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more like

ECT — memory loss — Weiner

This is important mainly for discussion section.

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Brief Report

The Effects of ECT Modifications on Autobiographical and Verbal Memory

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INTRODUCTION

Electroconvulsive therapy (ECT) produces memory impairment which may be modified (Valentine *et al.*, 1968; Squire, 1977; Weiner, 1979) by a choice of stimulus electrode placement (bilateral *vs.* unilateral nondominant) or electrical stimulus wave form (sinusoidal *vs.* brief-pulse). Regarding electrical stimulus wave form, it has been suggested that more amnesia may follow sinusoidal than brief-pulse ECT because more total electrical energy is delivered by the former than the latter treatment modality (Medlicott, 1948; Kendall *et al.*, 1956; Cronholm and Ottosson, 1963; d'Elia, 1974).

Several investigations have revealed that personal information inventories are sensitive means of assessing ECT-induced amnesia (Janis, 1950; Janis and Astrachan, 1951; Stieper *et al.*, 1951; Squire *et al.*, 1981; Weiner *et al.*, 1982). To date, however, no investigation has examined the effects of the aforementioned ECT modifications on memory for a specific autobiographical *episode* (e.g., "How did you celebrate your last birthday?"). These effects are examined in the present investigation.

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MATERIAL AND METHODS

Subjects

A group of 16 male inpatients, all meeting Research Diagnostic Criteria (Feighner *et al.*, 1972) for major depressive disorder, was studied. The Hamilton Interviewer-Rated Depression Scale (Hamilton, 1960) was administered before each patient's first ECT to measure severity of depression. Patients with any evidence or history of neurological dysfunction were excluded. No patient was tested who had received ECT within 12 months prior to his present ECT course. Dominance was determined by a battery modified from d'Elia (1970). All patients were strongly right-body dominant.

ECT Technique

Patients received either standard *bilateral* frontotemporal ECT or *unilateral nondominant* ECT (d'Elia, 1970, placement). Electrical stimulation was either bidirectional *brief pulse* (800-mA peak amplitude, 60 pulse-pairs/sec, 0.75- to 1.5-msec pulse duration, 1.25- to 2.00-sec pulse train duration; MECTA Corp. device) or bidirectional *sinusoidal* (140-170 V rms, 60 Hz, 0.5- to 1.0-sec train duration; Medcraft B-24 Mark III device). Thus four treatment groups were formed (unilateral nondominant pulse, unilateral nondominant sine, bilateral pulse, bilateral sine). Patients were randomly assigned to one of these four groups.

ECT was administered three times a week (M,W,F). Patients were premedicated with atropine (mean of 0.6 mg im) 30 min before ECT. Anesthesia was produced by intravenous methohexital, and subtotal muscle relaxation was achieved by intravenous succinylcholine. Ventilation with 100% O_2 was begun shortly after methohexital injection and was continued (except for several seconds during electrical stimulation) until satisfactory spontaneous respiration was achieved.

Seizures were monitored electroencephalographically. Seizure length was taken as time until cessation of epileptiform activity. The number of joules of electrical energy was measured with a custom-made integrating watt-second meter (Indiana University). Table I illustrates patient and ECT variables. The four groups were balanced with respect to all of these variables except electrical energy. Sinusoidal stimulation delivered more joules of electrical energy than did pulse stimulation (means: sine = 68.6 joules, pulse = 30.6 joules; $F = 13.6$, df = 1, 12, $p < 0.01$), a difference which is consistent with that reported elsewhere (e.g., Weiner, 1980).

