Retrograde Amnesia and Bilateral Electroconvulsive Therapy

Long-term Follow-up

Larry R. Squire, PhD; Pamela C. Slater; Patricia L. Miller

• **Memory for past events was assessed in 43 patients who had been prescribed bilateral electroconvulsive therapy (ECT) for relief of depressive illness. Four memory tests of personal or public events were administered before ECT, shortly after the fifth treatment, one week after completion of treatment, and about seven months later. The results indicated that ECT can initially disrupt recall of events that occurred many years previously, but recovery of these memories was virtually complete by seven months after treatment. It was also clear that persisting memory loss for information acquired only a few days before treatment can occur. For information acquired one to two years prior to treatment, recovery was substantial, but the results suggested that some memory problems might persist for events that occurred during this time period.**

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Electroconvulsive therapy (ECT) is considered one of the most effective treatments for relief of depressive illness.[1-2] The memory impairment associated with ECT has long been recognized as its major side effect, and several reviews of ECT and memory loss are available.[3-6] Memory dysfunction is greater after bilateral ECT than after right unilateral ECT,[7] wanes gradually after each treatment,[8] and is cumulative across treatments.[9,10] As measured by tests of the capacity to learn new material, memory functions gradually improve after treatment is completed.[6,11,12] In a recent study, performance was normal at six to nine months after bilateral or unilateral ECT on five different tests of the capacity to learn new material.[13]

However, it is possible that tests of remote memory could reveal persisting effects of ECT not detected by tests of the ability to learn new material. For example, in their classic study of traumatic amnesia, Russell and Nathan[14] noted that memory for pretrauma events could still be recovering after the capacity to learn new material had recovered to normal levels. Electroconvulsive therapy can affect memory for events that occurred years before treatment,[15-17] but objective tests of remote memory have rarely been administered long after ECT to determine the rate and extent of recovery. To our knowledge, only one study has prospectively followed up the effects of ECT on memory for the before-ECT period.[18] In this study, a defect in memory for autobiographical material was observed ten to 14 weeks after a course of bilateral ECT (mean, 17 treatments), but tests were not conducted to determine if this defect was reversible.

The present study investigated memory for past events on four occasions: before ECT, shortly after the fifth treatment, one week after the completion of treatment, and about seven months after treatment. Assessment of memory was conducted on each occasion with four different tests of remote memory that asked about personal or public events from the before-ECT period.

SUBJECTS AND METHODS

Four groups were constructed from a total of 43 psychiatric inpatients who had been prescribed a course of bilateral ECT at one of five local hospitals (Table). For group 4, a control group of seven psychiatric inpatients was included. For the ECT patients, the diagnoses recorded on admission by the patients' psychiatrists were severe depression (24 patients; this category included designations of psychotic depression, involutional melancholia, and primary affective disorder); manic-depressive psychosis, depressed phase (11 patients); depressive neurosis (six patients); schizoaffective disorder (one patient); and hysterical neurosis (one patient). For the control patients, the diagnoses were severe depression (five patients) and depressive neurosis (two patients). None of the patients in the control group was receiving ECT and none had received ECT in the past.

Patients with neurologic disorders, schizophrenia, or depression secondary to alcoholism or drug abuse were excluded. Twelve of the 43 patients had received ECT before, but none had received ECT within the previous 12 months. Decisions regarding the number of treatments and the prescription of psychotropic drugs during and after the course of ECT were made by the individual psychiatrists.

Electroconvulsive therapy was administered three times a week on alternate days after medication with atropine sulfate, methohexital sodium, and succinylcholine chloride. Treatments were given with 140 to 170 V (mean, 152.2 ± 1.9 V) for 0.5 to 1.0 s; electrode placement was bitemporal. In all cases, the attending physician reported that the current produced a grand mal seizure.

Test 1: Public-Events Recognition

This test has been described in detail previously.[10,19] A multiple-choice test of 50 items was prepared in three equivalent forms that asked questions about persons, places, or events that were in the news during the 1950s, 1960s, or 1970s. Each form contained 18

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From the Veterans Administration Medical Center, San Diego (Dr Squire); and the Department of Psychiatry, University of California School of Medicine, La Jolla, Calif (Dr Squire, Ms Slater, and Ms Miller).

Reprint requests to Veterans Administration Medical Center, 3350 La Jolla Village Dr, San Diego, CA 92161 (Dr Squire).

Subjects and Memory Tests					
Group	Test*	N	Age, yr, Mean (Range)	Sex	No. of Treatments, Mean (Range)
1	1. Recognition of public events, 1950-1975	15	43.3(28-65)	12 F, 3 M	9.1(5-13)
2	2. Recall of public events, 1950-1975	10	40.9(27-64)	10 F, 0 M	13.6(5-21)
3	3. Detailed recall of former television programs, 1967-1974	18†	42.1(23-62)	12 F, 6 M	9.8(5-21)
4	4. Recall of personal memories, 1925-1974	10‡	41.8(26-64)	8 F, 2 M	9.4(6-13)
4 (Control group)	4. Recall of personal memories, 1925-1974	7	41.0(24-55)	5 F, 2 M	...

*Patients were tested before electroconvulsive therapy (ECT), shortly after the fifth treatment, one week after ECT, and seven months after ECT.
†Two of these patients also took test 2.
‡Eight of these patients also took test 1.

questions about the 1950s, 16 about the 1960s, and 16 about the 1970s. During 1974 and 1975, 15 patients completed one form of test 1 one day before the first treatment, a second form one hour after the fifth treatment, and a third form one week after the completion of the treatment series (mean, 9.1 treatments; range, five to 13 treatments). The order of administration of the three forms was counterbalanced across subjects. Approximately seven months later (mean, 6.6 months), all three forms of the test were administered to the same 15 persons.

