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The Cognitive Side Effects of Electroconvulsive Therapy[a]

Discussion of Part VI

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It is a well-documented fact that electroconvulsive therapy (ECT) produces cognitive impairment. This type of side effect has been a major concern of both practitioners and their patients since the treatment was first introduced in 1938. Interest in finding ways to reduce these cognitive deficits has been at the core of research efforts in more recent years, and modification of the parameters of ECT, e.g., modality, stimulus waveform, and dosage, have met with apparent success. Research into the specificities of these cognitive deficits, and how they relate to the parameters of treatment, will not only aid us in dealing with the deficits directly, but will enable us to better understand how the treatment affects a wide range of neuropsychological functions, thereby providing data on the possible mechanisms of action of ECT as well as on the neuropsychological aspects of depression.

The papers presented in this session are primarily devoted to further exploration of the ways in which the parameters of treatment relate to cognitive dysfunction. Research advances in this area have pointed to the fact that the associated side effects of ECT are not general, but specific. They are specific to the direct effects of the stimulation, to the characteristics of the behaviors being studied, and to the time at which these assessments are made.

A wide range of research interests are presented. In some cases the data support previously reported findings, while in other cases the data are representative of new areas of study. I will briefly review the major findings in the area of ECT-related cognitive functions as they are presented in this session, and show, where possible, how these deficits relate directly to the parameters of the treatment.

The first major parameter to undergo study was that of electrode placement. It was clearly observed that the memory loss often associated with bilateral placement of electrodes was markedly reduced when the electrodes were placed on one side of the head (nondominant side). This reduction in cognitive impairment, with unilateral treatment, was primarily for verbal memory, although early studies suggested that nonverbal memory was similarly affected. The differential effects of treatment modality on verbal memory are a robust finding, which has held up through many experimental trials. We see from the data presented in this session that the differences between bilateral and unilateral electrode placement for verbal materials hold for the different stimulus waveforms (Weiner's study) and for low-dosage treatment (Sackeim's study).

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The differential effects of electrode placement on memory for nonverbal materials are not as clear-cut. This may be due, in part, to the difficult task of selecting stimulus materials that are sensitive to right hemisphere processing. The geometric shapes, for example, in the Sackeim *et al.* study were verbally encodable, and were, in fact, processed like verbal materials, while the nonsense shapes, which were not as easily encodable, showed treatment effects suggesting that they were being processed by the right hemisphere.

Pure nonverbal materials might be equally affected by the two treatment modalities, since the right hemisphere is being stimulated in both bilateral and unilateral electrode placements. It is interesting to note that the processing of the nonsense shapes in the Sackeim *et al.* study was sensitive to response to treatment, e.g., early in the course of treatment individuals who were later classified as responders showed greater deficit in their retrograde memory for nonsense shapes than did individuals who did not respond to the treatment. These data suggest that right hemisphere processing is differentially affected by the therapeutic aspects of the treatment. It is possible that tests of this kind could be used to predict ultimate response to treatment early in its course, and thereby restrict treatment to patients likely to respond.

Recent interest in the postictal period, i.e., the time immediately following the occurrence of the seizure, has revealed substantial differences in orientation for the two treatment modalities. Daniel and Crovitz, using a 12-item questionnaire, report marked differences between the two modes for both traditional sine-wave stimulation and for brief pulse. Greater cumulated disorientation, over the course of treatment, was observed in the bilateral groups. Similar modality differences are reported by Sackeim *et al.*, using low-dosage, titrated energy levels. Use of low-dosage treatment, however, apparently eliminates the cumulative disorientation effects for the bilateral group, while resulting in cumulative improvement in orientation times for the unilateral group. It may be that the shorter orientation times in the unilateral group at the end of the treatment course were related to the decreases in seizure durations observed in this group. Correlations between seizure duration and time to orient were found to be significant for this group.

Modifications of the stimulus waveform used to elicit the therapeutic seizure were first introduced in the 1940s. It was believed that the amount of energy needed to elicit a seizure, using a brief pulse, was substantially lower than that needed to elicit a seizure using a sine wave, and that this reduction in amount of energy might have a significant effect on cognitive impairment. Weiner and his associates report in this session that sine-wave stimulation causes greater cognitive impairment than does brief-pulse stimulation without compromising clinical benefit. Using a wide variety of carefully selected neuropsychological tests, they concluded that stimulus waveform has a more potent effect on cognitive functioning than does modality, although modality differences were also apparent in both stimulus waveform groups.

It is possible that it is not the absolute amount of energy applied to the brain that produces the cognitive impairment, but rather the amount in excess of an individual's threshold. Recent efforts (Sackeim *et al.*) have been made to develop a procedure for titrating energy levels for individuals, thereby reducing the amount of energy applied. The lower levels of energy have resulted in reduced impairment in both immediate and short-term cognitive functioning. In addition, there is no evidence for cumulative impairment over the course of the treatment, for either postictal orientation time or retrograde amnesia. While the cognitive impairment associated with the low-dosage treatment shows typical modality effects, low-dosage unilateral treatment was not found to be as effective a treatment as low-dosage bilateral treatment, despite the fact that available characteristics of the seizure obtained appeared to be equivalent.

The substantially shorter postictal orientation times for the low-dosage treatment

group have definite advantages for the patient. Most of the patients oriented within a 45-minute period following their treatment, and were able to return to their wards and participate in ward activities by lunchtime. For outpatients, this shorter recovery time enabled them to return to their homes and to resume their domestic responsibilities by early afternoon, if they wished.

