ECT - memory loss
nv

0022-3018/91/1799-0526$03.00/0
THE JOURNAL OF NERVOUS AND MENTAL DISEASE

Vol. 179, No. 9
Printed in U.S.A.

Early and Long-Term Effects of Electroconvulsive Therapy and Depression on Memory and Other Cognitive Functions

AVRAHAM CALEV, D.PHIL.,[1,3] DORON NIGAL, M.A.,[1] BARUCH SHAPIRA, M.D., [1,2] NURITH TUBI, M.A.,[1] SHELLA CHAZAN, M.A.,[1] YORAM BEN-YEHUDA, B.A.,[1] SOL KUGELMASS, PH.D.,[3] AND BERNARD LERER, M.D.[1,2]

Twenty-seven medication-free, depressed patients (Research Diagnostic Criteria, endogenous subtype) were administered a comprehensive battery testing memory and other cognitive functions before and after a series of bilateral, brief-pulse electroconvulsive therapy (ECT) administered according to a dosage-titration procedure (8.9 ± 1.981 treatments). A subset of patients (N = 14) were reexamined at 1 month and 6 months after the conclusion of the treatment. Anterograde (verbal and visuospatial tasks), as well as retrograde (famous and personal events), memory function was significantly impaired at the end of the ECT series. By 1 month follow-up, performance had improved to pre-ECT (depression) levels on both anterograde and retrograde tasks and exceeded these by 6 months. The memory deficits induced by ECT were not a consequence of generalized cognitive impairment. Furthermore, depression and ECT were shown to independently affect memory, and recovery from depression was not a consequence of the amnestic action of the treatment. The results generally confirm previous reports regarding the nature of ECT-induced memory impairment, in a different language and culture. They suggest that long-term effects of the treatment on memory are even less prominent than previously observed.

—*J Nerv Ment Dis* 179:526-533, 1991

Although electroconvulsive therapy (ECT) is widely recognized as a highly effective treatment for severe depression, it also produces well-characterized amnestic phenomena. Depressed patients treated with ECT manifest an anterograde memory deficit, that is, difficulty remembering materials learned after termination of the treatment series (Squire, 1977). This deficit is characterized by rapid forgetting (*e.g.*, Calev et al., 1989; Squire and Slater, 1978). Patients also show a retrograde memory deficit, that is, difficulty retrieving materials learned before the ECT treatment series commenced (*e.g.*, Calev et al., 1989; Squire et al., 1981). This deficit has been reportedly characterized by an amnestic time gradient, whereby the distant past is remembered better than more recent events (*e.g.*, Calev et al., 1989; Squire et al., 1981). Events related to the period immediately prior to ECT administration are reported to be least well remembered or permanently lost (Squire et al., 1981). Patients also experience a subjective memory impairment, which has been reported to last longer than the objective impairment (*e.g.*, Squire and Slater, 1983).

Recovery from depression as a consequence of ECT is thought to be a process independent of deterioration in memory function (Squire, 1984), as the two types of changes do not correlate (*e.g.*, Korin et al., 1956). It has also been suggested that cognitive tasks other than memory are minimally affected by ECT (*e.g.*, Taylor and Abrams, 1985), except under special circumstances (*e.g.*, Pettinati and Bonner, 1984), and that memory tasks that are minimally affected by other types of amnesia, such as immediate digit span, are also minimally affected by ECT (*e.g.*, Calev et al., 1989).

Although the above characterization of ECT-induced memory impairment is based on a large number of studies, some were methodologically inadequate (see Johnstone et al., 1980, for review), and findings have not always been consistently replicated (Fromm-Auch, 1982). Concern within the medical profession and among the general public regarding the adverse effect of ECT on memory limits access to this treatment. Therefore, it is important to provide a comprehensive replication of the findings, preferably using different memory tests and in a different language and culture. This was one purpose of the present study.

A second purpose of this study was to examine the nature of memory deficits induced by ECT in the context of the dosage-titration procedure, recommended

[1]Department of Research, Herzog Memorial Hospital, Jerusalem, Israel. Send reprint requests to Dr. Calev at Department of Research, Herzog Memorial Hospital, P.O. Box 140, Jerusalem, 91001, Israel.
[2]Department of Psychiatry, Hebrew University, Jerusalem, Israel.
[3]Department of Psychology, Hebrew University, Jerusalem, Israel.
The study was supported in part by NIMH Grant 40734.

by Sackeim et al. (1986). This procedure ensures that electrical stimulus intensity is limited to a prescribed level above the initial threshold for seizure induction and seeks to avoid unnecessary supramaximal stimulation. Under these conditions, one would expect to find the same pattern of memory deficits reported previously, but a lesser degree of severity.