Table I. Patient and ECT Variables

Variable	Range	Mean	Standard deviation
Age (years)	28-73	58.2	13.2
Hamilton score	30-62	47.7	11.8
Education (years)	4-16	10.2	3.1
Methohexital (mg)	60-80	65.6	8.9
Succinylcholine (mg)	60-120	73.8	18.2
Seizure length (sec)	25-195	57.2	41.7
Joules of energy	13-129	49.6	31.3

Memory Testing

Base-line memory testing was attempted 45 min (mean: 50 min) before each patient's sixth ECT. At this time, patients were read the "Airplane List" (Crovitz, 1979) three times. This story contains ten target words structured in a bizarre-imagery chain-mnemonic format to encourage deep and elaborate encoding (Crovitz, 1979). After each reading, free-recall memory was tested. Following the third free-recall testing, multiple-choice recognition memory was tested. The correct word was randomly interspersed with four distractor words. The last testing mode (story-cued recognition) involved reading each sentence of the story one at a time, with a missing blank(s) where the target word belonged. The same choices used in multiple-choice testing were printed below each sentence. Patients were instructed to guess on both recognition tests if they did not know the correct word.

Twenty-four hours after ECT, each patient was first asked "Do you remember being told a story containing ten words yesterday morning before your treatment?" The patient's "yes" or "no" response was accepted on face value as indicating the presence or absence of autobiographical memory for having heard the Airplane List. Each patient was informed that he *was* told a story before his treatment, and was asked to free-recall words from the story. Multiple-choice and story-cued recognition testing were then performed exactly as was done before ECT.

RESULTS

Table II displays autobiographical memory as a function of electrode placement and stimulus wave form. An exact Mantel-Haenszel Test (Thomas, 1975) revealed less autobiographical memory following bilateral than unilateral

Table II. Autobiographical Memory as a Function of Electrode Placement and Stimulus Wave Form

Autobiographical memory present?	Treatment modality			
	Bilateral sine ($n = 3$)	Bilateral pulse ($n = 4$)	Unilateral sine ($n = 5$)	Unilateral pulse ($n = 4$)
Yes	0	0	4	3
No	3	4	1	1

nondominant ECT ($p < 0.01$), but no effect due to stimulus wave form ($p > 0.20$). There was no difference in joules of electrical energy ($t = 0.87$, $p > 0.20$) or seconds of seizure length ($t = 0.49$, $p > 0.20$) between patients with and without autobiographical memory.

Figure 1 displays the amount of pre–post ECT forgetting of Airplane List words as a function of treatment group. Analysis of variance revealed a significant main effect for electrode placement ($F = 9.2$, df = 1, 12, $p < 0.05$), with greater forgetting following bilateral than unilateral ECT. There was no main effect for stimulus wave form ($F = 1.9$, df = 1, 12, $p > 0.10$), and there was no

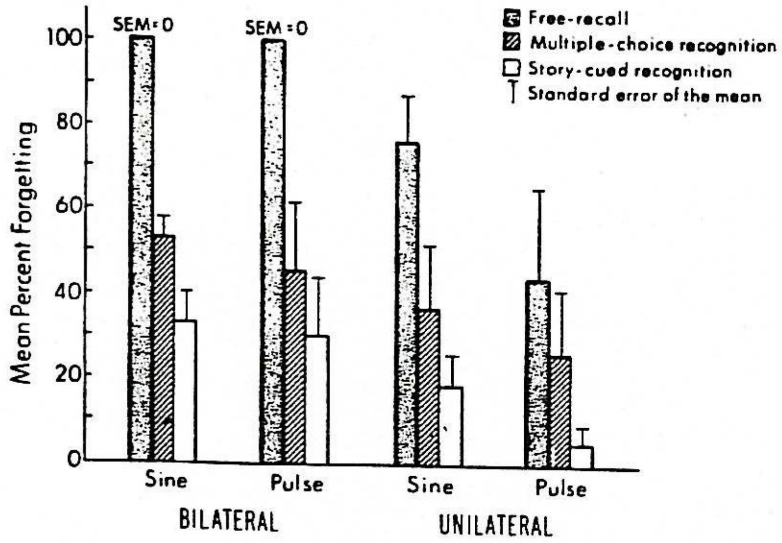

Fig. 1. Mean percentage of words forgotten before and after ECT in relation to treatment group.

interaction of electrode placement with stimulus wave form ($F = 0.9$, df = 1, 12, $p > 0.20$). Pairwise Tukey tests revealed that bilateral ECT produced more forgetting than unilateral ECT on free-recall testing ($p < 0.05$), but not on multiple-choice or story-cued recognition testing ($p > 0.05$).

