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Colonel R. W. Armstrong, R.A.M.C., for ed in the compilation of this article, and

## PROLONGED MEMORY DEFECTS FOLLOWING ELECTRO-THERAPY.\*

By M. B. BRODY, M.D.(Sheffield), D.P.M.,  
Senior Resident Physician, Runwell Hospital, Essex.

LEVY *et al.* (1942) reported impaired memory in 8 out of 11 patients treated by electric shock. Impairment lasted from one to several weeks, and in one patient was present after several months. Grinker, discussing this paper, compared the psychometric and clinical picture following electro-therapy with that seen in the "punch drunk" syndrome, in which careful testing, he warned, reveals permanent damage. This to my best knowledge is the only note hitherto made that impairment of memory occurring during or after electro-therapy has any serious significance. The following case-notes revealing memory defects lasting a year or more suggest that Grinker's apprehensions may be justified.

CASE 1.—Unmarried female, Aged 48. Admitted with manic-depressive insanity in a depressed phase. She had 15 treatments in September and October, 1941, of which six produced *grands maux*. During the treatment she complained that she could not remember names and addresses of relatives and familiar friends. She became very apprehensive of the treatment, which she said was making her worse. She was discharged recovered in May, 1943. Interviewed recently, more than two years after treatment, she was well and working, but said that her memory still let her down sometimes. She said, "I cannot seem to remember but it comes back later on. It takes me a long time to remember. My memory seems 'slower.' It lets me down over just small things that I am doing, like posting a letter." She still finds it difficult to remember people's names, an especially striking example occurring only a few weeks ago. At first, she said, it used to worry her, but now "it does not because it is so much better." Her memory improved for about six months after the end of treatment, but has not changed since then.

An interesting point in this case is that a few months previous to her course of electro-therapy she had undergone a course of cardiazol treatment, which is usually thought to cause more apprehension and to be more unpleasant than electro-therapy. Nevertheless she had continued with this treatment, and had not complained of memory impairment either during the course or afterwards, whereas her electro-therapy had to be terminated because her memory disturbance worried her so much.

CASE 2.—Married female, aged 32. An hysterical type, admitted with superimposed acute depression. She had four treatments, all of which produced *grands maux*, in March and April, 1942. She bitterly complained after each of memory disturbance, and the treatment was eventually stopped because, for this reason, she opposed it so strongly. She was discharged from hospital in April, 1942. She was readmitted for three weeks in November and December, 1943, with mild reactive depression, which rapidly cleared on adjusting the environmental situation which had precipitated it.

Seen 18 months after electro-therapy, she said her memory still failed her at times. "Incidents," she said, "occur on and off. I can go several weeks without trouble and then might get two or three in a day. One day three things were missing, the poker, the paper, and something else I cannot remember. I found the poker in the dustbin; I must have put it there without remembering. We never found the paper and I am always very careful of the paper." In her household duties: "I want to go and do things and go to do it and find I have already done it." She further explained: "For example, I looked for the duster in a drawer to dust another room. I looked all over for it and found that I had taken it into the room which I was going to dust. . . . I have to think what I am doing so that I know I have done it. . . . It is uncanny when you do things and find you cannot remember it." She, too, has difficulty when meeting friends: "I have met one or two people who seem to know all about me and I cannot remember anything about them. I look silly at them and I get frightened of meeting people." Her memory let her down in other ways too, but she found it impossible to describe them.

CASE 3.—Widow, aged 54, admitted with mild arteriosclerosis and hypochondriasis. She

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had twelve treatments in July and August, 1942, with six *grands mals*. She was discharged from hospital in September, 1942. During the treatment she complained that she could not remember the addresses of her son and of other near relatives, nor the details of her financial affairs. Seen 18 months after the end of treatment, she admitted that her memory still lets her down. She also finds that her memory fails her mainly in familiar matters, such as placing people who seem to know all about her, thus embarrassing her. A striking example was that—"The other day I went to see some relatives. I have been there a lot and I know the house very well. I wanted to go to the lavatory and I went upstairs and could not find it. I had forgotten that it was on the ground floor." She, too, said that her memory repeatedly failed her, but she could not remember all the incidents. Her memory had improved for about nine months after treatment, but had since been stationary. "I do not think about it much because it is so much better, but it used to worry me a lot."

CASE 4.—Married female, aged 45, admitted with agitated melancholia. She had a full course of electro-therapy in March and April, 1942, and was discharged recovered a month later. When she left hospital she was still complaining of some impairment of memory, particularly failure to remember place-names and addresses. This improved after a few weeks. She was readmitted in December, 1942, again in an agitated, depressed, and auto-accusatory condition. She still complained of some failure in memory, but this was thought to be due, not to her previous treatment, but to her preoccupation with somato-psychic delusions. Fourteen electric treatments were given between December 17, 1942, and January 4, 1943, of which only two produced *grands mals*. She was discharged recovered on January 6, 1943, and has remained well since.