A third purpose of the present study was to parcel out the effects of depression and ECT on memory. Since depressives are known to suffer from a memory deficit independent of ECT (*e.g.*, Calev et al., 1986), it is important to compare the same patients' memory function when depressed and free of medication with their performance post-ECT after recovery of the depression and after the effects of both depression and ECT have abated.

Methods

Subjects

Twenty-seven depressed patients participated in the study. All fulfilled Research Diagnostic Criteria (RDC) for major depressive disorder, endogenous subtype (Spitzer et al., 1977). They were hospitalized in the Resistant Depression Unit of Ezrath Nashim Hospital (Jerusalem, Israel) and fulfilled no less than one of the following clinical indications for ECT administration: an adequate, but unsuccessful, trial of at least one (usually two) tricyclic antidepressants; psychotic depression; suicidal risk; and sensitivity to side effects of antidepressants or medical contraindication to antidepressants, but not to ECT. Inclusion criteria further demanded a pretreatment Hamilton Depression Scale (24 items) score of 18 or above and written informed consent, and the patient had to be between the ages of 21 and 65. Patients were excluded if there was evidence of seizure disorder, other neurological dysfunction, alcohol or substance abuse, ECT administration in the preceding 12 months, or preexisting intellectual or memory impairment not related to depression. All patients were drug free for at least 2 weeks before treatment (except for chloral hydrate for nocturnal sedation). No patient was in an acute psychotic state at the time of testing and all were judged as able to comprehend the nature and purpose of the tests. All available patients were considered for the study.

These procedures resulted in a sample consisting of seven men and 20 women with a mean age of 54.1 ± 12.86, a mean age at first hospitalization of 36.1 ± 1.88, a mean cumulative hospitalization stay of 1.9 ± 1.47 years, and a mean IQ of 96.1 ± 17.21 according to a short form of the Wechsler Adult Intelligence Scale (see *Testing Procedure*, below). The mean verbal IQ of the sample was 104.6 ± 19.44 and the mean performance IQ was 86.7 ± 14.84, as expected in depressives. The Bender Gestalt Test showed similar intellectual impairment. Using the Hutt (1977) scoring procedure, the mean performance was 65.0 ± 23.07 and recall of the figures was somewhat low ($\bar{X}$ = 3.1 ± 2.18), as expected in depressives. The mean Hamilton Depression Scale score of the group was 31.4 ± 4.98.

Treatment Procedure

All subjects had given informed consent to participate in an ongoing double-blind study comparing the therapeutic efficacy and cognitive adverse effects of two-times- versus three-times-a-week schedules of bilateral, brief-pulse, constant-current ECT administration. Under this protocol, patients in the twice weekly treatment group received one simulated ECT per week (anesthesia, atropine, and muscle relaxant only) in addition to two real ECTs. Simulated ECT was not expected to appreciably affect memory performance (*e.g.*, Johnstone et al., 1980). Subjects were randomly assigned to the twice-a-week (N = 15) and three-times-a-week (N = 16) treatment groups.

The subjects received a total of 8 to 12 real ECTs, except for six patients whose treatment was terminated after four to seven real ECTs because of early remission. The mean number of ECTs administered was 8.9 ± 1.98. In all cases, except for the patients whose ECT course was terminated early, posttreatment cognitive retesting was conducted after a total of 12 treatments (including simulated treatments). Nine patients received additional real ECTs ($\bar{X}$ = 4.1 ± 1.90) subsequent to their post-ECT cognitive retesting because clinical remission was judged to be inadequate. These patients' follow-up testing was done 6 months after their last treatment.

The ECT was administered using the MECTA or THYMATRON constant-current apparatus. Electrode placement was bilateral frontotemporal and stimulus intensity was determined using a dosage titration procedure similar to that recommended by Sackeim et al. (1986). Under this procedure, seizure threshold was determined during the first ECT by a method of limits technique, and subsequent stimulus intensity was 150% of initial threshold. Seizure duration was determined clinically in an upper limb to which arterial supply had been occluded prior to administration of the muscle relaxant (Fink and Johnson, 1982), as well as by means of single-channel EEG monitoring. Stimulus intensity was increased if clinical seizure length dropped below 25 seconds during subsequent treatments.

Anesthesia was induced with thiopentone sodium (2 to 3 mg/kg), and succinylcholine (.75 mg/kg) was used to prevent peripheral muscle activity. Atropine (.5 mg/kg) was administered before treatment.