Test 2: Public-Events Recall

From the 150 questions on test 1, a representative subset of 74 questions was selected to form test 2, as described previously.[20] The wording of the questions was altered so that memory could be tested by recall rather than by multiple-choice. Two equivalent forms were prepared, each with 37 questions (12 for the 1950s, 12 for the 1960s, and 13 for the 1970s). During 1975 and 1976, ten patients received one form of test 2 one day before the treatment and the other form one hour after the fifth treatment. The order of administration of the two forms was counterbalanced. The same ten patients also received both forms of the test one week after treatment (mean, 13.6 treatments; range, five to 21 treatments) and again approximately seven months after treatment (mean, 6.9 months).

Test 3: Recall of Television Programs

Methods for constructing tests based on former, one-season television programs have been reported previously.[17,21,22] These tests were originally designed to permit an equivalent sampling of events from different time periods. The test used here involved 25 former television programs that were broadcasted for only one season from 1967 through 1974. Popular exposure to programs selected from three different time periods (1967 to 1968, N = 8; 1970, N = 7; and 1973 to 1974, N = 10) was estimated by the following viewing data provided by the A. C. Nielsen Co. From 1967 to 1974, the percentage of American households having a television set rose only slightly, from 94% to 97%. In American households having a television set, the percentage of time spent watching prime-time television did not vary from year to year by more than 2% during the period 1967 to 1974. Individual Nielsen ratings, which were provided for all of the programs in the test, indicated that the popularity of the programs selected from each time period had been quite similar ($F = 1.1$, $df = 2,22$, $P > .3$).

During 1975 and 1976, 18 patients were tested. At the time the test was administered, the three groups of programs used in the test had broadcast approximately one to three years, three to six years, and seven to nine years previously. Patients were given the name of each program and then were asked to tell about the plot, characters, and actors' names as well as about details of episodes that they could remember. The order of the programs on the test was random with respect to the time period that they were taken from. Responses were recorded, transcribed, and scored according to how many accurate details could be recalled. Trained raters have been shown to be highly reliable in scoring such interview and to vary less than 10% from each other in their judgment of th number of facts produced.[20] This test was administered before th first treatment, one to two hours after the fifth treatment, on week after the final treatment (mean, 9.8 treatments; range, fi to 21 treatments), and approximately seven months after th completion of treatment (mean, 7.4 months).

Test 4: Recall of Personal Events

This test was based on the pioneering studies by Janis and Jan and Astrachan that concerned ECT and memory for autob graphical material.[18,23] Prior to ECT, patients were asked a seri of questions designed to elicit detailed recall of personal memori and public events that had occurred in the recent and remote pa The questions asked patients to recall (1) the appearance of th elementary school, (2) the names of elementary-school classmat (3) the names of schoolteachers, (4) the names of high-sch classmates, (5) events of the day that President Kennedy w assassinated, (6) details about nine former television progra that were broadcasted for two years beginning in the period fr 1960 to 1970, (7) details about their most recent job, (8) events a names associated with the Watergate scandal, (9) events of t day from the Christmas before last (1973), and (10) events of t day on which they had come to the hospital for the pres admission. Responses to these interviews were recorded on ta transcribed, and scored according to how many accurate deta could be recalled, as was just described for test 3.

During 1975, these questions were given to ten patients, eight whom also took test 1. Testing occurred on three occasions: bef ECT, shortly after ECT, and about seven months (mean, months) after the completion of treatment (mean, 9.4 treatme range, six to 13 treatments). For six patients, the second testi occasion was scheduled one week after the completion of tr ment; the remaining four were tested six to ten hours after fifth treatment in the series. Results from these two test ti were quite similar and they were combined to demonstrate short-term effects of ECT. A control group (N = 7) of psychia inpatients who were not receiving ECT was also tested on th occasions. The average interval between their first and sec tests was four weeks. The average interval between their se and third tests was 7.3 months.

Previous studies of remote memory and ECT have indic that memories acquired a few years prior to ECT can be without the disturbance of older memories.[13-17] Accordingly, scoring purposes the first six questions were considered t questions about the remote past. These questions concer events that had occurred at least three years previously an average of 24 years previously. The last three questions about the more recent past. Thus, the eighth question concer events from the time of the Watergate burglary in June 197 about the time of President Nixon's resignation in August 1 For patients in this study, these events were six to 37 month at the time of ECT. Of course, some knowledge of this ma

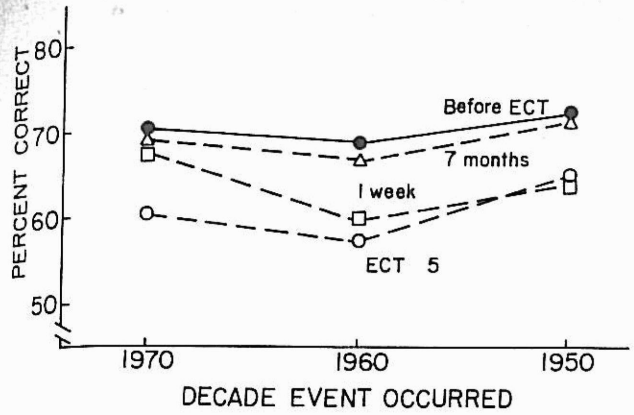

Fig 1.—Remote memory for public events that occurred from 1950 to 1975 was assessed by a four-alternative multiple-choice test (N = 15). Four tests were given in 1974 and 1975: before electroconvulsive therapy (ECT), after fifth treatment, one week after ECT, and seven months after ECT.

