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The Persistence of Electroconvulsive Therapy-Induced Changes in the Electroencephalogram

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The literature concerning the effects of electroconvulsive therapy (ECT) upon the EEG is reviewed with respect to the degree and persistence of abnormalities. The most common electrophysiological dysfunction consists of generalized regular and irregular slow wave activity. This slowing typically disappears by a few weeks to a few months following completion of the ECT course but in rare cases may persist for longer periods. Patients given large numbers of ECT treatments tend to show more prolonged alterations. Possible correlations of these EEG changes with a variety of parameters are discussed.

Electroconvulsive therapy (ECT) is an effective agent for inducing remissions in patients with severe depressive or acute schizophrenic episodes (11). Its utilization, however, has diminished since the development of effective psychopharmacological agents for the treatment of these disorders. A major reason for this decrease has been concern regarding the acute organic brain syndrome produced by ECT. This syndrome is characterized behaviorally by confusion and both anterograde and retrograde memory impairment (34). Neurophysiologically, it is manifested most clearly by generalized slowing in the EEG (32), as will be described in greater detail below. Although the neuropathological data relating to ECT are incomplete, the available evidence does not support the presence of significant pathological alterations (1, 4). Although memory deficits are generally thought to disappear by a month following ECT (9), there is suggestive evidence that subtle changes may persist in at least some patients (16, 28, 34), particularly those receiving relatively large numbers of treatments. How long the EEG slowing associated with ECT persists has likewise been unclear. In a 1952 review, Chusid and Pacella stated that "the EEG disturbances ... usually disappear within one to three months after termination of an average course of treatments" (8, p. 106). It is the purpose of the present paper, nearly 3 decades later, to review again the ECT literature relevant to this topic and investigate which factors affect the rate at which the EEG abnormalities disappear.

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Acute EEG Changes Associated with ECT

Over the course of a series of ECT treatments, a number of changes are apparent in the interictal EEG. From a pathophysiological standpoint, the most significant of these is a diffuse increase in the level of slow wave activity, which builds up over a course of ECT and begins to decrease immediately thereafter. Two morphologically and physiologically different patterns of slowing are present. The first of these consists of diffuse regular activity in the theta and delta frequency ranges, and is present in a uniform fashion during the waking state. With bilateral stimulus electrode placement, this polymorphic slowing is occasionally slightly greater over the left cerebral hemisphere, but with unilateral ECT the slowing is typically more prominent ipsilaterally. The second type of slowing is characterized by intermittent runs of regular delta activity which are usually bilaterally synchronous and frontally predominant. Both slowing patterns are nonspecific in nature and can be observed with a great variety of other etiologies reflecting diffuse CNS impairment, ranging from postictal conditions in epilepsy to toxic and metabolic encephalopathies (18).

General Characteristics of Data Included in Review

Only those studies were included in which at least a qualitative comparison was made between a baseline recording and follow-up records made not less than 10 days following completion of the ECT course. Very few studies were controlled and a high degree of methodological diversity was present. Potentially important factors which varied among the studies included: a) the number, age, and diagnostic character of subjects; b) the average number of ECT treatments per subject; c) the frequency of ECT treatments; d) stimulus electrode placement; e) electrical stimulus parameters; f)

presence and extent of treatment modification by muscle relaxation, anesthesia, and anticholinergic premedications; g) history of concurrent or previous somatic psychiatric treatments, *e.g.*, psychopharmacological agents, insulin coma, chemically induced convulsive treatments, and previous courses of ECT; h) the specific criteria for EEG abnormality; i) the degree of quantification and statistical analysis of results; and j) total duration of post-ECT EEG follow-up.

The contributions of many of these factors will be discussed below. A total of 21 studies, ranging in date from 1942 to 1975, have been reviewed.

How Long Does EEG Slowing Persist?

During the first few days following completion of a course of ECT, the vast majority of patients demonstrate a significant degree of slowing, with Klotz (19) reporting a figure of 82 per cent. Eleven studies felt some degree of slowing was still present at several weeks, with reports ranging from "few" to "most" (3, 13, 19–23, 25, 27, 29, 35), whereas only two did not (6, 24). In the two largest patient series reviewed, Klotz (19) reported that 13 per cent of his patients' EEGs had not returned to baseline by 1 month, whereas extrapolation of Fukuda and Matsuda's (13) results produce an analogous figure of 8 per cent. By 3 months, however, four studies, in addition to the two mentioned above, concluded that EEG slowing had returned to baseline levels (3, 5, 15, 29).