Materials

Five tests were used to assess anterograde memory performance. They were:

a) Complex Figure Reproduction. This visuospatial task (*e.g.*, Squire and Slater, 1978) consists of the Rey-Osterreith, the Taylor, and the Ritchie figures used as three parallel forms. In this test, the subject was asked to copy the figure twice, and then reproduce it from memory immediately after a delay of about 30 minutes, and again about 24 hours later.

b) Verbal Paired-Associates Recall and Recognition Tasks. This test (for details, Calev et al., 1989) consisted of 10 pairs of unrelated nouns, and included four learning trials followed by an immediate recall test, a 30-minute delayed recall, and a 24-hour delayed recall, all tested at the beginning of the next session (Table 1). Due to a change in the protocol, the last five subjects also took forced-choice recognition tests on the three testing occasions, after recall. This change was unlikely to appreciably affect the recall results because within-patient comparisons were made. These tests consisted of each word pair presented on a card along with four other word pairs that were not presented during the learning trials. These tests were included (1) to make the memory task easier, since recognition is easier, and (2) because this recognition task is minimally dependent on associative ability.

c) Categorized Word List Recall. This test (see details in Calev et al.'s (1983) experiment), like the paired-associates task, measures verbal recall and forgetting that depend on the subject's associative ability. Unlike the paired-associates task, this test has the advantage of having equivalent discriminating power on the immediate- and delayed-recall testing.

d) Verbal versus Visuospatial Recall. This test (details in Calev et al., 1986) compares verbal and visuospatial recall performance, because of equivalence in discriminating power. As a result of change in the protocol, the test was given again for retest purposes to 14 patients at the end of that session, after performance of the Personal Memory and Subjective Memory questionnaires (see Table 1), to assess delayed recall.

e) Immediate Memory Span. This task (taken from the Wechsler Intelligence Scale) evaluates short-term retention dependent upon echoic memory or rehearsal and has been reported to be minimally affected by ECT-induced or other amnesias. It was included as a control task.

Two tests were used to assess retrograde memory performance. They were:

a) the Famous Events Questionnaire. This questionnaire (Squire et al., 1981; for details, see Calev et al., 1989) is known to be sensitive to amnesia. It covered four equally represented time periods: 1954–1963, 1964–1972, 1973–1984, and the last year before the ECT series.

b) the Personal Memory Questionnaire. This questionnaire, which tests for autobiographic memory, was adapted from Weiner et al. (1986). Unlike the Famous Events Questionnaire, it is not affected by personal interests and has proven most sensitive to detecting time-graded memory deficits after ECT (Weiner et al., 1986; Hebrew version described by Calev et al., 1989), according to Ribot's (1882) law of amnesia.

In addition to these retrograde and anterograde memory tests, a Subjective Memory Questionnaire (Squire and Zouzounis, 1988) was used to evaluate the degree to which patients felt their memory performance was impaired after ECT.

Testing Procedure

Three days before ECT administration, the following background measures were taken: a) Hamilton Depression Scale ratings by a trained psychiatrist; b) the Mini-Mental State Examination (Folstein et al., 1975); c) the Bender Gestalt Test (copying and reproduction), used as a general measure of organicity; d) a short form of the Wechsler Adult Intelligence Scale (WAIS), consisting of the information, analogies, block design, and picture completion subtests; and e) the vocabulary scale of the Wechsler Intelligence Scale for Children (WISC; used in the absence of a WAIS equivalent), used as a criterion measure of adequate Hebrew vocabulary (equivalent score of 7 or more required). At the end of this day's testing, every other patient was tested on the Categorized Word List Recall Test. These patients were retested about 24 hours later.

These measures and all other tests given are summarized in Table 1 according to their order of administration. Although the tasks are reliable and resistant to interference, this constant order was kept to further minimize possible differences in interference on the four testing occasions. The testing occasions were 3 days before the first ECT treatment, the day after the last real ECT treatment, and at 1- and 6-month follow-up.

In order to ensure that patients did not show a general organic mental syndrome following ECT, during the post-ECT memory testing, a minimum score of 75% of that of baseline was required on the Mini-Mental State Examination. None of the 13 subjects tested failed to reach this criterion.

Following the ECT series, patients were drug-free for 7 days and then, unless contraindicated, commenced treatment with lithium carbonate to maintain a serum level of .8 to 1.0 mEq/l. There were, however, 11 patients who received additional or other treatments. Five of these received lithium plus imipramine,

TABLE 1
Summary of Assessment Procedures

	Pre-ECT	Post-ECT	1-Mo Follow-up	6-Mo Follow-up
Background Testing				
Hamilton Depression Scale	+[a]	+	+	+
Mini-Mental State Examination	+	−	−	−
Bender Gestalt Test	+	−	−	−
Wechsler Adult Intelligence Scale	+	−	−	−
Vocabulary Subtest	+	−	−	−
Categorized Word List Recall[b]	+	−	−	−
Day 1 Memory Testing				
Categorized Word List Recall Retest[b]	+	−	−	−
Mini-Mental State Examination	+	+	−	−
	(about 5-min break)			
Paired-Associates Learning Recall and Recognition	+	+	+	+
Complex Figure Copying and Reproduction	+	+	−	+
Digit Span (Forward, Backward)	+	+	+	+
Famous Events Questionnaire	+	+	+	+
Paired-Associates, about 30 min, Retest	+	+	+	+
Complex Figure, about 30 min, Retest	+	+	−	+
Day 2 Memory Testing				
Paired-Associates, about 24 hrs, Retest	+	+	+	+
Complex Figure, about 24 hrs, Retest	+	+	−	+
Verbal and Visuospatial Recall	−	+	−	−
Personal Memory Questionnaire	+	+	−	+
	(about 5 min break)			
Subjective Memory	−	+	+	+
Verbal versus Visuospatial Retest	−	+	−	−
Categorized Word List Recall[b]	−	+	−	−
Day 3 Memory Testing				
Categorized Word List Retest[b]	−	+	−	−

