Review

Memory Functions as Affected by ECT

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There are some issues that invite continuing disagreement. For example, certain empirical questions about electroconvulsive therapy (ECT) that seem at first glance rather simple to answer by experiment are still widely debated. Does ECT permanently impair memory? Memory impairment is a weighty issue because it is central to all discussions of adverse effects of ECT. From the patient's point of view, memory impairment is the most prominent and troublesome adverse effect of ECT. Moreover, neuropsychological tests that quantify memory impairment are extremely sensitive to brain injury.

The purpose of this chapter is to summarize what has been learned about ECT and memory loss. Specifically, how severe is the memory impairment, and how long does it last? Readers are invited to consult a number of recent reviews that consider these issues in somewhat more detail (1-4). The discussion here focuses in turn on anterograde amnesia (loss of the ability to accomplish new learning), retrograde amnesia (loss of memory for events that occurred before ECT), and memory complaints. Pertinent information will also be reviewed concerning the difference between bilateral and unilateral treatment. The discussion concerns the effects of a typical course of treatment, i.e., 6-12 treatments, and it is based primarily on studies in which ECT was given with a device delivering sine wave current. Recently, it has been reported that the cognitive side effects

associated with ECT can be reduced by using brief pulse stimulation instead of sine wave stimulation (see 5, 6). This issue will be touched on at the end of the chapter.

Memory loss following ECT is a selective neuropsychological impairment. It has been known for a long time that injury in either of two areas of the brain leads to an amnesic syndrome. The medial temporal region, including the hippocampal formation and the amygdala, and the diencephalic midline, including the dorsomedial nucleus of the thalamus and the mammillary bodies, have been most often implicated in the disorder (7-9). Amnesia is a circumscribed deficit that includes both anterograde and retrograde amnesia, in the absence of other defects of cognitive function. For example, amnesic patients can have intact intelligence test scores, intact language and praxic functions, and normal premorbid personality.

After the initial confusional period lasting approximately 30 minutes after each seizure, the memory loss associated with ECT resembles this classical picture of amnesia. It can be severe, and it occurs against a background of good performance on many cognitive tests that tap areas of function other than memory. The amnesia is particularly well circumscribed during the first several treatments as other cognitive impairment can appear later in the treatment course (3, 10). For these reasons, it seems reasonable to think that ECT is having a particularly strong impact on the brain structures that have been linked to

amnesia. This same point has been made previously (13), with emphasis on the medial temporal region and the fact that the hippocampal formation has a very low seizure threshold.

Anterograde amnesia. The anterograde amnesia associated with ECT diminishes between treatments and cumulates across treatments. During the first few hours after each treatment, and particularly after a few treatments have already been given, the anterograde amnesia can be as severe after ECT as in other conditions of amnesia--for example, in the amnesia associated with the alcoholic Korsakoff syndrome (12). In a test of paired-associate learning, which asks subjects to learn 10 new associations (e.g., army-table), normal control subjects remembered an average of about 5 of the pairs after one presentation of the list and 8 to 10 of the pairs after three presentations. In contrast, amnesic patients, including patients tested two hours after the fourth bilateral ECT, had great difficulty remembering any of the pairs and averaged about 2 pairs correct after three presentations of the list.

It is easy to document the recovery of new learning ability that occurs between each treatment. In one study lists of 10 words were presented to patients at each of four intervals (45 min, 65 min, 85 min, and 9 hours) after the fourth or fifth treatment (13). Memory was tested 15 minutes after each list presentation by multiple-choice method. Over the intervals tested, performance improved from an initial level that was no

better than would have been achieved by chance to a level of about 8 correct words out of 10. This marked initial deficit was observed only for patients receiving bilateral ECT. Patients receiving right unilateral ECT achieved 8 to 9 words correct at all test intervals. A group of depressed patients not receiving ECT averaged 9.5 words correct.

Although the verbal memory impairment associated with right unilateral ECT is considerably less than that associated with bilateral ECT, the advantage of right unilateral ECT is not so great when so-called non-verbal memory tests are used. These tests assess the learning and retention of faces, nonsense shapes, spatial layouts, and other material that is difficult to encode in words. It is known that memory for such material depends on the integrity of the right temporal lobe (14). Memory for this material is also affected by right unilateral ECT more than verbal material is affected (6, 15).