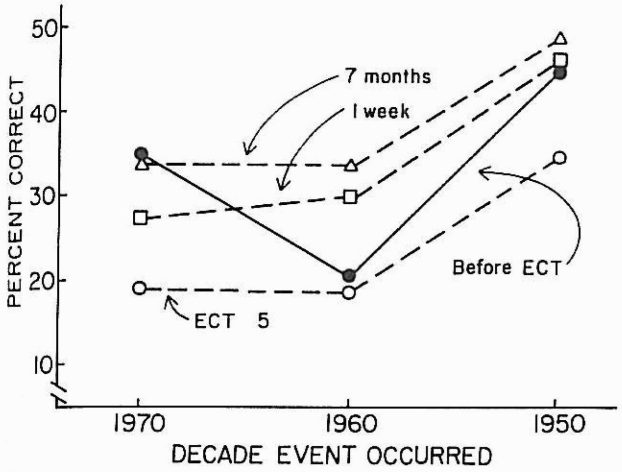

Fig 2.—Remote memory for public events that occurred between 1950 and 1975 was assessed by a recall test (N = 10). Four tests were given in 1975 and 1976: before electroconvulsive therapy (ECT), after fifth treatment, one week after ECT, and seven months after ECT.

could have been based on even more recent events since news coverage of Watergate personalities continued to some extent during 1975. The ninth question (Christmas 1973) concerned events that were 14 to 19 months old at the time of ECT. The tenth question (hospital admission day) concerned events that were two to 36 days old (mean, 11 days) at the time of ECT. Finally, the seventh question (most recent job) involved events that were recent for some patients and remote for others. Accordingly, results for the seventh question were excluded when remote memory and recent memory were considered separately, as will be discussed.

To score test 4, we used the total number of details elicited by the first interview as the before-ECT score. The scores for shortly after ECT and seven months after ECT were the total number of details elicited by the second and third interviews, respectively. These scores included details that had already been recalled during the first interview and also details that were elicited for the first time during the second or third interviews. When information recalled during the first interview was not spontaneously recalled in later interviews, patients were prompted with the omitted information and were asked whether it was familiar to them. Details recalled after this reminding procedure were scored as "reminded" and those still not recalled after reminding were scored as "omitted."

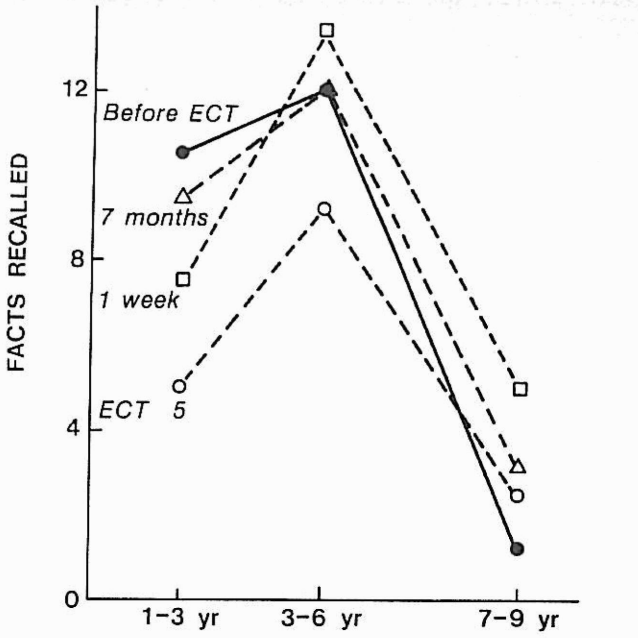

Fig 3.—Number of facts recalled about former television programs as function of how long prior to electroconvulsive therapy (ECT) programs were broadcasted. Scores are means of four tests (before ECT, after fifth treatment, one week after ECT, and several months after ECT) (N = 18).

Repeated Testing

Since subjects took the same forms of tests 1 through 4 on two or more occasions, we considered that performance might noticeably improve with repeated exposure to the same test material, particularly when only one or two weeks separated the testing sessions. To test this possibility, we gave tests 1 and 2 to control subjects (N = 10 for each test) on two occasions about two weeks apart. Performance was slightly improved on the second testing session (3.7% for test 1 and 8.0% for test 2). It seems unlikely that patients receiving ECT could have benefited by repeated testing, even to this small degree, since patients receiving ECT generally did not remember having taken the tests previously. To the extent that they did remember the tests, repeated testing would result in a slight underestimate of memory dysfunction shortly after ECT.

We also considered that patients receiving ECT might remember the tests taken one week after ECT well enough to affect their performance at the long-term follow-up six or seven months later. However, results for test 4, which will be described, indicated that even control patients did not exhibit a measurable influence of prior testing on performance at follow-up. Taken together, these considerations suggested that repeated testing exerted a negligible effect on the results and should not complicate their interpretation.

RESULTS

Test 1: Public-Events Recognition

Figure 1 shows the performance of patients who took the public-events recognition test. A 4 × 3 analysis of variance with repeated measures[24] revealed a significant effect of test time ($F = 4.0$, $df = 3,42$, $P < .02$). The Tukey test for individual comparisons[24] indicated that performance was significantly impaired shortly after the fifth ECT ($P < .01$) and was still impaired one week after ECT ($P < .05$). Seven months after ECT, performance was significantly better than after the fifth ECT ($P < .01$) and not measurably different from before ECT ($P > .3$).