[a] +, administered; −, not administered.
[b] Test performed alternately at either the pre- or the post-ECT testing.

one received lithium plus phenelzine, two received imipramine, two received imipramine plus haloperidol, and one received phenelzine. Any effect of these drugs on memory would be to lower memory performance (*e.g.*, Calev et al., 1989); therefore, the improved follow-up performance reported below is not attributable to these drugs.

It should be noted that due to circumstantial problems, such as absence of the tester, noncooperation or refusal on certain tasks, or absence of relatives to corroborate personal memory items, not all patients were available as subjects for all tests. This was more pronounced on the two follow-up testing occasions, when most patients were already living in the community. Another reason for the smaller number of subjects in these later tests was that not all patients had reached 6-month follow-up by the time the present analysis was conducted. Nevertheless, at least 10 subjects were available for each test on all occasions, including 6-month follow-up.

As the study used a within-subjects design, the analysis of follow-up data is valid. Furthermore, the characteristics of the 14 patients available at follow-up testing were very similar to those of the entire group at baseline.

Data Analysis

Data were analyzed when possible using parametric tests (analysis of variance and *t*-tests) and a within-subjects design. The memory scores used were arcsin of proportion of items recalled or forgotten. No transformation was required for tasks that did not deviate from 50% accuracy or normality. Data which, after transformation, did not meet criteria for parametric analyses were analyzed using nonparametric tests. In the figures, mean and standard error values are presented.

Results

Intercorrelations among Clinical State, Memory, and Physiological Measures

The depressive symptoms of the patients improved significantly over the period observed ($F[3,57] = 57.9$, $p < .0001$). This improvement was predominantly due to the acute treatment period, during which up to 12 ECT treatments were given ($F[1,27] = 72.7$, $p <$

.0001). There was no change in depressive symptoms from 1- to 6-month follow-up ($F[1,19] = 0.55$, NS). During this time, no ECT treatments were given.

The lifting of depression, as estimated by changes in the Hamilton Depressive Scale, was not significantly correlated with changes for the worse in memory performance on any of the memory tests used. Similarly, a multiple regression analysis indicated that the bulk of changes for the worse in the different memory measures (each test represented by one measure known to be the most sensitive to memory deficit, *i.e.*, the Complex Figure Reproduction and the Paired-Associates 24-hour delayed recall tests, and digits forward and digits backward, famous events and personal memory total scores) could not predict the change in depressive symptoms due to ECT ($F[12,4] = 1.87$, NS). Therefore, memory impairment and alleviation of depression appear as two parallel but unrelated processes, and depression changes do not confound memory changes.

The lifting of depression as estimated by changes in Hamilton Depression Scale scores from the pre- to post-ECT memory testing was not significantly correlated with any physiological measure associated with ECT, namely seizure duration, number of ECTs, and drug doses. A multiple regression analysis failed to predict change in depression from change in all these measures taken together ($F[5,20] = .36$, NS).

Correlations between these physiological measures and the change in memory scores were also examined. No significant correlation between physiology and memory emerged within the range of stimulus parameters used in the present study.

Anterograde Memory Performance

1. Complex Figure Reproduction. This nonverbal task showed (Figure 1, left panel) significantly more rapid forgetting at post-ECT than at pre-ECT testing ($F[2,48] = 5.2$, $p < .009$ for the interaction). The subgroup of patients tested at 6-month follow-up (Figure 1, right panel) showed a trend toward improvement and had a better performance than at baseline ($F[2,22] = 2.77$, $p < .084$). Immediate recall performance only at 6-month follow-up was better than the pre- and post-ECT performances ($F[2,22] = 3.44$, $p < .05$), which were equivalent. The rate of forgetting at 6 months was not different from baseline.

