#25

Effects of ECT upon Brain Electrical Activity

Richard D. Weiner, M.D., Ph.D.[1,2]

Helen J. Rogers, Ph.D.[1]

Jonathan R.T. Davidson, M.B., D.P.M.[1,2]

E. Michael Kahn, M.D.[1]

[1] Department of Psychiatry, Duke University Medical Center

[2] Psychiatry Service, Durham VA Medical Center

Introduction

Electroconvulsive therapy (ECT) acts through the elicitation of a series of brief paroxysmal electrophysiologic events involving neurons throughout the brain. The mechanisms by which seizure activity produces both therapeutic and adverse effects are a major focus of this conference. The data presented here, however, will center both upon the characteristics of the seizures themselves, and also upon the interictal neurophysiologic changes which are produced as a result of such seizure activity. It is felt that attention to the electrophysiologic domain, particularly with respect to the effects of variations in ECT technique, may provide useful information not only clinically, but in the understanding of mechanisms as well.

Methods

The data to be presented are part of a larger study, for which some preliminary results have already been reported.[1-3] Other findings relating to cognitive effects will be presented later in this symposium.[4] With respect to electrophysiologic variables, data was collected from a total of 74 subjects before, during, and after a course of ECT to which they were referred for clinical indications, independent of the research protocol. A reference group consisted of 21 depressed psychiatric inpatients not referred for ECT.

Experimental subjects were randomly assigned to receive their ECT treatments using either bilateral or right unilateral electrode placement, and either brief pulse or sine wave stimulus. This resulted in four experimental groups: pulse unilateral (PUL), sine unilateral (SUL), pulse bilateral (PBL), and sine bilateral (SBL) (Table 1). In the rare case where a subject's behavioral dominance was equivocal on a performance battery,[5] assignment to bilateral electrode placement was made. In order to maximize efficacy for unilateral placement, a high centroparietal location was used in conjunction with a standard frontotemporal location. The pulse stimulus was generated by

a Mecta Corp. MECTA ECT device, with typical starting parameters of 60 pulse pairs per second, 0.75 msec pulse width, and 1.25 seconds duration. The sine wave stimulus was generated by a Medcraft Corp. B-24 Mark III ECT device with typical starting parameters of 140 volts rms for 0.6 seconds. Stimulus intensity was titrated so as to produce seizures greater than 25 seconds by EEG criteria. Seizures more than 60 seconds in duration were followed by a decrease in stimulus intensity at the next treatment session unless such settings had already proven ineffective in eliciting an adequate seizure. In all cases, ECT was given three times weekly, with the endpoint of the ECT course determined by the subject's attending psychiatrist.

Single-channel EEG monitoring of the seizure was obtained using the MECTA ECT device, which has such capability built in. A custom switch (Mecta Corp.) allowed the seizure monitoring to also be carried out in conjunction with the Medcraft apparatus. EEG electrodes were placed in a headband, with bifrontopolar placement for bilateral ECT and left frontopolar to left anterior temporal locations for right unilateral ECT. The latter configuration was chosen so as to assure the presence of bilaterally generalized seizures with the unilateral technique. The seizure recordings were later rated, blind to subject group, with regard to duration of paroxysmal activity, degree of postictal suppression, and the presence or absence of various ictal stages, as outlined in Figure 1.

Prior to ECT and both 2-3 days and 6 months following completion of the ECT course, 8-channel EEG recordings were made, using standard referential and bipolar montages and incorporating runs during photic stimulation and hyperventilation. These EEG's were interpreted, blind to subject group, by one of the investigators (R.D.W.), who is a trained clinical encephalographer. An objective visual rating instrument was designed for this purpose, in order to allow an assessment of various EEG features thought to be affected by ECT

(Table 2). Using a series of 5-point ratings, ranging from "absent" to "severe," measures were determined for both overall abnormality and frequency of the dominant posterior rhythm, along with composite indices for extent and symmetry of slowing and for hyperventilation-induced changes.

