CHAPTER IV

ADVERSE EFFECTS OF ECT

Section I. *Memory and ECT*

Memory loss has long been recognized to be a prominent effect of electroconvulsive therapy (ECT). For a decade or two after the introduction of ECT, loss of memory was believed to contribute to ECT's therapeutic effect (1). Today the view is considerably different. First, several investigators have demonstrated that the extent of memory impairment is not correlated with clinical improvement (2, 3, 4). Second, following the development of right unilateral ECT (5), it became clear that this mode of convulsive therapy results in markedly less memory impairment than conventional bilateral ECT (6, 7, 8, 9). Yet right unilateral ECT is clinically as effective, or nearly as effective, as bilateral ECT (10). Accordingly, all available evidence supports the contention that memory loss is an undesirable side effect of ECT, not related to therapeutic efficacy.

Like the organic amnesias that result from head trauma (11), Korsakoff psychosis (12), diencephalic tumor (13), or temporal lobe dysfunction (14), the amnesia associated with ECT is both antero-

grade and retrograde. Amnesia occurs for the events prior to each seizure and an impairment in the ability to commit new events to long term memory is evident following each seizure. This impairment in learning new material diminishes gradually following each seizure (15) and is cumulative with successive treatments.

Several general reviews of the amnesic effects of ECT are available (16, 17, 18). This review will summarize the current evidence regarding the nature and extent of memory impairment. First, the anterograde amnesic effects of bilateral ECT will be compared to the effects of right unilateral ECT. Second, retrograde effects of ECT on remote memory will be reviewed. Third, the effects of extended treatments of ECT on memory will be summarized. Fourth, recent findings involving the reinstatement procedure will be described. Results with this procedure in animal studies suggested that learned material not ordinarily affected by electroconvulsive shock (ECS) may be forgotten if a reminder of the material is presented just prior to ECS (19, 20, 21). These reports raised the possibility that eliciting depressive ideation just prior to ECT could be therapeutically advantageous since ECT might produce amnesia for such ideation. Finally, memory capacity many months after ECT will be considered, in terms of objective and subjective estimates of ability.

Anterograde amnesia: bilateral vs. right unilateral ECT

It has been demonstrated that bilateral ECT produces a greater impairment of new learning capacity than right unilateral ECT (6, 7, 8, 9). Typically, however, learning ability has been assessed with verbal memory tests of the type particularly sensitive to dysfunction of the left cerebral hemisphere. The possibility has therefore remained that, if memory were assessed with nonverbal tests designed specifically to detect dysfunction of the right hemisphere, the amnesic effects of right unilateral ECT might be similar to or greater than the amnesic effects of bilateral ECT. In two studies of patients receiving bilateral or unilateral ECT (6, 22), impairment of "nonverbal" memory associated with bilateral ECT was slightly greater than the impairment associated with right unilateral ECT. However, in the absence of information about how patients with identified unilateral cerebral lesions would perform on these "nonverbal" tests, it is difficult to be sure how specifically sensitive these tests are to right unilateral hemispheric dysfunction.

Recently, verbal and nonverbal memory before and after ECT has been assessed in patients receiving bilateral or right unilateral treatment (23). To assess verbal memory, patients were read a short story and immediately thereafter were asked to recall as much of it as

possible. Delayed recall was tested on a second occasion 16 to hours later. Patients with identified dysfunction of the left temp lobe are known to perform more poorly on this test than patients v similar dysfunction of the frontal, parietal, or right temporal regi (24). To assess nonverbal memory, patients were asked to cop complex geometric design (25, 26). Sixteen to 19 hours later, with forewarning, they were asked to copy it from memory. Patients w right temporal lesions are known to be deficient on this memory ta whereas patients with left temporal lesions exhibit no impairm (27). Tests were administered one to two days before ECT and ag with equivalent forms six to 10 hours after the fifth treatment of series.