2. Paired-Associates Recall and Recognition. Subjects showed (Figure 2, left panel) significantly more rapid forgetting at the post-ECT rather than at the pre-ECT testing ($F[2,32] = 3.43$, $p < .045$ for the interaction). The subgroup tested using a recognition paradigm (Figure 2, middle panel) also showed more rapid forgetting after ECT ($F[2,8] = 4.46$, $p < .05$ for the interaction). There was a recall, but not a recognition, deficit at immediate recall testing ($t[16] = 3.11$, $p < .007$). The effect of pre-ECT depression on overall recall performance was very similar to the effect of ECT at 1-month follow-up (Figure 2, right panel). Since depression at 1- and 6-month follow-up was about the same, the significantly better performance at 6 months, compared with the performance at 1 month ($F[1,9] = 11.13$, $p < .008$), indicates that after recovery from ECT, performance is better than it is during the untreated depressive state. At follow-up, there was no evidence of rapid forgetting.

3. Categorized Word List Recall. On this verbal associative recall task, patients showed significant immediate and delayed-recall deficits ($t[21] = 2.11$, $p < .05$ and $t[21] = 3.21$, $p < .0042$, respectively). However, here the interaction effect showing the trend for more rapid forgetting after rather than before ECT did not reach significance ($F[1,21] = 1.79$, $p < .195$, NS). When using a more sensitive measure, that is, percentage of forgetting, this forgetting effect was marginally significant ($U = 36.5$, $p < .069$, used because scores deviated from normality). Depressed, pre-ECT patients performed better than post-ECT patients ($F[1,21] = 7.95$, $p < .01$) on the two tests taken together.

4. Verbal versus Visuospatial Recall. Patients did not show a significant difference between verbal and visuospatial recall both on immediate ($t[19] = .54$, NS;

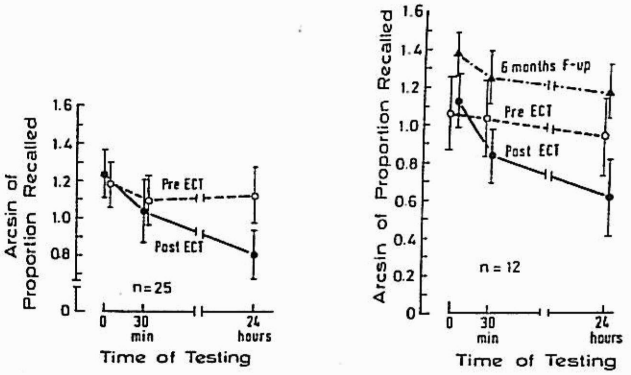

FIG. 1: Complex figure reproduction performance.

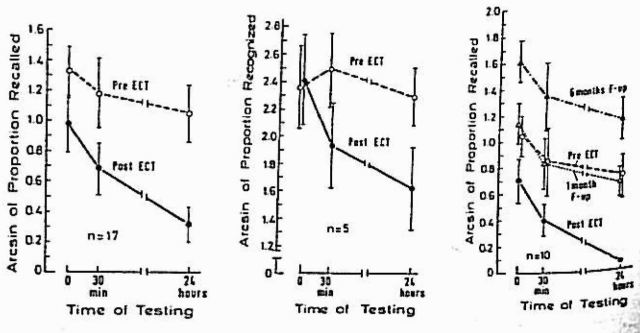

FIG. 2: Paired-associates recall and recognition performance.

$M_{z1} = -2.21 \pm .50$, $M_{z2} = -2.2 \pm .52$, respectively) and delayed ($t[13] = .95$, NS; $M_{z1} = -2.9 \pm .65$, $M_{z2} = -2.4 \pm .84$) testing, thus suggesting equivalent dysfuntion of visuospatial and verbal recall.

5. Immediate Memory Span. On both "forward" and "backward" immediate serial recall of digits, patients showed no performance change from the pre- to post-ECT testing (Figure 3). This suggests that the adverse effect of ECT is of similar magnitude to the adverse effect of depression on immediate digit recall. When the effects of both ECT and depression were minimal, at 1- and 6-month follow-up, performance on both digits forward ($F[1,12] = 5.758$, $p < .035$) and digits backwards improved ($F[1,12] = 7.314$, $p < .02$).

Retrograde Memory Performance

1. Famous Events Recall. The recall of famous events from the remote past (Figure 4) showed, as expected, a post-ECT deficit and recovery afterward ($F[3,33] = 12.05$, $p < .0001$). As in anterograde paired-associates performance, patients' 1-month follow-up performance was at about the pre-ECT (depression) level. Performance improvement from 1- to 6-month follow-up was close to significance ($F[1,12] = 4.11$, $p < .066$). Given the fact that depression levels remained constant during this period, one can assume that only the adverse effect of ECT on memory, not that of depression, has diminished. This suggests a net adverse effect of depression on remote memory. Also, a post-ECT amnestic time-gradient effect emerged ($F[3,72] = 3.83$, $p < .014$ for the interaction). This did not, however, show in the three latest periods, which belong to the subjects' adult life. Therefore, the interaction effect observed should be taken to suggest a larger episodic, rather than semantic (knowledge), memory deficit, and not an amnestic time gradient.