DISCUSSION

Sinusoidal stimulation did not produce significantly greater autobiographical or verbal amnesia than did brief-pulse stimulation. Other studies have reported more amnesia following sinusoidal than pulse stimulation, but these studies contain the following serious methodological inadequacies: failure to establish statistical significance for alleged intertreatment amnestic differences (Medlicott, 1948; Epstein and Wender, 1956; Valentine *et al.*, 1968); confounding of results by postictal confusion (Medlicott, 1948; Valentine *et al.*, 1968); failure to specify whether patients were oxygenated (Medlicott, 1948; Kendall *et al.*, 1956; Valentine *et al.*, 1968); intertreatment difference in hypoxia (Epstein and Wender, 1956); and intertreatment differences in treatment number and spacing (Kendall *et al.*, 1956). Our study contains none of these methodological inadequacies, and no statistically significant effect of stimulus wave form on memory functions was observed.

Regarding electrode placement, our results are consistent with other reports of greater retrograde amnesia following bilateral than unilateral nondominant ECT (e.g., Lancaster *et al.*, 1958; Cannicott and Waggoner, 1967; Costello *et al.*, 1970; d'Elia, 1970; Weiner *et al.*, 1982). However, this is the first investigation to demonstrate a statistically significant greater impairment in memory for an autobiographical *episode* following bilateral than unilateral nondominant ECT.

The forgetting of an autobiographical episode as simple as having heard the Airplane List before ECT is not a trivial phenomenon. Similar ECT-induced autobiographical memory failures, if added across a course of ECT, may produce *gross* autobiographical memory gaps that may be disconcerting to a patient and a patient's family, because the patient's sense of continuity with his or her own past may be disrupted. It is not yet known how far back in time autobiographical deficits extend. Nor is it known whether low-energy brief-pulse ECT will reduce these deficits if autobiographical memory is evaluated more thoroughly than in the present investigation.

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Brief Report

Glucose-6-Phosphate Dehydrogenase Deficiency in a Psychiatric Population: A Preliminary Study

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Glucose-6-phosphate dehydrogenase (G6PD) is the rate-limiting enzyme of the hexose monophosphate shunt. Deficiency of G6PD is a recessive X-linked metabolic disorder (Beutler, 1974). Erythrocytes are particularly affected but other tissues have also been found to be deficient in this enzyme. G6PD deficiency may result in hemolytic anemia, particularly after the ingestion of certain drugs, fave beans, or after conditions of stress like bacterial infections. Hemolysis has also been known to occur following exposure to pollen. It is estimated that this enzyme deficiency affects around 100 million people around the world, but mainly blacks, Mediterraneans, and Sephardic Jews.

Following the report of two black men with G6PD deficiency who developed transient psychosis following the administration of primaquine sulfate (Dern *et al.*, 1963), G6PD deficiency was surveyed in hospitalized chronic schizophrenic patients (Dern *et al.*, 1963, Bowman *et al.*, 1965; and Fieve *et al.*, 1965). These studies showed no association between G6PD deficiency and psychosis, but there are questions about the diagnostic and assay reliability used in these studies. Heller *et al.* (1979) studied sickle cell disease and G6PD deficiency in over 65,000 admissions to Veterans Administration hospitals. They also found no correlation between G6PD deficiency and any psychiatric diagnosis.

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full ECT memory loss - Weiner

This study shows 6 months (or more) memory loss of personal history memories, ie, memory loss identical to the patients' reports.