Figure 1 indicates that patients about to begin a course of bilat or unilateral ECT were nearly identical in delayed recall of the st and in delayed reproduction of the geometric figure. After EC bilateral ECT caused a greater impairment in both verbal and nonv bal memory than unilateral ECT. Delayed recall of the story v markedly impaired by bilateral ECT ($p < .01$), but not affected by ri

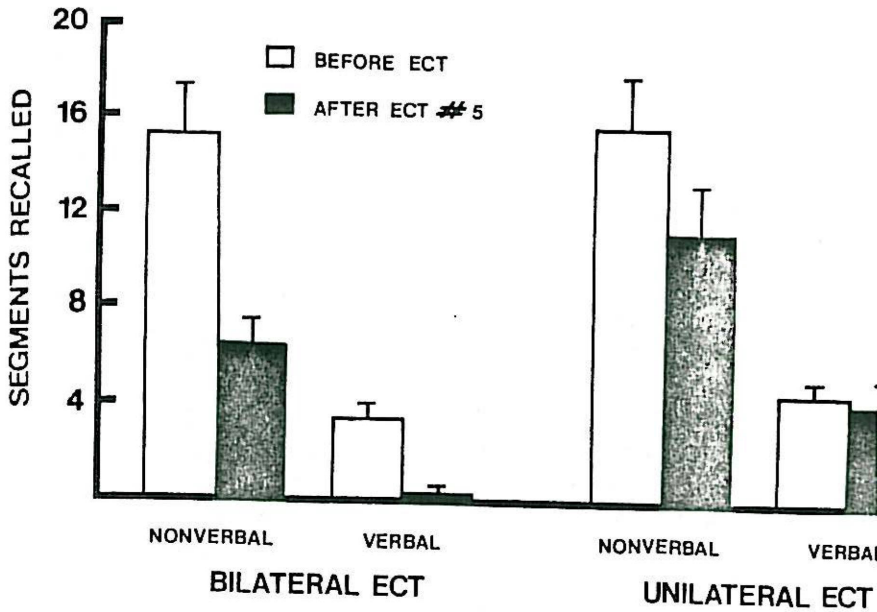

Figure 1. ECT and Memory Loss

Delayed retention scores on verbal and nonverbal memory tests for patien receiving bilateral ECT (N = 15) or right unilateral ECT (N = 9). Bracke indicate S.E.

occurred many years previously. Second, they indicate that bilateral ECT produces greater retrograde amnesia than right unilateral ECT. Right unilateral ECT caused no measurable loss of memory for remote events; by contrast, following a standard course of bilateral ECT, an impairment in memory for remote events persisted for at least two weeks.

Retrograde amnesia for remote events: Information about autobiographical material

The formal tests described above provide information about the effect of ECT on the ability to recognize public events that occurred from one to 16 years prior to treatment. There have also been some investigations of the effect of ECT on the ability to recall autobiographical material. In 1950, Janis (32) reported the results of a study frequently quoted by persons interested in and concerned about the effects of ECT on memory. Nineteen psychiatric patients who had been prescribed bilateral ECT, and 11 control patients not receiving ECT, were given a series of probing autobiographical interviews. These interviews concerned events relating to early schooling, job history, travel, the history of their mental problems, and other life experiences. The interviews were scheduled prior to ECT, four weeks after the completion of ECT (mean of 17 treatments), and again for five of the patients at 14 to 18 weeks after ECT. During the second interview, all patients who had received ECT exhibited amnesia for some of the material they produced in the first interview. Control patients exhibited virtually no amnesia. Finally, the five patients interviewed 14 to 18 weeks after ECT exhibited some recovery, but remained amnesic for some experiences (i.e., eight to nine experiences out of an unspecified number that had been produced during the initial interview). Since it has long been recognized that patients receiving ECT have persistent and probably permanent amnesia for much of the time period immediately surrounding the hospitalization period, it is important to ask to what time period did the memories belong that could not be recalled by Janis' patients. Unfortunately, because of limitations in this methodology and because of the design of the study, no general answer to this critical question is available. However, Janis did include five protocols as samples of persistent amnesia for pre-ECT events. An examination of these protocols indicates that for four out of five, the lost memories belonged to the time period just prior to hospitalization. For the remaining example, the lost memory seemed to relate to events that occurred sometime during the year preceding hospitalization. Accordingly, the

results of this study provide no evidence that memories acq
many years before ECT can be permanently lost as a result of
The critical question remaining then is: How far back in time b
ECT can the permanent amnesic effects of ECT extend? This que
will be considered in the next section: Issues of test sensitivity.