2. Personal Memory Performance. This measure of remote memory was obtained by dividing the post-ECT and 6-month follow-up memory performance scores by the baseline pre-ECT memory score of these events. These proportion scores were then transformed into arcsin. The time gradient was defined by three time-period scores: a) the last hospitalization (within weeks or months of initial testing); b) events occurring during the last year before ECT series began; and c) events related to earlier periods. The results indicated that patients were more impaired in recall of personal events at the post-ECT testing ($\bar{X} = 1.48 \pm .83$) than they were at the 6-month follow-up ($\bar{X} = 2.0 \pm .77$) testing ($F[1,12] = 12.43$, $p < .005$). However, there was no significant interaction ($F[2,24] = .90$, NS), which again shows no evidence for an amnestic time gradient.

Subjective Memory

Since the scores of this questionnaire did not violate

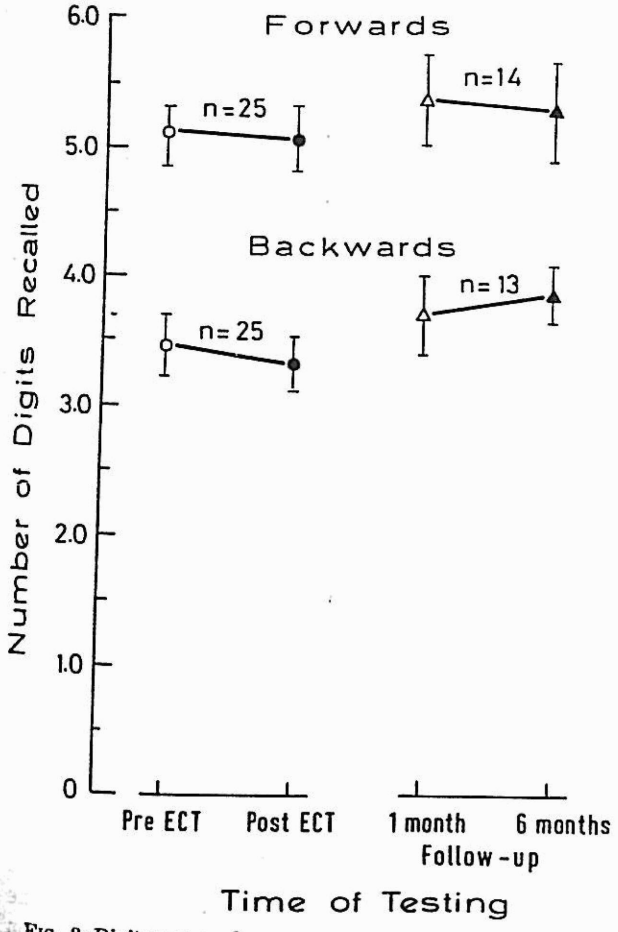

FIG. 3: Digit span performance.

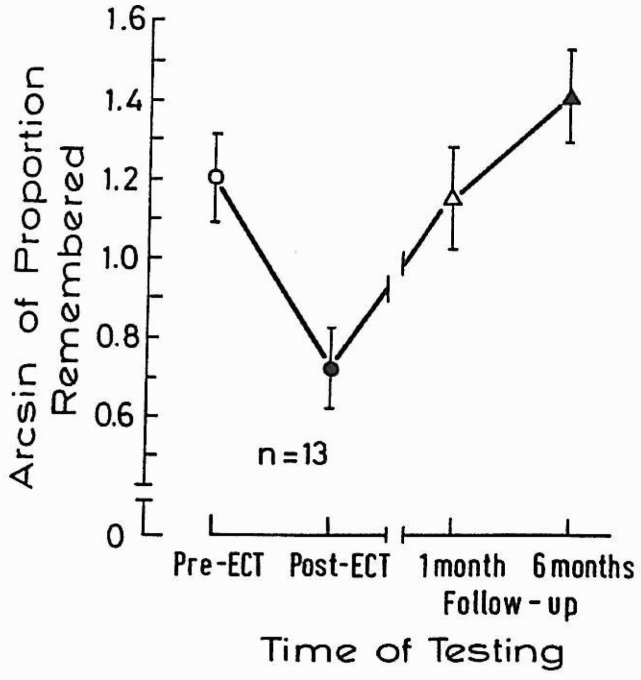

FIG. 4: Famous events recall performance.

normality and homogeneity of variance assumptions, they were analyzed parametrically, without transformation. Patients reported a subjective feeling of impairment only at 1-month follow-up ($\bar{X}$ = 105.6 ± 16.33, $t[22] = 2.45$, $p < .04$, relative to the expected mean of 95 for 19 items, each rated on a 1 to 9 scale, with a score of 5 representing no change in memory performance). There was a very slight nonsignificant tendency to feel impaired at the post-ECT testing occasion ($\bar{X}$ = 98.6 ± 22.35). Item analyses for the three tests failed to find significant amnestic linear trends (slope, .045) reported by Squire and Zouzounis (1988). This shows that no specific items in this questionnaire indicated a subjective memory impairment. The subjective memory feelings were not significantly correlated with any objective memory test or physiological measure. The improvement in depression, assessed using the Hamilton Depression Scale, was nonsignificantly correlated with better feelings about memory ability ($r = .33$, $N = 22$, $p < .14$).