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Effects of Stimulus Parameters on Cognitive Side Effects

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INTRODUCTION

This symposium has already focused on recent experimental data directed toward an understanding of the differential effects of electrode placement upon both therapeutic response and adverse cognitive effects with electroconvulsive therapy (ECT). In addition, we have yet to hear a number of further expositions on this subject. The available data, presented both here and elsewhere, suggest that unilateral nondominant (UL) ECT is roughly as effective as bilateral (BL) ECT in producing a remission in severely depressed patients.[1–3] At the same time, it must be pointed out that technical factors such as sufficient interelectrode distance and the assurance of suprathreshold stimuli also appear to play a role in the efficacy of UL treatments. In addition, there is also a possibility that some patients might respond better to the combination of more intense seizures and denser organic interictal changes produced by bilateral stimulation.

The situation with regard to adverse effects, however, is considerably clearer: unilateral nondominant ECT offers a distinct advantage to bilateral treatments with regard to the presence and extent of cognitive disruption, at least with respect to those functions that depend on the dominant hemisphere.[4] Still, the extent of data indicating that such amnestic differences exist longer than a few weeks has been largely limited to reports of self-ratings.[5–6]

Another form of ECT modification, discussed both within this volume as well as elsewhere in the literature, though to a lesser degree than electrode placement, is the

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stimulus waveform. Over the years, a number of attempts have been made to alter the electrical characteristics of the signal used to generate seizure activity with ECT.[1] Such attempts, while suffering from a variety of methodological inadequancies, have suggested that as long as the duration of the basic stimulus waveform unit does not become too abbreviated, a reasonable degree of therapeutic equivalence appears to exist among the various waveform morphologies.

The role of stimulus waveform in adverse central nervous system (CNS) effects has been a particularly problematic area of investigation. Early studies, which favored low-energy stimuli,[7] were confounded by concomitant differences in electrode placement. Later investigators reported mixed findings, with some claiming less impairment over a course of ECT given by lower energy stimuli,[8-12] and others finding no difference.[13,14] In no case, however, has evidence been presented for persistent deficits on the basis of waveform type.

While a larger number of studies have considered the possible beneficial and/or adverse effects or either electrode placement or stimulus waveform, few have evaluated these effects simultaneously. Valentine *et al.* observed an apparent additive effect of these two modifications on cognitive function during the postictal period.[12] To some degree, Daniel *et al.* found similar additive effects after an individual electrically induced seizure.[15-18] This latter group has also contributed relevant data concerning postictal orientation effects to the present volume.[19]

Still, there has been a notable absence of studies focusing upon differences in effects lasting beyond the postictal period. This is of particular interest, given recent claims that the theoretically most benign ECT combination, consisting of unilateral nondominant electrode placement and brief-pulse stimuli, may be at least relatively ineffective from a therapeutic standpoint.[20,21] In order to investigate more fully the acute and long-term effects of both electrode placement and stimulus waveform on cognitive function, we undertook a prospective study, some of whose results will be presented here. Electrophysiologic findings, suggesting an additive effect for bilateral electrode placement and high-energy sine-wave stimuli in the development of acute adverse cerebral changes with ECT, are presented elsewhere in this volume.[22]

METHODS

Subjects were severely ill psychiatric inpatients referred for ECT independently of the research protocol. All met Research Diagnostic Criteria for major depressive disorder,[23] had no ECT within the past year, and had no present or prior evidence of significant CNS disease. A reference group, consisting of similarly diagnosed inpatients not referred for ECT, was also included in the study design. Experimental subjects were randomly assigned to either bilateral or unilateral nondominant electrode placement and to either sine-wave (S) or brief-pulse (P) stimuli. A widely separated centroparietal to frontotemporal configuration,[24] applied using careful attention to electrode/scalp coupling, was chosen for the unilateral placement, in order to maximize efficiency of seizure induction.[2] MECTA (Mecta Corp.) and Medcraft B-24 Mark III (Medcraft Corp.) ECT devices, representing the most widespread pulse and sine-wave equipment available in the United States during the study period, were used to deliver the electrical stimulus.