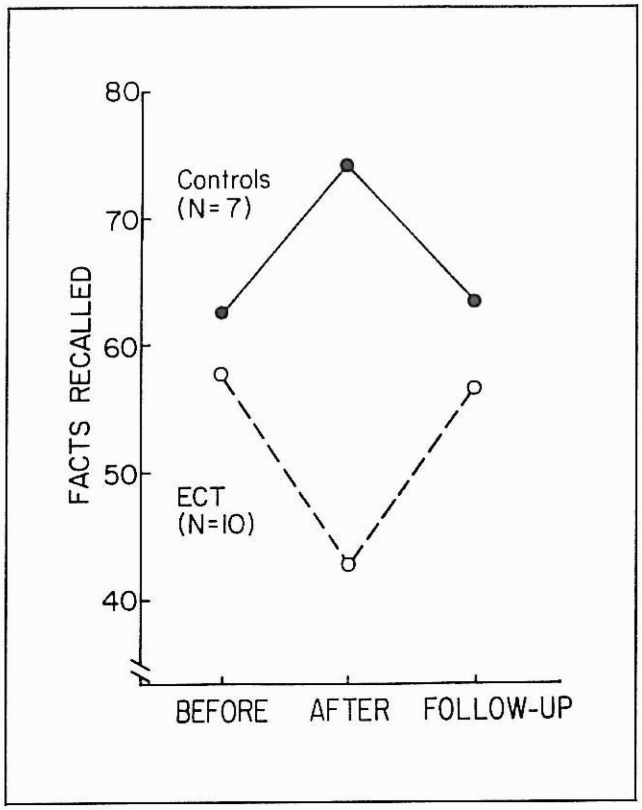

Fig 4.—Number of details recalled before electroconvulsive therapy (ECT), one to seven days after ECT, and at seven-month follow-up by patients in an interview about personal events that occurred from one week to 20 years previously. Control patients were tested at equivalent intervals.

Test 2: Public-Events Recall

Figure 2 shows the performance of patients who took the public-events recall test. A 4×3 analysis of variance showed a significant effect of test time on remote-memory scores ($F = 7.2$, $df = 3,27$, $P < .01$). Performance was significantly impaired shortly after ECT ($P < .01$) and had largely recovered by one week after ECT. One week after ECT, remote-memory scores were not significantly different from before ECT ($P > .3$), although scores for the 1970-1975 time period were still somewhat below the before-ECT level. By seven months after ECT, no defect in recall remained and performance was slightly better than before ECT.

Test 3: Recall of Television Programs

Figure 3 shows the performance of patients who took the television test. A 4×3 analysis of variance showed a significant interaction of test time and time period ($F = 5.3$, $df = 6,102$, $P < .01$). This interaction reflected the finding that ECT selectively affected recall of events that occurred one to two years prior to ECT without affecting recall of events that occurred prior to that time. For the 1973-1974 time period, recall was significantly affected shortly after ECT ($P < .01$). By one week after ECT, some recovery had occurred and the score for the 1973-1974 time period was between the before-ECT and after-ECT scores. By seven months after ECT, the ability to recall events from the 1973-1974 time period had recovered further and performance was significantly better than after the fifth ECT ($P < .05$) and not measurably different from before ECT ($P > .3$).

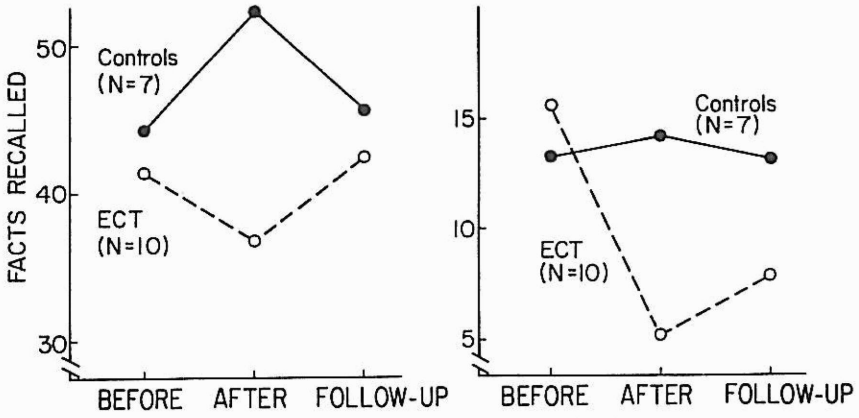

Fig 5.—Number of facts about remote (left) and recent (right) events remembered by patients who received electroconvulsive therapy (ECT) and control patients. Testing occurred before ECT, one to seven days after ECT, and at seven-month follow-up.

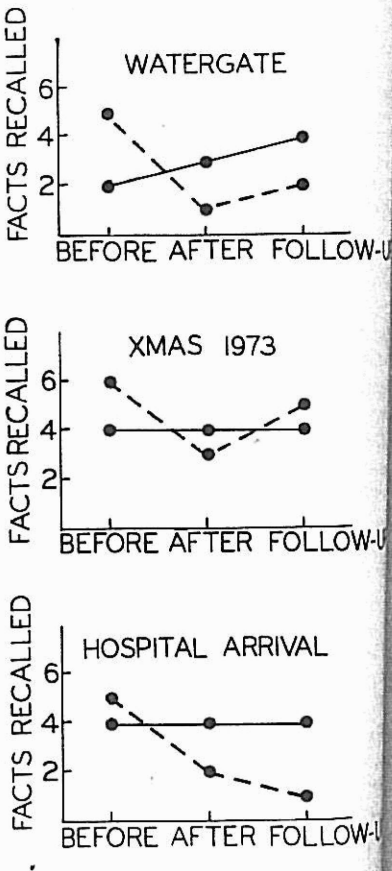

Fig 6.—Number of facts about three recent events recalled by patients receiving electroconvulsive therapy (ECT) (N = 10, dotted line) and control patients (N = 7, solid line). Testing occurred before ECT, one to seven days after ECT, and at seven-month follow-up. At time of first test, events were about one to 37 months old (Watergate), 14 to 19 months old (Christmas [Xmas] 1973), and two to 36 days old (mean, 11 days) (hospital arrival).