Issues of test sensitivity

Studies with objective memory tests for remote events (28
30) show that ECT can cause a temporal gradient of retrog
amnesia covering the past one to seven years and that, where info
tion is available about recovery, this effect can reverse spontaneo
(with no reason to suspect relearning) within a few weeks afte
completion of treatment. However, the multiple-choice tests on w
these conclusions about recovery are based are not as sensitiv
amnesia as tests that ask subjects to recall as much as possible ab
past event (33). Tests are needed that ask subjects to recall spe
time-dated memories before and after ECT. Studies of this type
in progress confirm (1) that memory for more recent events (or
three years prior to ECT) are much more affected by ECT
memory for more remote events; (2) memory for remote events ca
affected by ECT but clearly recover; (3) memory loss for very re
events may be permanent.

All the studies on retrograde amnesia for remote events follow
a conventional course of bilateral ECT can be summarized in
following way:

1. ECT can affect memories acquired many years prior to t
   ment;
2. the effect on memory is greater for recent memories and
   for more remote memories;
3. very remote memories appear to recover fully following
   in a manner that suggests that recovery is spontaneous
   does not require relearning;
4. memories acquired during the days prior to a course of
   may be permanently lost;
5. there is as yet no evidence to suggest that ECT prod
   permanent loss of memory for events occurring during the
   or two years preceding ECT; indeed, there is some evidenc
   indicate that memories acquired during this period do reco
   Nevertheless, a fully satisfactory study of this issue
   maximally sensitive tests has not yet been accomplished.

unilateral ECT ($p > .3$). Scores of the bilateral and unilateral groups were significantly different ($p < .01$). Delayed reproduction of the geometric figure was significantly impaired by bilateral ECT ($p < .01$). In this case, the difference between the scores of bilateral and right unilateral groups was short of significance ($p < .09$).

It has sometimes been assumed that right unilateral ECT causes as much memory impairment as bilateral ECT on those aspects of memory function identified with the right hemisphere. The present results clearly indicate that bilateral ECT impairs memory to a greater extent than right unilateral ECT, regardless of whether the tests used to assess memory are more sensitive to left or right hemispheric dysfunction. This finding may mean that following unilateral ECT the unaffected hemisphere can always contribute to some extent to performance. This notion is supported by the observation that bilateral medial temporal surgery affects both verbal and nonverbal memory to a greater extent than left or right unilateral temporal surgery (27).

Retrograde amnesia for remote events: Information about public events

It has been reported frequently that convulsive therapy can cause retrograde amnesia for events that occurred close to the time of treatment (16, 17, 18). It is now clear that retrograde amnesia can also extend to events that occurred many years previously (8, 28, 29, 30). In such studies, remote memory is assessed with objective tests that ask about relatively familiar past events. In one test (29) patients were asked to recognize the names of former television programs that were broadcast for a single season from 1957 to 1972 (31). The programs selected from different time periods were apparently exposed to national audiences to about the same extent, and memory for these programs was acquired close to the time the programs were on the air (31). Patients prescribed a course of bilateral ECT took one form of this test before ECT and another form one hour after the fifth ECT. Figure 2 indicates that ECT caused a temporal gradient of impairment in long-term memory. Programs broadcast one to three years previously were forgotten; programs broadcast four to 17 years previously were remembered as well after ECT as before. The memory loss associated with bilateral ECT largely recovered by one to two weeks after the completion of treatment. Further work indicated that right unilateral ECT caused no deficit in remote memory, as measured by this test (29).