Specific initial stimulus parameters for each device were chosen to be relatively equivalent with respect to seizure threshold. Single-channel EEG monitoring allowed iterative adjustment of intensity settings to produce seizures lasting longer than 25 seconds. Digital monitoring of stimulus energy was carried out to facilitate calculation

of a variety of electrical parameters. The number of ECT treatments was determined on clinical grounds by the subject's attending psychiatrist. Experimental subjects were tested before ECT, two to three days after the final ECT treatment, and six months following completion of the ECT course. Control subjects were tested at analogous time intervals. A variety of test measures, including those directed toward the assessment of therapeutic outcome, memory function, and EEG, were utilized. Analysis of variance and covariance, along with Pearson-product-moment correlations, formed the basis of statistical determinations.

RESULTS

A total of 53 experimental and 21 control subjects received both baseline and acute post-ECT course testing of clinical and memory parameters (TABLE 1). Thirty-nine of the experimental and 13 of the control subjects also completed the six-month follow-up testing. No differences on the basis of electrode placement or stimulus waveform were found for age ($m = 52.5$), years of education ($m = 11.0$), or socioeconomic status[25] ($m = 4.9$). UL subjects had somewhat lower IQs[26] than did BL subjects (86 vs. 96, $p < 0.01$). No BL vs. UL or S vs. P differences were found on the basis of history of previous ECT (30%), history of drug nonresponse during the present episode (50%), or evidence of psychosis during the present episode (50%).

TABLE 1. Number of Subjects Receiving Clinical and Memory Testing

	C	PUL	SUL	PBL	SBL
Acute effects	21	10	14	14	15
Long-term follow-up	13	8	10	9	12

As noted in a companion paper,[22] no intergroup differences were found on the basis of number of ECT treatments ($m = 9.5$), fraction of treatment sessions resulting in inadequate seizures (less than 25 seconds by single-channel EEG) ($m = 0.08$), or either mean or cumulative adequate seizure duration (57.2 seconds, 509 seconds). Seizure morphology, rated blind to type of ECT, revealed intergroup differences only with regard to postictal suppression.[22] This was particularly prominent for SBL ECT, supporting the hypothesis that this particular ECT combination is characterized by intense seizures.

Measures of stimulus intensity showed highly significant intergroup differences with respect to stimulus waveform ($p < 0.0001$), with sine-wave stimuli associated with 2.6 times the stimulus energy (Joules), 3.1 times the applied charge (coulombs), and 6.9 times the mean current (coulombs per second) as that associated with pulse stimuli. This difference in stimulus energy is similar to that reported elsewhere.[2] Subjects receiving UL ECT tended to receive lower intensity stimuli than those receiving BL treatments (e.g., for energy 36 vs. 44 Joules), though differences just missed statistical significance. In any regard, this ease in producing seizures with the UL technique helps to validate the relatively optimal mode of delivery of UL ECT used in the present investigation.

Therapeutic outcome measures included the Hamilton Depression Rating Scale (HDRS),[27] the Brief Psychiatric Rating Scale (BPRS),[28] the Zung Self-Rating Depression Scale (SDS),[29] and a retrospective four-point global rating based on the

discharge summary for the index hospitalization. All ratings were done blind to experimental subgroup. All groups, including controls, were equivalent with regard to baseline HDRS (m = 23.1, based on 17-item scale) and degree of acute improvement in HDRS, BPRS, and Zung SDS over the course of treatment (m = 11.7, 22.5, 15.2, respectively). A variety of responder criteria, based on combination of HDRS change and cutoff limits, were investigated, without the appearance of significant intergroup differences. Similarly, the retrospective four-point global rating also revealed no variation among subgroups. These findings together suggest an apparent acute therapeutic equivalence on the basis of both electrode placement and stimulus waveform. Finally, no intergroup differences were found in terms of HDRS, BPRS, and Zung SDS change scores between baseline and six-month post-ECT testing, all of which continued to show evidence of improvement (m = 13.9, 23.9, 11.4). As described elsewhere,[22] therapeutic response was not related to mean or cumulative seizure duration.