During these EEG recording sessions, several minutes of EEG data were also transferred on-line into a digital computer present in our laboratory. A special montage was used for this purpose, which also included an eye movement channel and a marker channel which was controlled by the computer to denote the beginning of each contiguous 4-second epoch of digitized data. This information was then used to allow manual rejection of data contaminated by artifact or drowsiness. For the purposes of the present investigation, only two channels of computerized data were subjected to further analysis. These consisted of homologous left and right frontocentral derivations (F3-C3 and F4-C4). Unrejected segments of EEG were analyzed off-line by Fast-Fourier transform. The results of the spectral analysis were then used to determine a slowing index, defined as mean of delta plus theta activity (1 to 7.75 Hz) for left and right frontocentral channels lumped together. In addition, a slowing symmetry index, defined as left minus right slowing, was also calculated. The choice of the specific frequency bands utilized was based upon a general acceptance of delta and theta band rhythms as pathologic manifestations of most encephalopathic entities, including ECT.[7]

Results and Discussion

No significant intergroup differences were found on the basis of subject age, number of ECT treatments received, number of missed seizures, and presence of psychotropic medication during the week prior to baseline testing. Likewise, an equivalency was demonstrated among the experimental groups with regard to both mean and cumulative adequate seizure duration (57.2 seconds, 509 seconds).

In view of claims that cumulative seizure duration might represent an objective means of "dosing" ECT,[8] the extent of correlation between this parameter and therapeutic response was determined, using the mean improvement in Hamilton Depression Rating Scale[9] ratings for this purpose. Interestingly, no significant relationship was found, suggesting that, when the presence of adequate seizures and a sufficient number of treatments are assured, the actual total amount of time spent seizing is of little therapeutic import.

In a related analysis, neither mean nor cumulative seizure duration were observed to have a significant effect upon degree of either memory impairment[4] or EEG slowing (which will be discussed below). Accordingly, both of these findings appear to demonstrate that the mechanism by which induced seizures produce both beneficial and adverse effects with ECT has to do with factors other than the mere duration of the paroxysmal activity.

The seizures produced with ECT have been described as quite similar, not only to those produced by pharmacoconvulsive agents, but also to those occurring spontaneously in individuals with major motor epilepsy.[10,11] While preictal and epileptic recruiting activity are frequently not observed, both polyspike and polyspike and slow wave stages, which are electrophysiologic concomitants of tonic and clonic behavioral stages respectively, are almost invariably present with a well-generalized ictal response (Figure 1). The polyspike and slow wave phase may either terminate abruptly or may dissipate over a period of time. Postictally, some degree of transient suppression, or flattening, of EEG activity may be present.

With only a single EEG recording channel in the present study, the symmetry of the ictal response, which has been reported as more intense over the stimulated hemisphere with unilateral ECT,[12] could not be investigated. An analysis of ictal and postictal stages for the single channel of available data was, however, carried out. This revealed that while the presence of

ictal stages was independent of ECT modality, the extent of postictal suppression, already established to be less with bilateral ECT, particularly over the cerebral hemisphere contralateral to stimulation, was found to be particularly intense with sine wave bilateral ECT (p [SBL > PBL, PUL, SUL] = 0.007, 0.002, 0.002).

This finding suggests that sine wave bilateral ECT, drawing upon its combination of bilateral stimulation with the presence of a long-duration for each phase of the stimulus cycle, may be characterized by particularly intense seizures. Empirical data reported during the pre-anesthetic/relaxant era, appear to substantiate this effect, with notations that patients receiving sine wave bilateral treatments were less responsive during the seizure, showed more intense convulsive movements, and took longer to arouse postically.[13,14] Other more recent findings which will be presented later in this Symposium,[15] dealing with the recovery of orientation post-ECT, are also supportive of the concept of a specificity of ECT modality on the basis of generalization and/or intensity of the ictal discharge. Finally, the acute postictal and interictal hypometabolic effects which have been reported by others to take place in association with ECT, and which will also be discussed elsewhere in this Conference,[16,17] are additionally quite compatible with this sort of hypothesis.

Over a course of ECT, some degree of EEG slowing often occurs. This slowing tends to be generalized, frontally predominant, and both regular and irregular in morphology. Electroencephalographically, such a pattern is considered nonspecific and is observed in a variety of conditions, including postictal dilirium in epileptics.[7] In addition to a considerable interindividual variability in extent of ECT-induced slowing, some investigations have reported that number of treatments and electrode placement also play a significant role.[11,18]

In terms of the present study, both visual ratings and computer analysis revealed that over a course of ECT, subjects receiving either bilateral electrode placement or sine wave stimuli demonstrated greater EEG slowing increases (TABLE 3). The mean spectral slowing indices, which were found to be more sensitive than visual ratings for subtle differences (e.g., PUL vs. C), are shown in Figure 2. These data represent the first time that increased ECT-induced EEG slowing has been shown to occur on the basis of stimulus waveform.