Once the course of ECT is completed, the capacity for new learning begins to recover. The point at which new learning ability reaches normal levels is difficult to identify exactly, and estimates will vary depending on the sensitivity of the test used to assess memory. One reviewer (16), considering a large number of studies, found an average return to baseline functions after 72 days. There are two ways to determine baseline. One way is to obtain pre-ECT performance scores. These scores, however, might have been lowered by the depressive illness for

which ECT was prescribed, and follow-up scores might therefore have to exceed this baseline by some unknown amount before they can be called normal. Another way to estimate baseline functions is to compare patients who have received ECT to other similar patients who have not received ECT.

In the past several years, studies have used both these methods. Testing instruments have included sensitive delayed recall tests, whereby subjects are asked to produce, without the help of cues, information that had been presented to them up to two weeks earlier. One test asked subjects to recall information that had been presented to them incidentally two weeks earlier, and which they had not been told would be later tested (17). The results from these studies (cf. 2, 5, 16, 17) have been quite consistent. Anterograde amnesia following bilateral ECT seems to have recovered by 6 months after treatment, and there is no good evidence that new learning ability is still deficient at this time. Presumably, once treatment is completed, recovery occurs gradually in a negatively accelerated fashion over a period of many weeks.

Retrograde amnesia. Remote memory for events that occurred before ECT can be evaluated either by tests that ask questions about public events, which are verifiable because the events were in the news, or by tests that ask about past autobiographical events. The latter are often difficult to verify, but the method has the advantage that a large amount of information can be

obtained from single subjects. One method for assessing public events that has been useful in evaluating the effects of ECT has been to ask about former television programs that had been broadcast for only one season during the past fifteen years (18). When tested by multiple-choice methods or by sensitive recall methods that asked for details about the programs, patients receiving bilateral ECT initially exhibited a temporally-limited gradient of retrograde amnesia. That is, shortly after the fifth treatment memory was lost for programs that had appeared one to three years previously, but unaffected for programs that had appeared longer ago. This impairment gradually subsided during the weeks after treatment and was not detectable six months later (19). Right unilateral ECT has considerably less effect on remote memory than bilateral ECT. As measured by the multiple-choice method, memory for past television programs was not affected at all in patients prescribed unilateral ECT, even as early as one hour after the fifth treatment (20).

Autobiographical memory after ECT was first evaluated systematically by Janis and co-workers in the early 1950s (21, 22). In his studies, patients who received 20 bilateral treatments later seemed to forget autobiographical information that had been reported successfully by the patients before treatment. This retrograde amnesia was present at four weeks after the treatment course, and was still present at 10-14 weeks after treatment in a subgroup of 5 patients who were followed

further. In view of the fact that the severity of retrograde amnesia following ECT is related to the recency of the to-be-remembered event, it seemed important to replicate the study by Janis and to include measures of the time period to which the tested material belonged.

In our study (19) patients prescribed bilateral ECT were asked 10 questions about their personal history, which covered the period from elementary school (name the teachers in your first six grades), to the period just prior to hospitalization (tell me everything you can remember about the day you came to the hospital for your present admission). The latter question concerned an event which had occurred from 2 to 36 days before the first ECT (mean = 11 days). These questions were given before ECT, shortly after ECT, and 7 months after ECT to 10 patients prescribed bilateral ECT. A group of 7 hospitalized depressed patients not prescribed ECT were also tested at equivalent intervals.

The results were that both the patients prescribed ECT and the control patients reported a large number of autobiographical details on their first testing session (about 58 details for each ECT patient and 62 details for each control patient). Following ECT there was a sharp reduction in the number of facts that could be recalled. At the follow-up period, seven months later, the ECT and control patients once again performed similarly. Thus, when all 10 questions were considered together, there was

no indication for a persisting deficit in remote memory.