There are seven studies, however, which continue to find a persistence of increased slowing at 3 months or more in at least some of their patients (2, 19, 23, 25, 27, 31, 36). Klotz (19), for example, demonstrated a persistence of increased slowing at 1 year in 1 per cent of his subject population. Proctor and Goodwin (27) felt that a few of their patients continued to show increased slowing "up to several months" following completion of the ECT treatments. J. G. Small (31, abstracted from Table 2, p. 58) found that the incidence of lateralized EEG slowing was 2.2 times greater at 60 to 90 days post-ECT than at baseline. Bagchi *et al.* (2) claimed that "mild but noticeable residuals" were still present in the EEGs of the four subjects they followed as long as 5 to 9 months after ECT, although they did not describe the specific findings. Pacella *et al.* (25) found that slowing in the anterior regions persisted past 3 months in 30 per cent of those patients receiving more than 13 treatments, but in none of the patients receiving fewer treatments (25). Mosovich and Katzenelbogen (23) reported an increased incidence in slowing at 10 months only in those patients whose EEGs during the interictal period had demonstrated signs of "cerebral dysrhythmia," an archaic term referring to the presence of paroxysmal slowing. Fifteen per cent of patients in that category who had received three to 15 treatments showed increased slowing at 10 months, whereas for those who had received more than 15 treatments the incidence rose to 50 per cent. The relatively high figures for persistent electrophysiological impairment in these latter two studies should be viewed with caution, since in both cases the increased slowing was often only present during hyperventilation. Since the time these studies were reported, in 1942 and 1948, respectively, generalized hyperventilation-induced slowing is no longer felt to be necessarily pathological (18). Nevertheless, overall these studies demonstrate that a small percentage of ECT patients may show continued impairment of electrophysiological brain activity 3 months after completion of the ECT course. The effect of an abnormal pre-ECT EEG upon persistence of EEG abnormalities was investigated by Taylor and Pacella (37). They found that five out of 56 subjects with abnormal pre-ECT EEGs showed greater than usual persistence of EEG abnormalities (over several months), suggesting that individuals in this category are more at risk for the development of long lasting CNS changes.

Role of Number of Treatments in the Persistence of EEG Changes

As described above, the studies by both Pacella *et al.* (25) and Mosovich and Katzenelbogen (23) demonstrate a positive correlation between incidence of persistent EEG abnormalities and the number of ECT treatments. In another study, Roth (29) divided his patient population into four groups on the basis of number of ECT treatments and followed EEGs until they returned to baseline conditions. In terms of both the waking record and thiopentone-induced slowing, he found a clear correspondence between the number of ECT treatments and the length of time it took for baseline EEG charcteristics to reappear. Only one study, that of Weil and Brinegar (38), found an absence of a correlation between number of treatments and either severity or persistence of EEG impairment. It is conceivable, however, that a possible difference between patient groups could have been obscured by their relatively brief follow-up period of 14 days. Nevertheless, on the whole the available evidence strongly suggests the existence of a positive correlation between number of ECT treatments and persistence of EEG abnormalities.

Role of Stimulus Electrode Position in Persistence of EEG Changes

When generalized seizures are evoked by stimulation of only one cerebral hemisphere instead of bilat-

erally, both verbal and nonverbal memory losses are diminished (34). There is no objective evidence, however, that memory deficits last longer with bilateral ECT than with unilateral ECT, although the incidence of complaints of persistent memory difficulties is higher with the former (30, 33). The acute differences in the effects of unilateral and bilateral ECT on the EEG have been discussed above. A number of the studies that were reviewed compared EEGs of patients receiving unilateral and bilateral ECT at follow-up periods greater than 10 days (5, 21, 27, 31, 35). Except for the study by Blaurock *et al.* (5), in which EEGs were only followed for 2 weeks, no evidence that bilateral ECT produces more persistent EEG slowing than unilateral ECT has yet been demonstrated. However, none of the above studies investigated the duration of EEG slowing in enough detail to provide a definitive answer.