Based upon the postictal suppression findings described above, it is tempting to postulate that, again, something more "intense" about the seizures produced by bilateral electrode placement and sine wave stimuli may be responsible for these differences. In fact, postictal suppression and EEG slowing were indeed found to be highly correlated. Another related result was the extent of hyperventilatory response, an effect which is known to be sensitive to encephalopathic changes, particularly those involving the diencephalon.[7] In the present sample, subjects receiving sine wave ECT were found to have a greater hyperventilatory response than those receiving pulse ECT (p = 0.05), despite the fact that no electrode placement specific effect was observed. Together, these data provide evidence to support the hypothesis that different types of ECT exert differential effects upon the brain substance.

Although, as noted earlier, some researchers have presented evidence for greater EEG slowing ipsilateral to the side of stimulation, this was not observed in the present study, at least in terms of intergroup differences. This, perhaps, is not surprising, given the tendency of encephalopathic changes involving deep midline structures to reflect themselves in a symmetrical fashion.[7] It may also reflect the use of a centroparietal electrode located close to the cerebral midline, as opposed to a more lateral

position. Still, analysis of symmetry relationships was productive of a tendency for sine wave bilateral stimuli to produce slightly greater left-than right-sided slowing (p < 0.02 for visual rating, p < 0.03 for computer analysis). This latter finding, which is compatible with some earlier studies,[11,19] may be secondary to an underlying predisposition for the left hemisphere to manifest signs of impairment, assuming an insult of sufficient magnitude.

Given the presence of acute adverse CNS changes with ECT, it is important to establish the extent of their persistence, especially with the widespread concern which exists regarding the possibility of irreversible brain damage with this treatment modality.[20] While previous investigators have reported that ECT-induced EEG slowing has a duration of weeks rather than months or years,[21] such work tended to be unsystematic in its approach and did not incorporate quantitative analytic techniques. In an attempt to compensate for these deficiencies, we looked at differences in visually rated and computer-analyzed EEG parameters between pre-ECT baseline testing and six months following completion of the ECT course. The computer-analyzed data for long-term slowing changes are shown in Figure 3.

Overall, in terms of intergroup effects, it appeared that acute slowing had dissipiated by the time of the 6-month follow-up test session. Still, when the results of individual cases were considered, it was found that the three individuals with the greatest amount of residual slowing all received sine wave bilateral ECT. While such a finding is not necessarily statistically meaningful, it may serve to illustrate the manner in which intergroup comparisons can wash out effects characterized by a low incidence of occurrence. In any event, it leaves open the issue of persistent CNS deficits, something which will be discussed elsewhere in this Symposium, with regard to alterations in memory function.[4]

Conclusions and Future Directions

The results presented above, combined with the related work of others, provide support for the hypothesis that variations in ECT technique produce seizures which differ from one another in some fundamental, though not well-understood fashion. Furthermore, such differences may well underlie the degree of CNS dysfunction produced by this treatment modality, irrespective of therapeutic effects. In particular, unilateral nondominant electrode placement and low-energy stimuli both appear to offer the opportunity to lower neurophysiologic morbidity with ECT, at least in terms of acute effects.

Presently, our laboratory is embarking upon a replication and extension of these findings. With respect to baseline and follow-up EEG data collection, we have, in order to gain better spatial resolution, now begun to utilize 19, as opposed to 2, channels of EEG. In addition to this expansion of acquisition capability, we are also carrying out topographic mapping of spectral EEG indices, based upon methods developed at NIMH and elsewhere.[22] This new technique provides two-dimensional color-coded or grey-scale displays of any scalp-recorded electrophysiologic parameter in a format which is both easy to interpret and anatomically relevant.