However, a persisting impairment was present nonetheless, and this became apparent when the results were tallied separately for three of the 10 questions that asked about relatively recent events. One of them, the hospital admission question, concerned an event that had occurred 11 days before treatment, another question concerned an event that had occurred 6 to 37 months before ECT, and a third question concerned an event that had occurred 14 to 19 months before ECT. Control subjects recalled an average of about 13 details concerning these three events at the time of the pre-ECT test and recalled almost as much information seven months later, without intervening ECT. The ECT patients initially recalled a little more information than the control patients about these same three events (about 16 details per person). However, 7 months later they forgot much of what they had previously reported and now recalled only 7 details per person. The great majority of this forgetting applied to the most recent event, i.e., the question about hospital admission.

When patients did not volunteer information that they had recalled before ECT, the omitted detail was given to them and they were asked whether or not it was familiar. This procedure was 71% effective for ECT patients and 100% effective for control patients. The information that was not recognized by ECT patients after the reminding procedure belonged mostly to recent time periods. Thus approximately 3.5 details per person from the

hospital admission question were regarded as unfamiliar at the follow-up test, 1.0 details per person from the other two recent-event questions, and 0.5 details per person from all the other questions together. These results provide evidence that information about recent events can be lost for a long time, possibly permanently, after bilateral ECT. These data are also compatible with a large literature concerning the effects of electroconvulsive shock (ECS) on memory in rodents, which show that retrograde amnesia is temporally-graded and that the most recent events are the most vulnerable (23). Although these retrograde effects have typically extended only to the seconds or minutes preceding a (single) ECS, retrograde amnesia in mice can affect memories acquired one to three weeks previously when four, spaced ECS are given (24).

It is not yet clear how to evaluate the finding that at seven months after treatment persons who had received bilateral ECT occasionally failed to recognize as familiar even remote events that had occurred many years ago. Specifically, 5 of the 10 persons in our sample denied familiarity to a total of 18 remote events that they had reported as facts before ECT, seven months earlier. Unfortunately, it was not possible to verify these pre-ECT reports, so it is not certain that the autobiographical information obtained was always accurate. If it was not accurate before ECT, of course, subsequent failure to recognize the material as familiar cannot be taken as evidence

for forgetting. On the other hand, it is not clear why ECT patients would be more likely than control patients to report inaccurate information. There is also another complicating aspect of these data. It is well known that subjects' reports of familiarity about a previously encountered item is determined in part by a subject's "response bias," quite independently of the strength of that item in memory. Perhaps ECT patients were more cautious than control patients. Future studies could use multiple-choice tests and verified material to determine whether long-lasting memory loss can actually occur after ECT for information acquired in the distant past.

Memory complaints. Many patients who have received ECT continue to report even several months after treatment that their memory is not as good as it used to be, and they attribute their memory problem to the ECT experience (25-27). When these reports of poor memory were evaluated with a self-rating scale (25), two important points emerged about the nature of memory complaints. First, memory functions were rated considerably better six months after bilateral ECT than one week after treatment. In this respect, the reports were viridical, because it is known that memory functions do improve during this interval. Second, the quality of the memory complaints seven months after ECT suggested that the patients may have persisted in interpreting their memory abilities just as they had experienced them shortly after ECT. That is, there could have been continuing doubts that memory had

fully recovered and a tendency to refer even normal failures of memory to the ECT. It is also possible that the complaints refer, at least in part, to the lacuna in memory that exists for the time period immediately around the treatment. As patients recover from anterograde amnesia, they do not recover the memories for events that occurred during the period of anterograde amnesia. In addition, persisting memory loss does occur for events that immediately preceded the treatment course.

In a later study, 31 patients who had received bilateral ECT were asked three years later to indicate the portions of past time period that they had trouble remembering (26). The median response was an anterograde amnesia of two months and a retrograde amnesia of six months. The anterograde amnesia is presumably related to the ECT and appears to be an accurate assessment of missing memories. The retrograde amnesia may also be accurate, but it is not clear how much of it should be related to the ECT and how much to the depression that led up to the ECT. The same patients, three years earlier, had indicated before ECT that it was difficult to remember the previous five months. These results show directly that persisting memory complaints are in part directed toward the lost time period around the treatment.