Role of Oxygenation, Muscle Relaxation, and Anesthesia on Persistence of EEG Changes

Until the 1960s ECT treatments were generally given without modification by muscle relaxants, anesthetics, or oxygenation. It is now clear that a significant level of cerebral anoxia occurs under such circumstances (14). Electrically induced seizures modified by oxygenation and muscular relaxation, however, do not appear to result in significant anoxic effects upon the brain (26). The discomfort of succinylcholine-induced respiratory paralysis has necessitated the use of fast acting general anesthetic agents. This, in turn, has resulted in a relative increase in the amount of electrical energy necessary to induce a generalized seizure. This appears to be the case even with the most commonly used anesthetic, methohexital, which is not otherwise known to raise seizure threshold. In effect, this represents a tradeoff between anoxic effects and musculoskeletal trauma, on the one hand, and increased seizure threshold and possible adverse effects of the electrical stimulus itself on the other. A comparison of the studies mentioned above in regard to possible effects of seizure modification upon EEG persistence does not reveal any significant correlation. No single one of these studies, however, incorporated separate patient groups receiving modified and unmodified ECT treatments. It is difficult, therefore, to determine the relative contribution of anoxic *vs.* electrical effects upon the persistence of ECT-induced neurological dysfunction as manifested in the EEG.

Effects of Other Parameters on the Persistence of EEG Changes

Callaway and Boucher (6) and Murillo and Exner (24) investigated the effect of regressive ECT (25 to 30 treatments over 1 to 2 weeks) upon the EEG, both agreeing that the records had normalized by 2 weeks following completion of the treatments. Neither study, however, included a comparison group of patients receiving standard three per week treatments. In addition, it is well known that patients undergoing regressive ECT undergo profound but apparently reversible organic deterioration, leading one to view the above relatively benign EEG findings with some uncertainty.

Attempts to relate degree of EEG slowing with either the amount of clinical improvement or the extent of memory deficits have not established consistent relationships (37). The time course for return of baseline memory functioning following a series of ECT treatments does in fact appear to follow roughly that described above for EEG slowing, but not enough information is available to make a more definitive comparison.

Persistence of EEG Changes with Chemically Induced Seizures

The electrophysiological correlates of electrically or chemically induced seizures are strikingly similar, whether monitored by scalp or intracerebral recording electrodes (7). Davis and Sulzbach (10) determined that pentylenetetrazol (Metrazol), an intravenous analeptic agent, produced generalized slowing which, in two patients, persisted at least 11 to 13 months (10). Although confounded by the concurrent use of insulin coma treatments, their results are supported by clinical observations made by Proctor and Goodwin (27). At 3 weeks following completion of a series of convulsive treatments, however, Levy *et al.* (20) felt that, even though as many patients receiving pentylenetetrazol as ECT showed EEG impairment, the severity of the abnormalities was greater with the latter. In their book on somatic therapies, Kalinowsky and Hippius (17) concluded that the EEG changes with both convulsive modalities are of equivalent persistence. Similarly, no significant differences in EEG slowing between ECT and flurothyl (Indoklon), an inhalant analeptic agent, were observed at follow-up intervals of 2 weeks (12) or 2 to 3 months (31).

The acute memory deficits with flurothyl appear to be less than those associated with ECT, although at 2 to 3 months no significant difference is present (30). The issue of memory deficits with pentylenetetrazol *vs.* ECT is largely unresolved, as the former fell into disuse before appropriate measures for memory testing became available.

The results of comparisons between EEG effects of electrically and chemically induced seizures suggest that EEG slowing is related more to the occurrence of a series of generalized seizures than to the precise

mode of seizure induction. This may be inconsistent with the finding mentioned earlier of partially lateralized EEG slowing following unilateral ECT, and it is therefore possible that, at least acutely, both seizures and electrical stimulus contribute to the development of EEG abnormalities.

Conclusions

1. Generalized EEG slowing, both regular and irregular in morphology, is the most prominent electrophysiological correlate of ECT. It is a nonspecific abnormality consistent with diffuse cortical and subcortical impairment.

2. In most cases, by 1 month after completion of a course of ECT, the slowing has returned to baseline levels, although the presence of mild slowing at this time is not uncommon.

3. The incidence of increased slowing by 3 months following completion of the ECT treatments is low.

4. Both the severity and the persistence of EEG slowing are proportional to the number of ECT treatments received.

5. Unilateral ECT typically produces slowing which is maximal over the ipsilateral hemisphere, despite generalization of the evoked seizure activity. It is still unclear whether or not EEG changes are more transient with unilateral than with bilateral ECT.

6. The major factor in the development of EEG slowing appears to be the occurrence of a series of generalized seizures. To a lesser degree, other factors, such as the form and intensity of the electrical stimulus and anoxia, may play a part.

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