Short orientation times also make it possible to gather data on a wide variety of neuropsychological functions, closer in time to the actual seizure than is possible with the more traditional forms of treatment and their prolonged orientations. These data will be more sensitive to the treatment parameters and provide better insight into possible mechanisms of action.

At one time the confusion produced by the treatment was believed to be a mechanism of action. It was thought that patients became disoriented and "forgot" what was bothering them. Recent research, however, has offered little support for this notion. Degree of cognitive impairment, per se, has not been found to be related to response to treatment.

The specificity of the treatment on cognitive functioning was first observed when comparisons of the effects of bilateral and unilateral treatment on verbal and nonverbal memory revealed that bilateral placement had a more profound effect on verbal functioning than did unilateral placement. The fact that materials processed by the different hemispheres would be differently affected by the treatment parameters has resulted in the selection of stimuli sensitive to brain lateralization. As mentioned above, early attempts to select nonverbal stimuli were not successful since nonverbal stimuli that can be easily verbally encoded are processed by the left hemisphere. Since then researchers have explored the effects of the treatment on a wide range of neuropsychological tasks. Just reviewing the materials utilized in the studies reported in this session, we see an extensive list including memory for words, paragraphs, geometric shapes (for verbal materials), and facial recognition (affective and neutral), form reproduction and memory for nonsense shapes (for nonverbal materials).

With the use of more appropriate nonverbal materials it now appears that the differences between the bilateral and unilateral treatments, previously reported for nonverbal materials were probably more a function of the stimulus properties than of the treatment modality, and that the effects of the two treatment modalities on nonverbal tasks are about equivalent (the Weiner and Sackeim studies).

Interest in the effects of the treatment on different kinds of memory has led to comparisons of retrograde amnesia (memory loss for material learned before treatment) with anterograde amnesia (inability to learn new material). Results have indicated that following ECT, anterograde amnesia is less pronounced than retrograde amnesia. Recovery of anterograde memory (Squire's study) seems to progress at a regular pace from time of last treatment and is usually back to normal at about six months, depending, of course, on the nature of the task. Retrograde memory loss often displays a temporally limited gradient, e.g., loss of more recently acquired information and less or no loss of material more remote in time. While retrograde amnesia also returns to normal by the end of six months, many individuals report losses persisting many months after treatment, and some patients report that this gap is never filled. Memory losses are often for the events immediately surrounding the treatment experience, and these losses are often the most frequent of patient complaints.

The magnitude of the memory loss is often directly related to the time from the last treatment, and seems to be a direct response to the treatment. With time, some of the loss is dissipated. Dr. Squire reports that anterograde learning is most impaired within the 45 minutes following the treatment, and then improves with increases in time. This gradient was found for the bilateral group, but not for the unilateral group, where only minimal deficits were observed shortly after the treatment. While these findings were

clearly reported for the verbal materials (paired associate word learning), his data for the nonverbal materials (faces and nonsense shapes) suggest that the unilateral and bilateral groups were similarly affected.

There is a general claim in the literature that the learning of new materials is not as affected by ECT as the ability to retain this information, e.g., retention is more strongly affected than acquisition, particularly when a substantial delay is imposed between the acquisition and retention of the materials.

Results from the Sackeim *et al.* study provide additional support for this hypothesis. Using paired-word and paired-face tasks, they reported that depressed patients differed from normal controls in their ability to acquire information prior to treatment, and that the ECT produced deficits in retention for both the verbal and nonverbal stimuli, suggesting that these two neuropsychological processes are differently affected by the treatment.

Along a different dimension, Weiner and his associates report that memory loss for personal information is affected by the treatment to a greater extent than is memory for impersonal material, the latter being measured in terms of recall for famous events and famous faces. Most important is the finding that bilateral treatment produced greater impairment for personal memory than did unilateral treatment. While Weiner's data lack corroborative control, this is probably an important step in the finer differentiation of the kinds of memory losses often complained about.

Freeman's paper on patients' attitudes towards ECT lends additional support to the importance of memory losses, since close to 75% of the patients reported that memory loss was the worst side effect experienced, with 30% stating that their memories have never returned to normal. He reported that those patients who had received unilateral treatment were more likely to report that they would not want to have ECT again. At first this seems contradictory, since bilateral treatment produces greater cognitive impairment. However, it is possible that the unilateral treatment was not as effective a treatment and that the patients were disappointed in the therapeutic effects of this treatment. It would have been interesting to compare the bilateral nonresponders to the bilateral responders to see if attitude towards ECT is related to response to treatment.

The lack of a relationship between subjective reports of memory loss and objective measures reported in the Weiner *et al.* study suggests that the former are more a function of the mood state of the patient (in fact correlations between Hamilton Rating Scale scores and the reports of subjective memory loss were high), while the latter are more a function of the "organic" state of the patient (no correlation with depression scores). It is possible that patients' complaints of memory loss are of a specific kind, a kind not reflected in the objective scores, and a kind exacerbated by depressive symptomatology.

In summary, the papers presented at this session represent current research efforts in the study of the cognitive effects of ECT. While many of the previously reported findings have been supported, new ones have been offered and have contributed to a better understanding of the specific effects of the treatment on cognitive functioning. Hopefully, research efforts will continue in this vein and the data culled from these efforts will help to further reduce the undesirable side effects of the treatment, enabling more patients to seek and utilize ECT as an effective treatment for depression.

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