On her return home she found her memory to be so bad that it worried her considerably. She found she could not recall how to cook dishes with which she was very familiar, and had to refer constantly to the cookery book. She could not remember where she had been accustomed to put things in her kitchen. She also complained of inability to remember names of places and persons, where she had met people, and so on. It must be remembered that she had been in hospital on the second occasion for only five weeks and that she was now cheerful and composed, and, although worried, quite ready, if the worst came to the worst, to accept this disturbance of memory as the price of her recovery. Matters improved in the next six months; but a year later she was still having difficulty with her memory. She wrote in January, 1944: "I find that my memory is now quite good for all practical purposes. I have accepted the fact that there are one or two apparently *permanent* blanks, but these do not hinder me from efficiently carrying out my daily duties. On occasions minor embarrassments have occurred, but, being well, I have been able to laugh them off. Perhaps I make more written notes of things than I used to, but I believe this is mostly necessary as one gets older." Pressed for further details she wrote: "Regarding the blanks I can only explain by giving one or two examples. I originally had a very good memory for places and people. About two years ago we moved into this house. I have not the slightest recollection of taking it over, or seeing it beforehand. Although detailed measurements in my own handwriting were produced, it awakened not the slightest chord of memory. Occasionally I concentrate in a determined manner, but so far can remember nothing more. Facing me on the opposite side of the road is the house I moved out of. I have entirely forgotten the layout of the upper part of the house, but know the lower floor perfectly. Three years ago (approximately) I undertook a journey to enter hospital for an operation on the rectum. I have a great interest in travel, yet I can remember nothing of the journey, the building, or the return home. I have just a memory of a painful recovery after the operation, and, as I progressed, a daily bath taken in a surprisingly rusty bath. I was not worried when I set out, and it was not my first operation and I can remember every detail of previous ones. There are many faces I see that I know I *should* know quite a lot about, but in only a few cases can I recall incidents connected with them. I find that I can adjust myself to these circumstances by being very careful in making strong denials, as fresh personal incidents constantly crop up. I do not worry over it, and find that I can manage very well, and am quite efficient in carrying out my duties. I am bright and alert, and see no reason to be concerned about patchy memories of the past." By "being careful in making strong denials" she means that although she may not remember people who meet her and claim to know her, she does not therefore deny their acquaintanceship.

CASE 5.—Widow, aged 41, suffering from anxiety neurosis. This woman, an out-patient not admitted to hospital, had seven treatments with five *grands mals*, the last early in March, 1943. Following this she was enormously improved, but complained that she was very forgetful. A year later she still cannot rely on her memory. In a letter she says: "The following are some of the things I forget: The names of people and places. When the title of a book is mentioned I may have a vague idea I have read it, but cannot recall what it is about. The same applies to films. My family tell me the outlines and I am able to recall other things at the same time. I forget to post letters and to buy small things, such as mending and toothpaste. I put things away in such safe places that when they are wanted again it takes hours to find them. This is not very clear, I am afraid, but it is difficult to explain. It did seem as if after the electric treatment there was only the present and the past had to be recalled a little at a time." She is positive about the disturbance of her recall for place-names. A much travelled woman, she used to be able to recall the places that she had visited very clearly in detail and by name. Now she finds this very difficult. An interesting point she made is that her memory improved when her daughter was called up, thus lessening her household responsibilities. During her daughter's

12, with six *grands mals*. She was discharged from ment she complained that she could not remember ives, nor the details of her financial affairs. Seen nited that her memory still lets her down. She amiliar matters, such as placing people who seem

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week-end leave, when responsibilities and calls on her memory returned to their previous level, she again exhibited defects on which her children commented before she herself noticed them. She is not unduly worried by her disturbance and, like patient No. 4, willingly accepts it as the price of her improvement.

More patients could be quoted, but I have deliberately selected only from those who are fully recovered from their other symptoms, out of hospital, and whose statements cannot justifiably be accounted for by depression, feeling of inadequacy, disturbance of the stream of thought or other such psychotic or neurotic abnormalities. Only one patient had arteriosclerosis and that mildly, and none was at an age when it could be argued that incipient senile dementia was revealed with the passing of more striking psychotic or psycho-neurotic symptoms. Further, most of the statements were made, not as complaints, but as items of interest. The similarity of the statements is also convincing.

The memory disturbance seems to be mainly in connection with long-known familiar material, particularly names of persons and places and habits of work. Three of the patients make the point that they have to observe themselves carefully or to make notes so as not to forget to perform, or that they have already performed, routine items of their daily work. Here, again, long-known familiar material is involved. Another prominent feature is the difficulty the patients have in explaining or illustrating their loss, perhaps because every-day trivialities are for the most part affected.

These observations, if confirmed, have implications. Even though the impairment of memory for the most part affects trivialities and is one to which an otherwise well patient can adjust, it necessarily imposes a mental strain. It also contra-indicates electro-therapy in those, for example teachers and transport workers, in whom inability to remember names of persons and places may seriously impair working capacity. Finally, it implies permanent, or semi-permanent, damage to the brain which, as Grinker hints, may later have untoward consequences.

It is a pleasure to thank Dr. R. Ström-Olsen, Physician Superintendent of Runwell Hospital, for his interest in these cases and for his permission to quote them.

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ANNALS OF THE NEW YORK ACADEMY OF SCIENCES

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## ELECTROCONVULSIVE THERAPY<sup>a</sup>

Clinical and Basic Research Issues

Editors and Conference Organizers

SIDNEY MALITZ and HAROLD A. SACKEIM

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## The Cognitive Side Effects of Electroconvulsive Therapy<sup>a</sup>

### 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).

<sup>a</sup>The preparation of this paper was supported in part by National Institute of Mental Health Grant No. MH 35636.

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

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one immediately following the treatment. Differences in orientation for the two 12-item questionnaire, report additional sine-wave stimulation over the course of treatment, and differences are reported by. Use of low-dosage treatment, stimulation effects for the bilateral in orientation times for the treatment. It is possible that decreases in seizure durations and time to orient were

that the therapeutic seizure were amount of energy needed to elicit more than that needed to elicit a amount of energy might have a effect. This associates report in this cognitive impairment than does benefit. Using a wide variety of that stimulus waveform has modality, although modality in groups.

energy applied to the brain that not in excess of an individual's need to develop a procedure for the amount of energy applied. Irritation in both immediate and no evidence for cumulative postictal orientation time or associated with the low-dosage unilateral treatment was not bilateral treatment, despite the fact appeared to be equivalent.

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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