Other tests have confirmed the clinical impression that ECT produces a greater loss of temporal order information than other

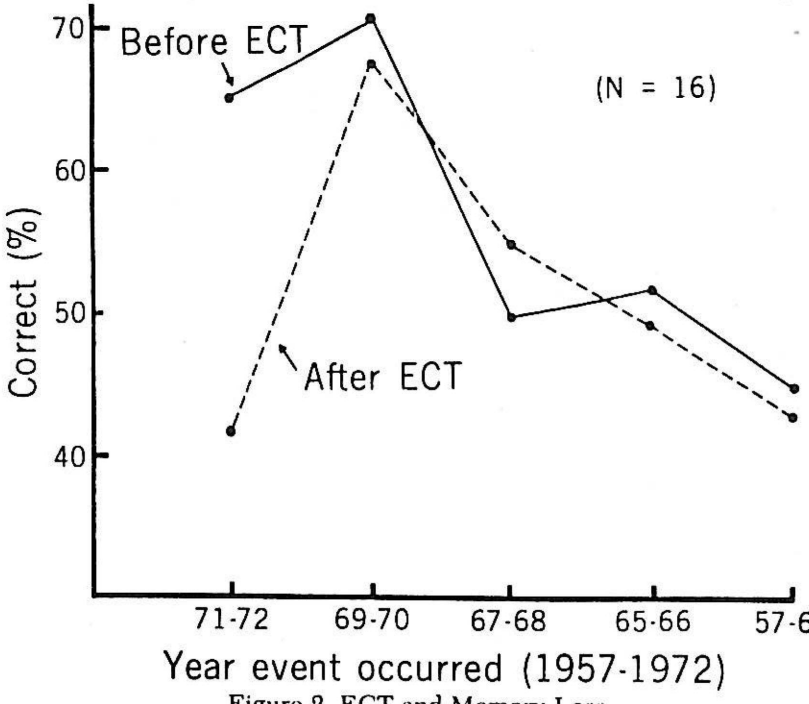

Figure 2. ECT and Memory Loss

A remote memory test was given before bilateral ECT and one hour after fifth treatment. ECT selectively impaired performance on questions cover the 1971-1972 period. The test was given in early 1974.

aspects of memory (30). Patients saw sets of three television prog names and were asked to choose which was broadcast most recen In each set of three the correct program name was broadcast for season from 1962 to 1973 and the other two (incorrect) program nar were broadcast five years previously, from 1957 to 1968. Follow five bilateral treatments, patients developed a marked impairmen their ability to make temporal judgements about this material. T impairment was temporally graded, extending to events that occur four to seven years before treatment, but not to events that occurred ei to 16 years before treatment. The deficit for temporal order infor tion was more persistent than the deficit for recognition of progr names, and remained unchanged at one to two weeks after completion of treatment. Work is in progress to determine how l this deficit remains.

The clinical relevance of these findings is twofold. First, th results indicate clearly that the amnesia associated with bilateral E affects not only recent events, but can also extend to events t

of the study, no general answer to this critical question is available. However, Janis did include five protocols as samples of persistent amnesia for pre-ECT events. An examination of these protocols indicates that for four out of five, the lost memories belonged to the time period just prior to hospitalization. For the remaining example, the lost memory seemed to relate to events that occurred sometime during the year preceding hospitalization. Accordingly, the

5. there is as yet no evidence to suggest that ECT produces permanent loss of memory for events occurring during the one or two years preceding ECT; indeed, there is some evidence to indicate that memories acquired during this period do recover. Nevertheless, a fully satisfactory study of this issue with maximally sensitive tests has not yet been accomplished.

Memory loss in patients receiving extended ECT

Most modern studies of ECT and memory loss concern patients receiving a conventional course of eight to 12 treatments. Accordingly, such studies do not speak to possible long-term effects on memory of an extended course of ECT (e.g., more than 50 treatments). Three studies have been reported that do assess memory capacity and other cognitive functions in patients who have received an extended course of ECT (34, 35, 36). These studies are retrospective investigations of patients who have in previous years received a total of more than 50 treatments. Such patients were compared to other patients matched as closely as possibly for age, sex, and psychiatric diagnosis. The results indicated that those patients who had received ECT performed worse on a variety of memory tests and other cognitive tests than the control group. However, these patients were either chronic schizophrenic inpatients who had been long-term inpatients or severely ill patients who had received cingulotomy in addition to ECT. In retrospective studies of this type, it is always difficult to know if differences between groups are attributable to ECT, or if those patients selected for extensive ECT were different from control patients before ECT in ways that affected their subsequent performance on neuropsychological tests. Accordingly, these studies cannot provide a conclusive answer to questions concerning possible permanent effects of extensive ECT.