Figure 4 shows the scores of ten patients who received ECT and seven control patients on the ten interview questions about past events. For this test, medians have been used to describe the performance of the two groups. Before ECT, the patients receiving ECT and the control patients (who were not scheduled for ECT) recalled about the same number of details (patients receiving ECT, 58 details; control patients, 62 details; $P > .2$). Shortly after ECT, the patients who had ECT recalled significantly fewer details than they had recalled originally (58 vs 43, $P < .05$). Control patients, who were tested after an equivalent interval, recalled a greater number of details than they had recalled originally (62 vs 74, $P < .05$). This increase in recall by control patients apparently reflected a facilitatory effect of the first interview on subsequent recall. Thus, because they had the experience of recalling information about past events during the first interview, control patients were later able to recall most of this material (ie, 89% of previously recalled details) and to add more material. By contrast, after ECT, the patients treated with ECT recalled only 64% of the details from their first interview and recalled little additional information. Note that if ECT had caused memory loss for only the first interview itself, then the total after-ECT score should have been about the same as the before-ECT score. Since recall was significantly poorer after ECT than before, ECT clearly produced a loss of memory for past events.

During the third interview several months later, both control patients and patients treated with ECT recalled about the same number of details that had been recalled originally ($P > .2$), and the scores of control patients and patients treated with ECT were not significantly different from each other ($P > .2$). Thus, when all ten interview questions were considered together, persistent effects of ECT on memory were not observed.

Figure 5 shows scores separately for six questions concerning remote events and for three questions concerning more recent events that occurred from one week to about three years before ECT. Memory for remote events (Fig 5, left) was slightly poorer shortly after ECT than before, but this difference was not significant ($P > .1$); seven months after ECT, performance was close to the before-ECT level (40 vs 42). By contrast, memory for more recent events (Fig 5, right) was markedly affected by ECT, and this deficit was still present seven months later (before ECT, 15.5 details; shortly after ECT, 5.5 details; seven months after ECT, eight details; before-ECT score vs follow-up score, $P < .01$). Thus, when the three questions about more recent events were considered alone, long-lasting effects of ECT on memory could be observed.

To evaluate further this long-term effect of ECT, the results for each of the three questions about recent events were examined separately. Figure 6 shows that persisting memory loss for the day of hospital admission, which was two to 36 days prior to ECT, accounted for much of the evidence for the long-lasting effects of ECT. Seven months after ECT, recall was poorer about this event than it was before ECT ($P < .05$). In addition, the follow-up score for the group treated with ECT was significantly lower than the corresponding score of the control group ($P < .02$). Figure 6 also shows that some memory loss seemed to persist for events of the Watergate scandal. Seven months after ECT, patients recalled fewer details about Watergate than they had recalled before ECT (five details before ECT vs two details long after ECT, $P < .05$). Finally, Fig 6 shows that ECT patients experienced no lasting memory loss for events of the Christmas before last (six details before ECT vs five details long after ECT, $P > .2$).

Test 4: The Reminding Procedure

During the first interview, a total of 599 details were recalled by the ten patients who received ECT and 498 details were recalled by the seven control patients. During the second and third interviews, none of the patients treated with ECT or the control patients recalled spontaneously all of the information that had been recalled previously. Whenever previously recalled information was omitted, this information was presented to the patients and they were asked if it was familiar (see the "Subjects and Methods" section). During the second interview, patients receiving ECT needed significantly more reminders than did control patients (median, 13 vs six reminders, $P < .02$). During the third interview six months later, patients receiving ECT needed reminders just as often as control patients (median, 7.5 vs 7.0 reminders, $P > .2$).

In most cases, patients recognized previously recalled information as familiar when given a reminder about it. For control patients, the reminding procedure was effective 100% of the time. For patients treated with ECT, the reminding procedure was effective 71% of the time. Considering all ten patients treated with ECT together, the reminder failed to elicit recognition on 120 occasions: 51 times shortly after ECT and 69 times long after ECT. Of these, 53% (25/51 and 38/69) involved failures to recognize previously recalled information about the day of hospital admission. That is, about half of the time that prompting did not elicit recognition of previously recalled information, the apparently forgotten material involved events that had occurred just a few days before treatment. This observation agrees with the results for free recall obtained from the period immediately prior to ECT (Fig 6, bottom), and suggests that events that occur in this time period can be lost from memory for a long time after treatment. Of the remaining occasions long after ECT when prompting failed to elicit recognition of previously recalled information, the circumstances were as follows: failure to recognize events from the Watergate and Christmas questions (13 occasions, three patients) and failure to recognize remote events (18 occasions, five patients).

It is clear that failure to recognize material when reminders were provided was considerably more frequent for recent events than for more remote events. Another way of making this point is to note that after prompting, patients receiving ECT failed to recognize a median of 4.5 events from the questions concerning the day of hospital admission, Watergate, and Christmas 1973 and a median of only 0.5 remote events ($P < .01$). Of the recent events, most of the recognition failures involved events of hospital admission day (median, 3.5 events). Taken together, the results from test 4 confirm and extend the observations of Janis.[18,24] Long-lasting, relatively subtle amnesias can occur after a course of eight to nine bilateral electroconvulsive treatments. These amnesias most prominently involve the period just prior to treatment.

COMMENT

This investigation was planned to assess how bilateral ECT affects memory for events that occurred before treatment. Four memory tests were administered before ECT, shortly after ECT, and several months after ECT. During the first week after treatment, memory dysfunction extended to events that occurred many years previously, and information acquired one week to two years prior to treatment was affected by ECT to a greater extent than information acquired many years before. Between one week and seven months after the completion of treatment, marked recovery of memory occurred. Recovery appeared to be substantially complete for information acquired many years previously (Fig 1 and 2). Recovery was also complete for some information that had presumably been acquired up to two years prior to treatment (Fig 3 and 6, center), although the results raised the possibility that recovery of some information acquired during this time period might be incomplete (Fig 6, top). Memory loss persisted for events that had occurred only a few days prior to treatment (Fig 6, bottom).