Figure 4 demonstrates a left hemispheric display of alpha activity in the resting state with eyes closed for a control subject. One can easily appreciate the classical frontal-occipital gradient of the resting alpha pattern, with darker patterns signifying greater alpha intensity (publication costs precluded the use of the considerably more striking color display). An example of left hemispheric slowing before and after a course of ECT is depicted in Figure 5. In this instance, both a diffuse, but frontally predominant, delta increase and a diffuse, centrally maximal, theta increase post-ECT can be easily appreciated. Potential asymmetries in spectral indices are particularly easy to visualize with this technique. Figure 6 portrays

left, right, and hemispheric difference maps for delta activity in an individual who, two days post-ECT, had intermittent runs of asymmetrical slowing.

Aside from the mapping of time-averaged spectral parameters associated with EEG background activity, our system can also map out the spatial electrical fields of transient electrophysiologic events, such as spikes or sharp waves. Figure 7 shows the left and right hemispheric fields associated with the peaks of two asymmetric sharp transients in a patient two days following completion of an ECT course. One could, of course, easily adapt this latter process to the investigation of ictal phenomena with ECT. In addition to the primary use of these types of EEG mapping, it can also be used to provide an electrophysiologic correlate to other imaging techniques, such as regional cerebral blood flow, position emission tomography, or nuclear magnetic resonance. This can be accomplished by using, where appropriate, specialized analytic techniques designed to extract cortical information from whole brain scans.

In summary, it is hoped, that with refinements in methodology such as these, a more definitive understanding of the electrophysiology of ECT can be established. The increase in knowledge gained should help to carry us closer to a characterization of the mechanisms underlying ECT, which is, of course, itself electrophysiologic in nature.

References

1. Weiner, R.D., Rogers, H.J., Davidson, J., and Miller, R.D. 1982. Evaluation of the central nervous system risks of ECT. Psychopharmacol. Bull. 18:29-31

2. Welch, C.A., Weiner, R.D., Weir, D., Cahill, J.F., Rogers, H.J., Davidson, J., Miller, R.D., and Mandel, M.R. 1982. Efficacy of ECT in the treatment of depression: Wave form and electrode placement considerations. Psychopharmacol. Bull. 18:31-34

3. Weiner, R.D., Rogers, H.J., Welch, C.A., Davidson, J.R.T., Miller, R.D., Weir, D., Cahill, J.F., and Squire, L.R. 1984. ECT stimulus parameters and electrode placement: Relevance to therapeutic and adverse effects, IN: ECT: Basic Mechanisms, (B. Lerer, R.D. Weiner, R.H. Belmaker, Eds.), London, John Libbey and Co., pp. 139-147

4. Weiner, R.D., Rogers, H.J., Davidson, J.R.T., and Squire, L.R. 1985. Effects of stimulus parameters on cognitive side effects. This Volume

5. d'Elia, G. 1970. Unilateral ECT. Acta Psychiatr. Scand. Suppl. 215:5-98

6. Weiner, R.D. Electroencephalographic correlates of ECT. 1982. Psychopharmacol. Bull. 18:78-79

7. Kiloh, L.G., McComas, A.J., Osselton, J.W., and Upton, A.R.M. 1982. Clinical Electroencephalography. Fourth Edition, London, Butterworths

8. Maletzky, B.M. 1978. Seizure duration and clinical effect in psychiatry. Compr. Psychiatry 19:541-550

9. Hamilton, M. 1960. A rating scale for depression. J. Neurol. Neurosurg. Psychiatr. 23:56-62

10. Chatrian, G.E. and Petersen, M.C. 1960. The convulsive patterns produced by Indoklon, Metrazol and electroshock: Some depth electrographic observations in human patients. Electroencephalogr. Clin. Neurophysiol. 12:715-725

11. Weiner, R.D. 1983. EEG related to electroconvulsive therapy, IN: EEG and Evoked Potentials in Psychiatry and Behavioral Neurology (J.R. Hughes, W.P. Wilson, Eds.), Boston, Butterworth Publishers, pp. 101-126

12. Staton, R.D., Hass, P.J., and Brumback, R.A. 1981. Electroencephalographic recording during bitemporal and unilateral nondominant hemisphere (Lancaster position) electroconvulsive therapy. J. Clin. Psychiatry 42:264-269