Reinstatement

Normally, the severity of retrograde amnesia is inversely related to the time interval between learning and amnesic treatment. Several animal studies have suggested, however, that material not ordinarily affected by convulsive stimulation may be forgotten if a reminder of previously learned material is presented just prior to treatment (19, 20, 21).

To assess the reinstatement phenomenon with human subjects (37), inpatients receiving bilateral ECT learned material 18 hours before ECT or about ten minutes prior to ECT. Alternatively, they learned 18 hours before ECT and then were given a reminder a few minutes before ECT. Retention was always tested six to ten hours after ECT. Figure 3A presents results for a 32-item recognition task, and Figure 3B presents results for 18 paired associates. Patients learning 18 hours before ECT consistently exhibited better retention than patients learning only a few minutes before ECT ($p < .05$). Patients

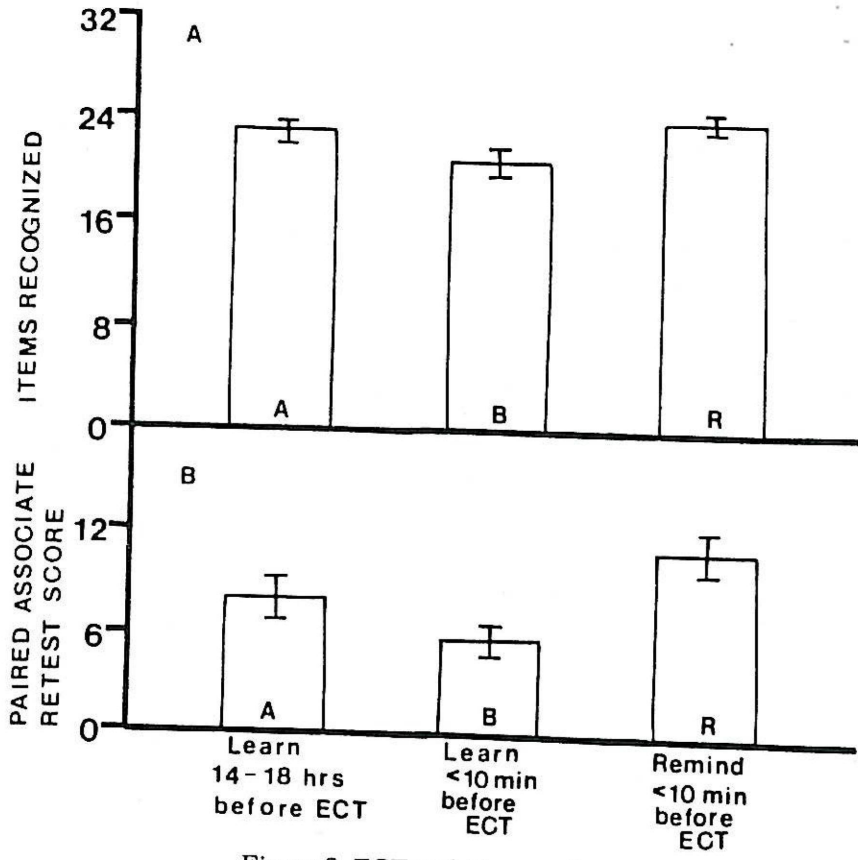

Figure 3. ECT and Memory Loss

Retention scores for 12 patients taking a recognition memory test (A) and a paired associate learning test (B). Learning occurred 14-18 hours before bilateral ECT (Conditions A and R) or just prior to ECT (Condition B). In Condition R, a reminder was given just prior to ECT. Retention was tested 6-10 hours after ECT.

given a reminder of previously learned material just prior to ECT retained this material as well or better than patients not given a reminder. Thus, recalling material from memory just prior to ECT did not produce amnesia. If anything, the reminder procedure improved retention. The results cannot rule out the possibility that amnesia might have been demonstrated if the interval between the reminder and ECT had been shorter than the three minutes required for administration of medications. Nevertheless, it is clear that amnesia need not occur even when a reminder is given at a time before ECT when memory for newly learned material is disrupted. This finding is of clinical interest because of the possibility that the reminder

patients to improve the effectiveness of electroconvulsive therapy. The results of the present study provide no evidence that such a procedure would be effective in a clinical population.