Depression

We cannot exclude the possibility that the fate of memories acquired just prior to ECT might have been influenced in part by the affective state of the patients prior to ECT. For example, patients in group 4 who were about to receive ECT could have been more depressed than control patients who were not scheduled for ECT and might therefore have acquired the details of the day of hospital admission (Fig 6, bottom) less efficiently than control patients. This possibility seems unlikely because before ECT the two groups of patients recalled nearly the same number of details about the day of hospital admission. Another reason for thinking that memory loss for past events after ECT was not strongly influenced by the length or severity of depressive illness is that retrograde amnesia after ECT varied from two years in one study[15] to about seven years in another study[16] depending simply on the memory test that was used and not on the nature of the illness. In addition, the finding here that memory loss was worse for events just before ECT than for events long before ECT is entirely consistent with findings from the study of head trauma[14] and from studies of convulsive stimulation in experimental animals[25] where the affective status of the subjects could not have contributed to amnesia. Nevertheless, until additional studies are done in which ECT and control groups are equated for length and severity of illness, it will be difficult to exclude the possibility that memory loss for past events after ECT might have some relationship to the depression that preceded ECT.

We also considered that persisting or remitting depressive illness might have influenced the memory-test scores obtained at follow-up. Whereas it is clear that depression can adversely affect performance on tests of ability to learn new material,[26,27] depression seems to have much less effect on the recall of past memories. In two previous studies, depressed psychiatric inpatients who were scheduled to begin a prescribed course of ECT scored as well on remote-memory tests as did their control groups.[15-17] Therefore, it seems unlikely that the memory-test scores obtained at follow-up were influenced by the affective state of the patients at the time of the test.

Psychotropic Drugs

We next considered that psychotropic drugs prescribed in addition to ECT might have influenced memory-test scores. We therefore compared results for patients who had been prescribed therapeutic doses of psychotropic drugs during their course of ECT (N = 23) with results for patients who either had not been prescribed drugs (N = 8) or who had been prescribed drugs at doses below therapeutic levels (N = 12). Accordingly, scores on tests 1 through 4 were converted to z scores, and t tests were used to compare group scores before ECT, shortly after ECT, and seven months after ECT. The ten patients who took more than one test were assigned the average of their z scores. For all test occasions before and after ECT, the 23 patients who were prescribed therapeutic doses of drugs performed nearly the same as the eight patients who were not prescribed drugs and also about the same as the 12 patients who were prescribed low doses of drugs ($t < 1.1$, $P > .3$ for all tests).

We also examined separately the results for test 4 (three questions about recent events) since these questions provided the only evidence for long-lasting effects of ECT on memory. Five of the ten patients who took this test had been prescribed therapeutic doses of drugs during their course of ECT and five had not. These two groups of patients did not differ from each other on any test occasion either before or after ECT ($P > .3$).

Finally, we considered that psychotropic drugs prescribed at the time of follow-up several months after ECT might have influenced the follow-up test scores. At follow-up, 28 patients were receiving therapeutic doses of prescribed psychotropic drugs, six were receiving drugs at doses below therapeutic levels, and nine were not receiving drugs. Patients who received therapeutic doses of drugs performed somewhat more poorly across all tests than patients who received low doses of drugs or no drugs ($t = 1.9$, $P < .1$). However, on the only test that provided evidence for long-lasting effects of ECT (test 4, three questions about recent events), patients who received therapeutic doses of drugs actually scored somewhat higher than the other patients (median, eight vs five facts recalled). Taken together, these analyses suggest that psychotropic medication did not contribute to memory problems.

Autobiographical Memory

Part of the objective of the present study was to assess memory functions before and after ECT by the method originally used by Janis.[18-24] Janis assessed memory for autobiographical material before bilateral ECT and again four weeks[24] or ten to 14 weeks[18] after a course of about 2 treatments. In these studies, patients frequently failed to recall material during the second test that had been recalled spontaneously before ECT. This material was sometimes not recognized even when memory cues were provided by the interviewer to elicit the missing information. When patients were able to provide an answer, those who had received ECT took longer than control patients to bring their answer to mind and their answers contained fewer details. It was concluded that ECT produced subtle disturbances in recall that long outlasted the temporary confused state.

These studies are unique in the literature of ECT and memory loss because they suggest that long-lasting, albeit subtle, defects in memory can occur after a course of ECT. In our study of memory for autobiographical material (test 4), we sought to replicate these observations and to assess three additional questions. (1) Are long-lasting memory defects present after a course of the eight or nine bilateral treatments, the average number typically used to relieve depressive symptoms according to contemporary psychiatric practice? (2) In the earlier studies, instances of amnesia were still present at the longest follow-up time, 14 to 16 weeks after ECT.[18] Are these defects in recall still present several months after ECT? (3) If there is persistent

amnesia, to what time period does the forgotten information belong? That is, does it involve the remote past or is it limited to more recent time periods?

The results of test 4 indicated that memory tests of autobiographical material can be a sensitive technique for assessing amnesia after ECT. Amnesia for events that had occurred before treatment was demonstrated, and this amnesia long outlasted the temporarily confused state. However, the seven-month follow-up indicated that memory had substantially recovered for events that had occurred long before treatment. Strong evidence for persistent memory loss was limited to events that had occurred a few days or weeks prior to treatment.

It is not clear how to best interpret the finding that patients who received ECT occasionally failed, even with prompts, to remember information that presumably had been learned long ago. We did not expect that at seven months after treatment patients who received ECT should ever have difficulty recognizing previously recalled information about remote events since the results from all four tests indicated that remote memory had fully recovered by this time. Yet, the results of the reminding procedure were that at seven months after ECT, five of the ten patients occasionally denied recognizing material about remote events that they had recalled spontaneously before ECT. By contrast, the seven control patients never failed to recognize information that they had spontaneously recalled during the first interview.