13. Liberson, W.T. 1948. Brief stimulus therapy: physiological and clinical observations. Am. J. Psychiatry 105:28-39

14. Marshall, T.J. and Dobbs, D. 1959. Treatment technique and apnea in electroshock. Dis. Nerv. Syst. 20:582-583

15. Crovitz, H.F. et al. 1985. Effects on acute orientation processes, This volume

16. Silverskiold, P. et al. 1985. Late effects on RCBF, EEG, psychometric testing and clinical outcome, This volume

17. Prohovnik, I. et al. 1985. Effects on regional cerebral blood flow: modality and therapeutic outcome, This volume

18. Fink, M. 1979. Convulsive therapy - theory and practice. New York, Raven Press

19. Volavka, J. 1974. Is EEG slowing related to therapeutic effect of convulsive therapy? IN: Psychobiology of convulsive therapy, (Fink, M., Kety, S., McGaugh, J., and Williams, TA, Eds.), Washington, D.C., V.H. Winston and Sons, pp. 35-40

20. Weiner, R.D. Does ECT cause brain damage? 1984. The Behavioral and Brain Sciences 7:1-53

21. Weiner, R.D. 1980. The persistence of ECT-induced changes in the electroencephalogram. J. Nerv. Ment. Dis. 168:224-228

22. Coppola, R., Buchsbaum, M.S., and Rigal, F. 1982. Computer generation of surface distribution maps of measures of brain activity. Comput. Biol. Med. 12:191-199

TABLE 1

NUMBER OF SUBJECTS RECEIVING EEG TESTING

	C	PUL	SUL	PBL	SBL
ICTAL AND ACUTE INTERICTAL EFFECTS	21	14	18	24	18
SIX-MONTH FOLLOW-UP	12	11	11	13	11

TABLE 2

EEG-VISUAL RATING METHOD

A. TYPES OF SLOWING - RATED AS ABSENT, BORDERLINE,
    MILD, MODERATE, OR SEVERE BY OBJECTIVE CRITERIA

      1. SPONTANEOUS SLOWING
      2. FRONTAL INTERMITTENT SLOWING
      3. OTHER RHYTHMIC SLOWING
      4. ASYMMETRY OF SLOWING
      5. HYPERVENTILATION-INDUCED SLOWING

B. FREQUENCY OF POSTERIOR RHYTHM

C. OVERALL LEVEL OF ABNORMALITY - RATED ABSENT TO
    SEVERE AS ABOVE

TABLE 3

ACUTE EEG SLOWING INCREASES

2-3 DAY POST-ECT vs. BASELINE

	P-VALUES (2 x 2 + 1 ANOVAS)		
	BL > UL	BL > C	UL > C
VISUALLY RATED	0.03	0.0001	0.0001
COMPUTER ANALYZED	0.02	0.0001	0.05
	S > P	S > C	P > C
VISUALLY RATED	0.03	0.0001	0.0001
COMPUTER ANALYZED	(0.07)	0.002	0.02

ICTAL + POSTICTAL STAGES WITH ECT

Figure 1

ACUTE BIFRONTOCENTRAL COMPUTER–ANALYZED SLOWING
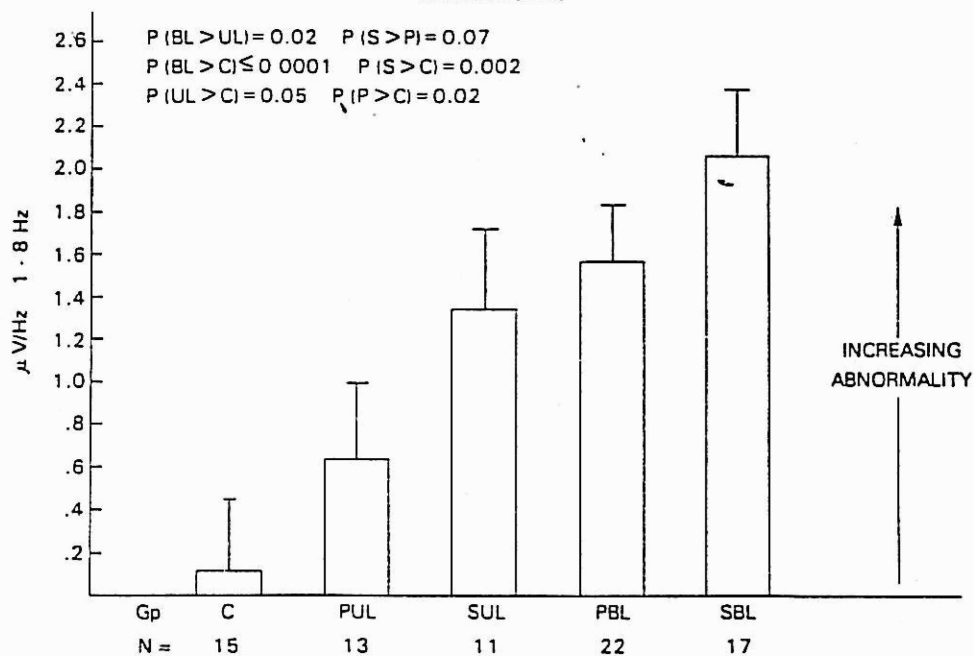
Difference between 2 - 3 Day Post-ECT and Baseline
Means (s.e)