The difference between bilateral and unilateral ECT, noted in formal tests of anterograde and retrograde amnesia, is also reflected in the self-ratings. In contrast to patients

prescribed bilateral ECT, who report markedly reduced memory functions one week after treatment, patients prescribed unilateral ECT do not report that memory is more impaired after treatment than before. However, depressed patients who had not received ECT actually reported significantly improved memory functions during this same interval, so it is possible that unilateral ECT also causes memory complaints. A study involving randomized assignment to ECT and non-ECT groups, where the role of pre-existing group differences could be controlled, would be required to settle this issue.

Discussion. The effects of ECT on memory functions can be summarized in the following way. Patients who receive ECT have impaired memory. Eventually, and certainly by 6 months after treatment, they perform as well on new learning tests and on remote memory tests as they performed before treatment and as well as other patients who have not received ECT. However, information acquired during the days and weeks prior to and following ECT may be permanently lost. Bilateral ECT affects memory considerably more than right unilateral ECT, and this difference is reflected as well in patients own reports of their memory functions.

An important new finding is that the use of brief-pulse stimulation instead of sine wave stimulation can reduce the memory impairment still further, beyond the reduction achieved by using right unilateral sine wave instead of bilateral ECT sine

wave (5). Brief pulse stimulation can elicit a seizure with approximately one-third the electrical energy produced by conventional sine-wave current, and this difference in electrical energy (e.g., about 22 joules vs. about 60 joules) probably accounts for its advantage. Interestingly, two previous studies of memory and ECS in animals failed to demonstrate any role for total electrical energy in determining the severity of amnesia (24, 28). As recently as 1982 (3) review articles of ECT could fairly conclude that waveform was probably not an important factor in determining the severity of memory dysfunction.

It is worth emphasizing that reduction of memory impairment by using pulse stimulation may be expected to occur only when the available parameters on the MECTA machine, the most common device in use that delivers brief-pulse stimulation, are set correctly, i.e., so as to optimize seizure induction, but not to exceed seizure threshold by too much. On the one hand, Sackheim and colleagues (6) report that a carefully titrated course of right unilateral, brief-pulse ECT, designed to be as close to seizure threshold as possible, did not achieve good therapeutic efficacy. On the other hand, Weiner and his colleagues (5) report good efficacy with parameters set, on average, as follows: frequency = 60; pulse width = .75 msec; pulse duration = 1.25 sec, for a total of about 22 joules of energy. If maximum dial settings are used to deliver brief-pulse stimulation (2.0 sec duration and 1.5 msec pulse width), the total number of joules increases from 22

to 70, and the energy advantage of pulse stimulation over conventional sine wave stimulaion is lost. Since the parameters must be selected individually for each patient, and since there is considerable variability in seizure threshold among patents, special care may be needed when using the MECTA machine to obtain the full energy advantage without missing seizures or otherwise compromising efficacy.

In any case, it does now seem possible to deliver a therapeutically effective course of right unilateral ECT using brief-pulse stimulation; and to produce less memory impairment than with right unilateral sine wave and markedly less impairment than with bilateral sine wave. It is not yet certain how to characterize the level of memory impairment associated with brief-pulse stimulation. The relative rankings of the four treatment combinations can be given in order of increasing memory impairment: unilateral pulse, unilateral sine-wave, bilateral pulse, bilateral sine wave (5). Moreover, the general conclusions summarized here, i.e., regarding the impairment associated with bilateral sine wave treatment, presumably apply as well to each of the other treatment combinations, but the severity of the effects on memory and the time needed for recovery are different for each combination.

It is not known whether a similar or different story must be told for patients who have received large numbers of ECT (e.g., more than 50). It is not known whether the persisting report by

patients of memory difficulty after ECT refers entirely to problems in remembering events that occurred close to the time of treatment. The perception of memory difficulty could in part refer to a subtle compromise of memory functions, but one that would show up only on a test instrument more sensitive than any yet devised. Alternatively, a sense of continuing memory problems might occur because persons who have made a gradual recovery from amnesia tend to doubt that they are fully recovered. We all occasionally have faulty memories. How can we know when memory failures are normal and when they might be attributable to a previous course of ECT? It is not known to what extent persons in this circumstance could be helped by continued consultation or reality testing after ECT, or whether such a perception would be so resistant to change that it must be considered an important cost of ECT. These and other questions remain, but science can address them all.

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