Although these results raise the possibility that persistent, subtle defects in memory after ECT can extend to remote memory in some patients, this conclusion cannot be a strong one. It is possible that patients who received ECT were less willing than control patients to acknowledge that a prompt was familiar. Alternatively, since material recalled during the autobiographical interviews was not corroborated, it is possible that during the first interview patients who received ECT made more errors in recall than control patients. Subsequently, they would not recall this material spontaneously and, because they had amnesia for the first interview, they would not recognize the reminders.

All of the conclusions just presented are limited, of course, to patients who receive an average of about nine bilateral treatments, and they in no way rule out the possibility that more severe or long-lasting cognitive impairment might result from a longer course of bilateral ECT (eg, more than 50 treatments[28,29]). These conclusions also apply only to bilateral ECT. Unilateral, nondominant ECT is known to be associated with less anterograde amnesia than bilateral ECT.[4-7] Although objective tests of memory for past events have rarely been given to patients receiving unilateral ECT, the available evidence suggests that unilateral treatment is associated with considerably less retrograde amnesia than bilateral treatment.[15,30]

To summarize, memory functions were assessed before and on three different occasions after ECT with four tests of memory that asked about personal and public events from the period before ECT. The results lead to the following general conclusions about ECT and memory loss: (1) memory for remote events that occurred many years previously can initially be disrupted by bilateral ECT, but memory for these events appears to be fully recovered seven months later; (2) memory loss for events that occurred only a few days before treatment persisted; and (3) memory for events that occurred during the period one month to two years before treatment was also vulnerable to ECT. Whereas it is clear that recovery of many of these memories can be substantially complete, the results raise the possibility that persisting loss might occur for some memories formed during this time period.

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significant side effect of neuroleptic treatment and may be associated with exacerbation of psychosis, anxiety, depression or even "abject terror" (1). The proper treatment of neuroleptic-induced akathisia can reduce positive and negative symptoms of schizophrenia in addition to the subjective experience of akathisia (1). Diazepam is reportedly effective in reducing symptoms of neuroleptic-induced akathisia in some patients with schizophrenia (2, 3); alprazolam might be expected to share this property.

Although an alprazolam-induced reduction in akathisia may conceivably have contributed to the marked therapeutic effects we observed in our schizophrenic patients, we feel it is unlikely that it fully accounted for the improvement we observed. Our patients were stabilized on a fluphenazine regimen for at least 4 weeks without reporting symptoms of restlessness, discomfort, or anxiety. No exacerbation of psychosis was observed following initiation of fluphenazine treatment; the patients showed clinically significant improvements on fluphenazine treatment compared with placebo alone. Further, our patients were treated with clinically appropriate doses of benztropine mesylate in conjunction with fluphenazine. Antiparkinsonian drug treatment has been reported to ameliorate neuroleptic-induced akathisia in approximately 50% of patients (4); however, in some patients diazepam may be more effective (3).

We would agree that future studies of the addition of alprazolam to standard neuroleptic treatment of schizophrenia should specifically evaluate akathisia as well as other extrapyramidal symptoms and should compare the efficacy of alprazolam with that of other benzodiazepines. Such studies are in progress in our laboratory.

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OWEN M. WOLKOWITZ, M.D.
DAVID PICKAR, M.D.
ALLEN R. DORAN, M.D.
ALAN BREIER, M.D.
STEVEN M. PAUL, M.D.
Bethesda, Md.

On Brief-Pulse Versus Sine-Wave ECT

SIR: I have long admired the unique ability of Larry R. Squire, Ph.D., to conduct high-quality research in a suboptimal setting. However, the recent paper from his laboratory, "ECT and Memory: Brief Pulse Versus Sine Wave" (May 1986 issue), written with Joyce A. Zouzounis, M.S., suffers from too many problems in method to go unchallenged. For example, assignment of subjects to treatment groups was nonrandom. Treatment electrode placements and stimulus waveforms were confounded. Nine patients were included who received treatment with both types of electrode placements. ECT stimulus settings were nonsystematic and varied according to the treating physician's preference. Patient impedances and, therefore, stimulus energies were estimated, not measured. Memory assessments were performed after unequal numbers of treatments. Unilateral ECT electrode placements were mostly nonstandard and varied systematically with stimulus type. Memory testing was apparently not performed blind to treatment assignment. Unlike sine-wave ECT, brief-pulse ECT was almost always administered at maximum dose, reducing the likelihood of finding a difference between methods. Treatment electrode diameters, which substantially affect electrical dose, varied systematically among treatment groups. Finally, for at least one critical comparison (paired-associate learning), the sample size appears to have been insufficient ($N=6$ in each group) to enable the investigators to reject the null hypothesis with adequate power.

Although described in the Method section of the paper, most of these problems were not considered in the Discussion, and none was noted in the précis. The unwary reader, therefore, may be misled by the prestige of both author and journal to accepting the conclusions of a seriously flawed study.

RICHARD ABRAMS, M.D.
North Chicago, Ill.

Dr. Squire and Ms. Zouzounis Reply

SIR: Dr. Abrams raises a number of concerns about the method of our study. However, many of them are not relevant to the study's main findings, and some of them miss the point of the study altogether. A written response to each of Dr. Abrams's points is available on request. In the space available here, we wish to discuss an important misunderstanding that has arisen about our study and its implications.

Contrary to reports by Dr. Weiner et al. (1, 2) from a research setting that brief-pulse ECT produces less severe memory impairment than sine-wave ECT, we found in a clinical setting that the two modes of treatment were identical except during the first hour immediately after the seizure. An examination of the machine settings used to deliver ECT suggested that the physicians who administered ECT in our study used higher settings than those used in the studies of Weiner et al. In particular, in the case of bilateral brief-pulse ECT, our physicians tended to use maximum settings for the three adjustable parameters (pulse width, duration of pulse train, and frequency). This resulted in an estimated energy level of 52 joules (J) for the average bilateral brief-pulse treatment, compared with about 25 J in the studies by Weiner et al. We interpreted our findings to mean that a memory advantage for brief-pulse ECT over sine-wave ECT is not likely to occur unless treatments are titrated individually for each patient and delivered closer to seizure threshold. At higher intensities, seizures may be more intense and more generalized, thereby attenuating or eliminating potential differences between ECT waveforms.