Long-term effects of ECT on memory

A recent study reviewed the available literature on follow-up studies of ECT and memory and reported the results of a long-term follow-up study of patients who had received bilateral ECT, right unilateral ECT, or hospitalization without ECT six to nine months previously (38). Memory functions were assessed with six different tests of learning and remote memory capacity, and self-ratings of memory functions were obtained from all subjects. A group of inpatients was also included, who at the time of testing were receiving a course of bilateral ECT. This study can be summarized by stating that the three follow-up groups did not differ from each other on any of the memory tests. However, the group tested a few hours after the fifth bilateral treatment was consistently impaired. Figure 4 presents results for one of the memory tests. As might be expected, the inpatients performed more poorly than the other groups. Considerable forgetting occurred in all groups at one day and two weeks after learning, but there was no measurable difference between the retention scores of the three follow-up groups ($p > .3$).

Although no objective evidence could be obtained for persistent memory impairment long after ECT, subjects who had received bilateral ECT frequently felt that their memory was not as good as it used to be (38). Figure 5 presents additional data on memory complaints for a larger sample of subjects who had received bilateral ECT or right unilateral ECT six to nine months before. Of 55 persons who had received bilateral ECT (mean number of treatments = 9.9), 37 (67%) indicated that their memory was not as good as it used to be. By contrast, of 15 persons who had received right unilateral ECT (mean number of treatments = 9.4), only four (27%) felt that their memory was impaired. Such an asymmetry in the distribution of memory complaints of bilateral and right unilateral groups could have occurred by chance less than one in fifty times. Most persons with complaints felt that ECT was the cause of their memory problems. Eleven of the 37 persons who had complaints after bilateral ECT selected from four statements the one they felt best described their circumstances. None felt that they had "severe memory problems that interfere with almost everything I do"; two felt that they had "many memory problems that