Non-Memory Measures

1. Complex Figure Copying. There was no significant change in the patients' copying score of the complex figures ($F[2,26] = .11$, NS; pre-ECT, $\bar{X}$ = 24.3 ± 11.96; post-ECT, $\bar{X}$ = 24.1 ± 10.54; 6-month follow-up, $\bar{X}$ = 25.0 ± 10.84).

2. Paired-Associates Learning. The first three learning trials in the paired-associates task were statistically independent of the memory (retention) performance and were, therefore, analyzed separately. A repeated-measures analysis of variance revealed no difference in learning rates on the four testing occasions ($F[6,52] = 1.57$, NS).

3. Mini-Mental State Examination. The Mini-Mental State Examination, which consists of memory and other cognitive items, showed, as expected, significantly lower post-ECT than pre-ECT performance for the 13 patients tested ($F[1,12] = 7.48$, $p < .026$; M_1 = 23.0 ± 4.95, M_2 = 25.2 ± 4.05, respectively). The change (9.7%) was far from the organic syndrome criterion of 25%. When the cognitive item scores involving negligible memory components were analyzed separately, no significant change from the pre- to the post-ECT performance emerged ($t[12] = 1.76$, NS; M_1 = 21.5 ± 3.3, M_2 = 20.2 ± 4.58, respectively). In contrast, the items intended to test for memory ability (registration and recall) showed a significant difference between the pre- and the post-ECT tests ($t[12] = 4.77$, $p < .012$; M_1 = 4.77 ± 1.01, M_2 = 3.85 ± .99, respectively).

Discussion

The results presented characterize the effects on memory and other cognitive functions of bilateral, brief-pulse ECT administered to endogenously depressed patients according to a titrated, moderately suprathreshold treatment paradigm. They generally confirm an earlier report from our group (Calev et al., 1989). The present study used a considerably more comprehensive test battery and encompassed an extended follow-up period, compared with our earlier report. Previous findings on the nature of post-ECT amnesia (Squire, 1984), with some important exceptions, are replicated in the context of a different culture and using a different language. This replication emerges in the context of a mean of 8.9 ECT administrations in the series and a dosage-titration procedure (Sackeim et al., 1986), limiting stimulus intensity to approximately 150% above threshold.

The results confirm that recovery from depression is a process independent of deterioration in memory performance. This replicates former findings (see *Introduction*) and suggests that depression does not improve because of the memory deficits that ECT induces.

Several points regarding the independent effects of ECT and depression on memory are highlighted by the findings. On immediate testing, the anterograde (recent) memory deficit caused by ECT was of similar magnitude to that associated with depression. There are, however, two sets of data that render the recent memory deficit caused by ECT distinguishable from that associated with depression. a) Delayed memory testing revealed more rapid forgetting after ECT than in the depression pre-ECT state. b) Immediate memory performance, *when dependent on associative ability*, revealed a larger deficit after ECT than in the depressed pre-ECT state.

Rapid forgetting, the first of the above findings, is a well-documented consequence of ECT (Calev et al., 1989; Squire and Slater, 1978). Associative memory deficit, however, has not been previously demonstrated in relation to ECT. This latter finding may be explained by frontotemporal electrode placement, which adversely affects both pure memory (due to the temporal effect of ECT; Squire, 1984) and memory dependent on associative (organizational) ability (due to the presumed frontal effect of ECT).

The results also replicate and highlight other previously reported anterograde effects of ECT on memory. They clearly demonstrate that after bilateral ECT, the verbal memory deficit is of comparable magnitude to the visuospatial memory deficit. Both sets of verbal and visuospatial tasks showed rapid forgetting, as in previous studies.

An additional objective of the study was to examine the long-term effects of ECT on memory function. The results suggest that the adverse effects of depression

on memory are of similar magnitude to the adverse effects of the treatment demonstrable 1 month after ECT. By 6 months, performance tended to improve to levels higher than observed during the depressed state. This complete recovery of retrograde memory function, which we observed, is at variance with previous reports (*e.g.*, Squire et al., 1981; Weiner et al., 1986). Moreover, contrary to previous observations (Squire et al., 1981), no permanent loss of memory for events transpiring during the last hospitalization and no time gradient was observed. These findings were unexpected and perhaps may be shown with more sensitive tests designed for this purpose. They do, however, suggest that impairment of retrograde memory function is not necessarily a consistent, long-term consequence of ECT. Furthermore, the finding of a strong trend for improved remote performance at 6 months relative to pre-ECT levels suggests that depression affects remote memory in addition to its known effect on recent memory (*e.g.*, Calev et al., 1986).