Dr. Abrams states that brief-pulse ECT was always administered at maximum dose in our study and that, in general, ECT stimulus settings were nonsystematic and varied according to the physician's preference. This was the point of the study, and he repeats what we wrote. We found that physicians were preferring to use maximum settings, especially for brief-pulse ECT. We do not make the generalization that brief-pulse ECT always produces memory impairment similar to that produced by sine-wave ECT. We conclude only that in clinical settings, if physicians choose to

deliver brief-pulse ECT in the same manner as did the physicians whose patients we studied, brief-pulse ECT is not likely to live up to its research promise of reduced memory impairment. This was a study of how ECT is given in clinical practice, not an evaluation of what brief-pulse ECT can potentially offer.

None of Dr. Abrams's other comments on method are relevant to our finding that bilateral brief-pulse ECT produced considerable memory impairment and that it was similar to bilateral sine-wave ECT with respect to its effects on memory. For example, electrode size and placement were variable only for unilateral ECT, whereas the study concerned primarily bilateral ECT. Eliminating the few patients who received unilateral ECT before receiving bilateral ECT scarcely changed the scores. The experimenter was blind to the hypothesis of the study, and, besides, we had the wrong hypothesis. Brief-pulse and sine-wave subjects were tested after the same average number of treatments in experiment 1 and after exactly five treatments in experiment 2.

One way to state our findings is to say that, whatever potential advantage brief-pulse ECT might have (so far as memory is concerned), evidence remains to be presented that this advantage can be achieved or is being achieved in clinical practice. In our article, we discussed our findings in the light of the research of Dr. Weiner et al. (1, 2), and we suggested what might be done in clinical practice so that memory impairment could be reduced.

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LARRY R. SQUIRE, PH.D.
JOYCE A. ZOUZOUNIS, M.S.
San Diego, Calif.

Voluntary Euthanasia and the Hemlock Society

SIR: I believe that James Henderson Brown, M.B., F.R.C.P.E., F.R.C.P.(C), and associates, in "Is It Normal for Terminally Ill Patients to Desire Death?" (February 1986 issue), have made some important misstatements about the voluntary euthanasia movement in general and about the Hemlock Society in particular. In the first paragraph of the article, the authors suggest that organizations such as Hemlock believe that "people facing serious life problems, especially people with painful, disfiguring, or disabling terminal illness, should be given encouragement and assistance in thinking of suicide as a rational solution."

Since its founding in 1980, the Hemlock Society has been candid in its belief that a decision to terminate one's life is an intensely personal one, to be made—where possible—in concert with family members, close friends, and a personal physician. Hemlock has never encouraged suicide for any primarily emotional, traumatic, or financial reason in the absence of a terminal illness. The Society has, in fact, been strongly supportive of suicide prevention services, helping individuals through depressive episodes unassociated with terminal illness. The Society has also been openly supportive of palliative care services, such as the hospice movement, as alternatives for many terminally ill people.

There is also an issue of method, not raised by the authors, which may have affected their findings. According to the article, the sample included terminally ill people already admitted to an inpatient palliative care service "organized on hospice principles." One might assume that such persons had already made a conscious choice among possible ways of dying. They may already have decided that suicide was an unacceptable option. With such a biased sample, it seems simplistic to conclude that a patient who had just committed himself to living as long as possible is depressed and mentally disordered if he subsequently considers terminating his life prematurely. It would be illuminating, I believe, to repeat the study with individuals diagnosed as terminally ill (death to occur within, say, 6 months or less) but who had not yet made judgments and commitments about various courses of action.

Finally, although there is little connection between the various criminal codes nationwide and *DSM-III*, many jurisdictions specifically exclude suicide as a label for actions that, in cases of terminal illness, shorten life by the voluntary withholding or withdrawing of life-sustaining procedures.

DAVID B. CLARKE, JR., D.MN., J.D.
Legislative Advocate
Hemlock Society
Los Angeles, Calif.

Dr. Brown and Associates Reply

SIR: We apologize for failing to emphasize that the Hemlock Society, in its literature, advocates voluntary euthanasia for terminal illness only and discourages suicide for other reasons. We had no desire to misrepresent the Hemlock Society. However, our study was specifically concerned with terminal illness, and, therefore, we believe that a specific reference to the Hemlock Society was appropriate. Also, although the Hemlock Society officially discourages suicide for other than terminal illness, not all its members seem to accept this message. In the survey published by the Society in 1983 (1), 74% of the respondents did not agree that life would be worth living if one were incapable of living outside an institution, 61% did not agree that life would be worth living in the absence of loved ones or close friends, and 84% stated that obtaining expert advice on *suicide* (our emphasis) and euthanasia was a very important reason for joining the Society.

We were not aware of support by the Hemlock Society for suicide prevention services and palliative care services. Such support is not mentioned in the literature we have seen, and we should be very grateful if Mr. Clarke could draw our attention to any published references in which such support is expressed.

Mr. Clarke is quite correct in pointing out that the members of our patient group were in a palliative care setting and might be assumed to be biased toward solutions other than voluntary euthanasia. They were, however, not completely self-selected, since patients are accepted into the unit only on referral by a doctor. Their bias was also relative rather than absolute, since 10 of the 44 patients in one way or another looked favorably or had looked favorably on early death. We agree that it would be illuminating to do further studies with groups of patients selected in different ways, and we hope that our paper will stimulate further research.

Mr. Clarke is, however, quite incorrect when he implies that we concluded that any patient is "depressed and men-