P (BL > UL) = 0.02   P (S > P) = 0.07
P (BL > C) ≤ 0 0001   P (S > C) = 0.002
P (UL > C) = 0.05   P (P > C) = 0.02

INCREASING
ABNORMALITY

Gp	C	PUL	SUL	PBL	SBL
N =	15	13	11	22	17

Figure 2

LONGTERM COMPUTER ANALYZED BIFRONTOCENTRAL EEG SLOWING

(THETA + DELTA ACTIVITY)

Six Months Post-ECT Minus Baseline Score (+S.E.)
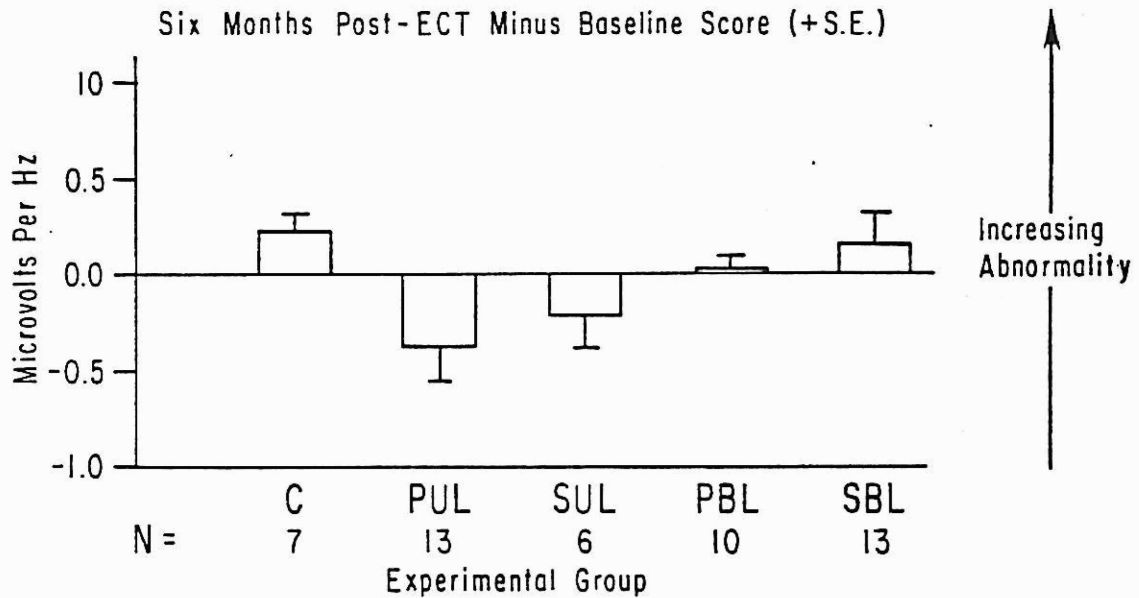

Figure 3

ALPHA, EYES CLOSED

174.
165.
157.
148.
140.
131.
122.
114.
105.
96.
88.
79.
71.
62.
53.
45.
36.

LEFT HEMIS.
EVA1A.1L

Figure 4

PRE-ECT   WA1S.2

DELTA   THETA
LEFT HEMIS.   LEFT HEMIS.

POST-ECT   WAR2S.2

DELTA   THETA
LEFT HEMIS.   LEFT HEMIS.

