applications to which they lend themselves, especially as the initial evaluation of potential new psychoactive compounds, nor in the management of treatment courses, especially of therapy resistant patients. The IPEG sessions in Boca Raton in May were a good sample of our present experience. Unfortunately, except for some work in pharmacokinetics of benzodiazepines by Greenblatt, and of opioids and anesthetics by anesthesiologists, little has been added to our theoretic or functional knowledge since the spate of NIMH/PSC supported studies between 1959 and 1975. These studies developed the main algorithms for data reduction which are still in use today. The main difference between 1990's and the 1970's is in the speed of data reduction, ability to record and analyze multi-lead inputs (compared to our single and 2-channel analyses), and the sharp reduction in costs; so much so that practically any academic laboratory can do superior (to 1970s) recording, data reduction, and data analyses for under $15,000 for 4 to 8 channels.

Unfortunately, the theoretic underpinnings remain the same as at that time. And, many of the applications which we recognized as useful and feasible, [and which are even more feasible today], have never had adequate trials. Further, the present loyalty to the neuroscience reductionist belief structure [which so dominates the ACNP, SBP, NIMH, and many academic psychiatric departments] rejects any human recording studies as too gross. The main exception are the polysomnographers with their activity in medical physiology and the idiosyncratic, essentially impractical, sleep EEG studies of Kupfer.

A few years ago I summarized my experience with pharmaco-EEG in a report which was not published. From time to time I have gone back to it, and I enclose an incomplete draft, dated October 1991. On another occasion, I was asked to review some reports by Herrmann which he submitted to the journal *Pharmacopsychiatry*. I wrote an editorial that accompanied the papers. Finally, I enclose a historical review which was published in 1984 which provides a basis for our present knowledge.

At the IPEG meeting in May, the applications of QEEG for pharmacokinetics was well demonstrated. Its use in pharmacodynamic studies in man was suggested, but there are few new studies such as Peter Irwin and I did two decades ago. The industrial laboratories are apparently funding quantitative pharmaco-EEG studies in various species. The pharmacologists are enthusiastic that they can identify our present list of human psychoactive drugs, but they have few examples of new compounds that have an identifiable pharmaco-EEG profile in an animal species which helped in the clinical study of the compound. [I am not impressed that this expenditure has much merit; rats, mice, dogs, and cats are quite distinct in their pharmacology from man (indeed, mice have been bred to be remarkably sensitive and insensitive to a host of CNS active compounds) and it is pure happenstance when a compound has an EEG effect in an animal that is predictive of its EEG pattern or sensitivity or clinical activity in man.]

As for multi-lead recordings (such as the BEAM), these have not been more helpful than single lead recordings in man. Herrmann and Coppola undertook detailed analyses of multi-lead recordings of compounds which had been classified by classical single channel recordings. Their findings were no more useful than what was already known, at much greater expense. There are some authors who argue that localized EEG changes **should** occur and they hope that such differences will have predictive merit. But, so far, the data are very weak.

With that introduction, I will answer your questions as best as I can.

1. The enclosed papers are a good beginning. Get the issue of *Pharmacopsychiatry* 24 (Nov):196-225, 1991. The three reports by Herrmann show what can be done with pharmaco-EEG studies.

2. The best citations for the relation between EEG changes and clinical response are cited in my report in progress.

3. Few studies fund pharmaco-EEG studies. I was recently contacted by Tetsushi Inada, Ph.D. (Kyowa Hakko Kogyo Co. Ltd., 599 Lexington Avenue, Suite 2780, New York City 10022). They have an antihistaminic compound and are seeking ways to define its central activity. They were impressed by our 1979 report of the EEG study of terfenadine and diphenhydramine (*Pharmakopsych. Neuro-Psychopharmakologie* 12:35-44). I sent them to Kurt Itil and have not had a follow-up.

4. I am always willing to visit McLean. It might be useful to arrange a Grand Rounds on pharmaco-EEG. I recently gave a talk for the neurologists: *Pharmaco-EEG: Science or Pseudo-Science.* Dr. Vasile should visit Itil in Tarrytown and get an idea of which directions he is taking this technique. Turan and Kurt are quite hospitable and seem willing to show off their techniques.