Unlike objective functioning, patients' subjective impressions of their memory function were at their worst at 1-month follow-up, rather than immediately after ECT. This latter finding needs further corroboration in view of some previous reports suggesting a long-lasting subjective impairment (*e.g.*, Squire and Slater, 1983). If correct, it can reassure the clinician that ECT does not cause *any* permanent or long-lasting impairment.

Unlike memory functioning, analysis of the nonmemory tasks used showed that these functions were not adversely affected by ECT. This confirms the view that ECT does not have appreciable long-standing effects on general mental function.

A task which was, like the nonmemory tasks, not expected to be adversely affected by ECT and which was included in the battery as a control task was digit span. This memory task, unlike others, had been located to a perisylvian parietal region. The effect of ECT on this task was indeed small. Performance after ECT was comparable to that observed during the pre-ECT depressive state. However, the main difference from other tasks was in recovery. Digit span performance (both "backward" and "forward") had improved by 1-month follow-up and was comparable to that of 6-month follow-up, unlike other tasks. This suggests that the perisylvian parietal location specific to digit span is less severely affected by ECT than are other locations related to memory.

References

Calev A, Ben-Tzvi E, Shapira B, et al (1989) Distinct memory impairments following electroconvulsive therapy and imipramine. *Psychol Med* 19:111–119.

Calev A, Korin Y, Shapira B, et al (1986) Verbal and nonverbal recall by depressed and euthymic affective patients. *Psychol Med* 16:789–794.

Calev A, Venables PH, Monk AF (1983) Evidence for distinct verbal memory pathologies in severely and mildly disturbed schizophrenics. *Schizophr Bull* 9:247–264.

Fink M, Johnson L (1982) Monitoring the duration of electroconvulsive therapy seizure—"Cuff" and EEG methods compared. *Arch Gen Psychiatry* 39:1189–91.

Folstein MF, Folstein SE, McHugh PR (1975) Mini-mental state. *J Psychiatry Res* 12:189–198.

Fromm-Auch D (1982) Comparison of unilateral and bilateral ECT: Evidence for selective memory impairment. *Br J Psychiatry* 141:608–613.

Hutt ML (1977) *The Hutt adaptation of the Bender-Gestalt Test.* New York: Grune and Stratton.

Johnstone EC, Lawler P, Stevens N, et al (1980) The Northwick Park electroconvulsive therapy trial. *Lancet* 20/27:1317–1320.

Korin H, Fink N, Kwalwasser S (1956) Relation of changes in memory and learning to improvement in electroshock. *Confines of Neurology* 16:88–96.

Pettinati HM, Bonner KM (1984) Cognitive functioning in depressed geriatric patients with history of ECT. *Am J Psychiatry* 141:49–52.

Ribot T (1882) *Diseases of memory.* New York: Appleton.

Sackeim HA, Portnoy S, Neeley P, et al (1986) Cognitive consequences of low dosage ECT. *Ann NY Acad Sci* 462:326–340.

Spitzer RL, Endicott J, Robins E (1977) *Research Diagnostic Criteria (RDC) for a selected group of functional disorders* (3rd ed). New York: New York Psychiatric Institute.

Squire LR (1977) ECT and memory loss. *Am J Psychiatry* 134:997–1001.

Squire LR (1984) ECT and memory dysfunction. In B Lerer, RD Werner, RH Belmaker (Eds), *ECT: Basic mechanisms* (pp. 156–163). London: John Libbey.

Squire LR, Slater PC (1978) Bilateral and unilateral ECT: Effects on verbal and nonverbal memory. *Am J Psychiatry* 11:1316–1320.

Squire LR, Slater PC (1983) Electroconvulsive therapy and complaints of memory dysfunction: A prospective three-year follow-up study. *Br J Psychiatry* 142:1–8.

Squire LR, Slater PC, Miller PL (1981) Retrograde amnesia and bilateral electroconvulsive therapy. *Arch Gen Psychiatry* 38:89–95.

Squire LR, Zouzounis JA (1988) Self-rating of memory dysfunction: Different findings in depression and amnesia. *J Clin Exp Neuropsychol* 10:722–738.

Taylor MA, Abrams R (1985) Short-term cognitive effects of unilateral and bilateral ECT. *Br J Psychiatry* 146:308–311.

Wechsler D (1987) *Wechsler Memory Scale—Revised Manual.* San Antonio: Psychological Corp., Janovich, Inc.

Weiner RD, Rogers HJ, Davidson JRT, et al (1986) Effects of stimulus parameters on cognitive side effects. In S Malitz, H Sackeim (Eds), *Electroconvulsive therapy: Clinical and basic issues.* New York: New York Academy of Sciences.