Figure 5

DELTA FREQUENCIES

LEFT
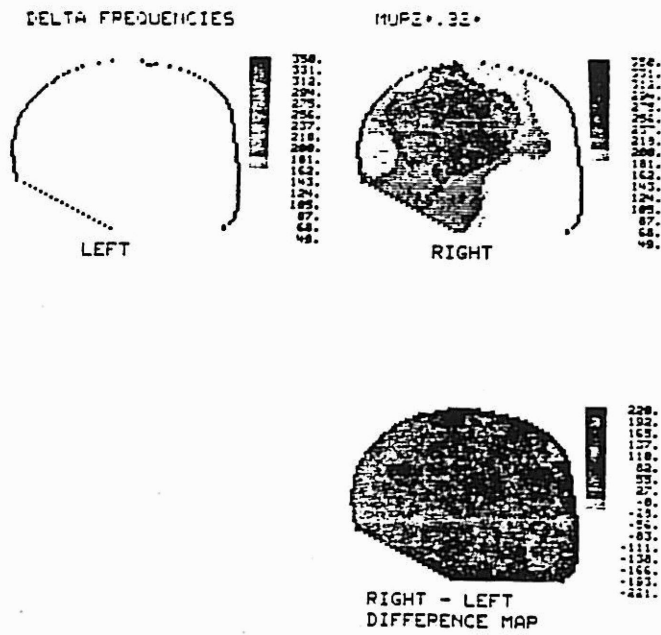
RIGHT

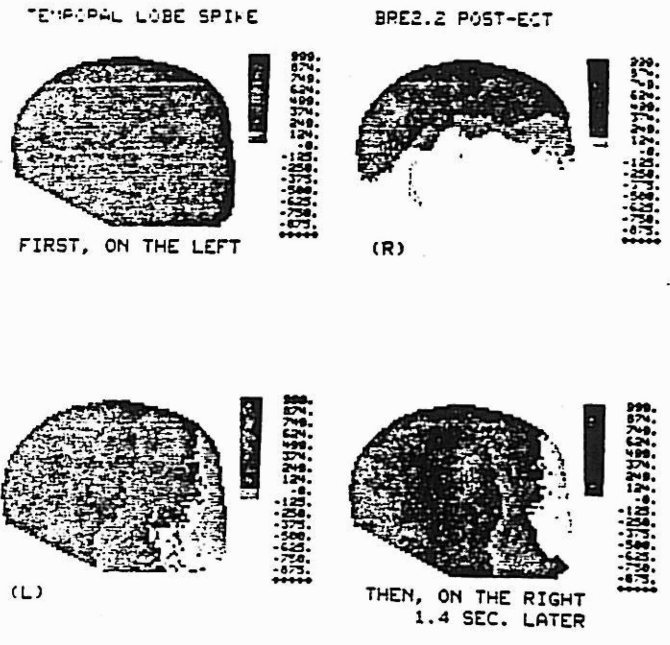RIGHT - LEFT
DIFFEPENCE MAP

Figure 6

Figure 7

Figure Legends

Figure 1: Ictal and postictal EEG stages with ECT.

(from Weiner, 1982.)

Figure 2: Acute bifrontocentral computer-analyzed slowing change with ECT (delta through theta bands).

Figure 3: Long-term bifrontocentral computer-analyzed slowing change with ECT (delta through theta bands).

Figure 4: Topographic map of left hemispheric alpha activity during the resting state with eyes closed (control subject). Scale in microvolts per Hertz. Nineteen standard scalp leads placed per International 10-20 format, with linked ear electrodes used as a reference.

Figure 5: Left hemispheric delta and theta activity before (upper) and 2 days after (lower) a course of pulse unilateral ECT. Scale, lead locations, and reference as in Figure 4.

Figure 6: (Upper) left and right delta activity during burst of asymmetrical slowing 2 days after a course of six pulse unilateral and 2 pulse bilateral ECT.

(Lower) hemispheric difference map (right-left) for the above. Scales, lead locations, and reference as in Figure 4.

Figure 7: Left and right hemispheric voltage field maps for peaks of shifting asymmetrical sharp transients occurring 2 days following a course of pulse bilateral ECT. Scale in analog-to-digital converter units. Lead locations and reference as in Figure 4.