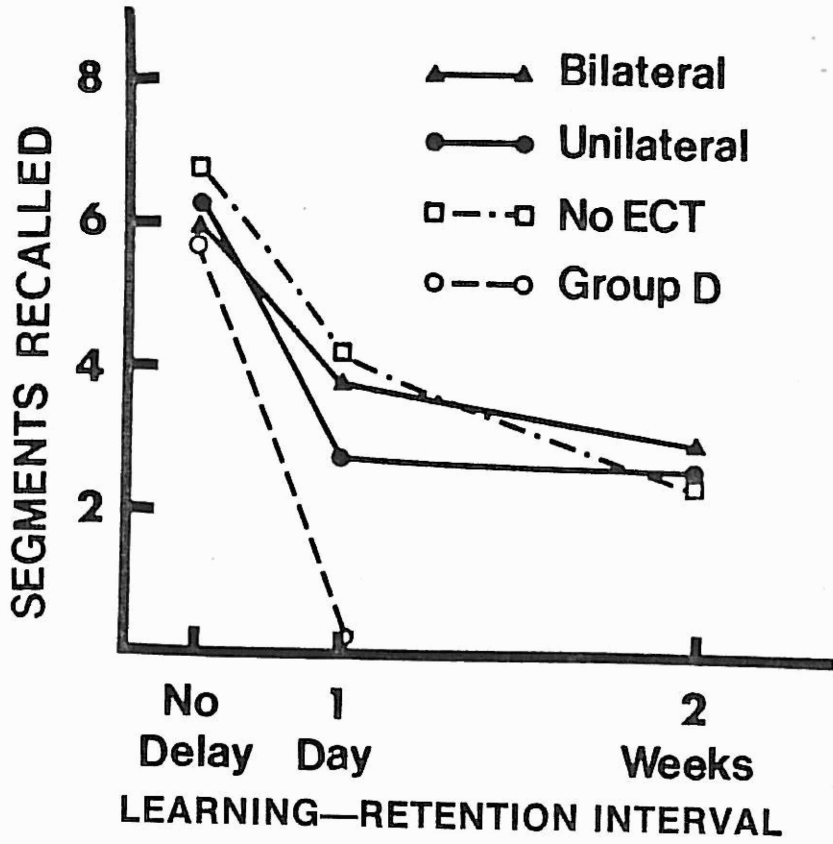

Figure 4. ECT and Memory Loss

Immediate and delayed recall of a short paragraph learned six to nine months after bilateral (N = 16), right unilateral (N = 10), or no ECT (N = 12). A group of inpatients, group D, (N = 15) was also tested 6-10 hours after their fifth bilateral treatment.

	Impairment	No Impairment
Bilateral ECT	37	18
Unilateral ECT	4	11

Figure 5. ECT and Memory Loss

Self-ratings of memory function six to nine months after bilateral or rig unilateral ECT. Patients with memory complaints related only to the period hospitalization were not scored as having perceived memory impairment.

are disturbing and that occur frequently"; six felt that they had "minor memory problems that occur frequently"; and three indicated that they had "only an occasional minor problem".

Unfortunately, the discrepancy between subjective and objective measures of memory function cannot be conclusively resolved. Three possible explanations of this discrepancy will be considered here. (1) The possibility cannot be ruled out that failures of recall persist after ECT that are not detected by conventional memory tests. (2) The possibility also cannot be ruled out that patients receiving bilateral ECT were different from patients receiving unilateral ECT in some way that favored the development of memory complaints. For example, patients receiving bilateral ECT might have initially been more depressed than patients receiving unilateral ECT, or they might initially have had different expectations about memory impairment. Thus, it should not be concluded that bilateral ECT will cause persistent memory complaints in any depressed patient. Whichever explanation is correct it seems clear that memory complaints long after ECT are common in persons judged clinically appropriate for bilateral treatments. (3) Finally, bilateral ECT might itself lead to a lingering sense of memory impairment. Thus, the marked impairment of recent and remote memory initially associated with bilateral ECT might cause some individuals to be more sensitive to subsequent failures in recall, even if they occur at a normal frequency. By this hypothesis, unilateral ECT, which causes less memory impairment than bilateral ECT, would not be expected to lead to memory complaints. Put in its strongest form, this explanation of memory complaints supposes that bilateral ECT might lead many individuals (with or without psychiatric illness) to have persistent illusion of memory impairment.

Summary

The findings reviewed above lead to the following general conclusions about ECT and memory loss:

1. bilateral ECT is associated with greater anterograde amnesia than right unilateral ECT, even when memory is assessed with tests known to be particularly sensitive to dysfunction of the right cerebral hemisphere;
2. bilateral ECT also produces more extensive retrograde amnesia for remote events than right unilateral ECT;
3. extensive ECT (e.g., more than 50 treatments) may lead to long-lasting or permanent impairment in memory capacity or cognitive function, but a definitive conclusion is not possible;
4. the activation of previously learned material just prior to EC does not cause amnesia for that material;
5. new learning capacity substantially recovers by six to ni months after the completion of bilateral or right unilate ECT, but persisting memory complaints are common in ind viduals who receive bilateral treatment;
6. memory for events that occurred long prior to ECT su stantially recovers by six to nine months after ECT; memory f events that occurred days prior to ECT may be permanent lost.

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APPENDIX II—AI

AMERICAN PSYCHI
TASK FORCE ON ELECTRO

INSTRUCTIONS: You will help us keep the cost of proces
answers according to the following rul

Please

- Use a soft black pencil
- Erase completely any answer you wish to change
- Answer e h question by writing the code number of the cor
provided.
- For some questions your answer may be a number with fewer
the extreme right in the space provided and fill the empty spa
your age were 9 years, you would complete item 1 as 0 9

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SECTION I

1. YOUR AGE AT LAST BIRTHDAY?

2. YOUR SEX? 1-Male 2-Female

3. NAM AND LOCATION OF MEDICAL SCHOOL FRO

OVER