Measures of memory function were subdivided into those assessing newly learned information (anterograde memory performance), information learned prior to the study (retrograde memory performance), and self-perceived, or subjective, memory function. Tasks were specifically chosen to be sensitive to ECT-induced effects, based upon previously reported findings. Specific anterograde memory measures included verbal paired associates,[30] paragraph retention,[31] and complex figure reproduction tasks, along with a newly designed instrument involving the learning and recognition of unfamiliar faces. All of these included 20-minute delayed recall testing. Retrograde memory function was evaluated using newly designed and periodically updated famous events and famous faces recall tasks, in addition to an autobiographical, or personal, memory questionnaire. Subjective memory function was tested using a modified version of Squire's Subjective Memory Questionnaire.[32]

The personal memory questionnaire was developed to cover a number of items relevant to the subject's life experiences, especially the last several years prior to baseline testing. A careful focus upon this difficult area of memory function was chosen because of earlier findings by others,[33] and is consistent with the nature of memory complaints by ECT patients themselves. This questionnaire included material on the following topics: place of residence, neighbors, family members, close friends, last birthday, last New Year's Eve, last overnight trip out of town, favorite television show, last movie seen at a theater, current hospitalization, and recent outstanding experiences. Only questions responded to at baseline were used at post-ECT test sessions.

Acute effects of ECT upon memory function were evaluated by determining the difference between baseline and two to three day post-ECT course scores, except for the personal memory task, where the percentage of items not recalled after ECT was calculated. TABLE 2 presents a listing of significant acute differences in memory function on the basis of electrode placement and stimulus waveform. In terms of acute effects of ECT upon anterograde measures, the verbal paired associate task proved quite sensitive in separating UL from BL subjects and P from S subjects. As in all cases to be discussed here, both BL and S treatments were associated with greater deficits. In addition, S and BL subjects also tended to perform much worse than control subjects. In what proved an extremely common phenomenon throughout these data, the SBL group was clearly the most impaired. The PUL group, on the other hand, in a manner consistent throughout virtually the entire data set, did not differ from the control group. The complex figure reproduction task was quite sensitive in separating S from P subjects ($p < 0.0008$), but was relatively insensitive in separating UL from BL subjects. This is not surprising, given the fact that nonverbally encodable figural information relies heavily upon the nondominant cerebral hemisphere. Control

subjects, in this regard, performed much better than both SUL and SBL subjects. The use of baseline HDRS scores as a covariate with regard to acute memory change scores produced no alterations in the above findings. Because of intergroup baseline differences, the IQ score was also used as a covariate, resulting in additional findings favoring UL ECT over BL ECT for both paragraph recall and complex figure reproduction ($p(BL > UL) < 0.03, 0.009$).

In terms of acute effects on retrograde memory measures, the famous events recall task was sensitive in differentiating the acute effects of both UL from BL, and P from S ECT. The SBL group was again more impaired than all others ($p < 0.0001$). The famous faces recall task was somewhat less sensitive in discriminating acute effects of ECT on the basis of electrode placement and waveform. The personal memory recall questionnaire, however, proved to be a very sensitive memory measure (FIGURE 1). All groups except control and PUL showed significant levels of relative impairment in the percent of initial items not recalled at the two to three day post-ECT test session. Main

TABLE 2. Acute Memory Impairment (Two to Three Days Post-ECT vs. Baseline Scores)

	p-Values (2 × 2 + 1 ANOVAS)					
	BL > UL	BL > C	UL > C	S > P	S > C	P > C
Anterograde Deficits (Based on Delayed Recall)						
Verbal paired associates	0.002	0.0001	NS	0.002	0.0001	NS
Paragraph recall	NS	0.01	NS	0.002	0.0008	NS
Unfamiliar faces recognition	NS	NS	NS	NS	NS	NS
Complex figure reproduction	NS	0.0008	0.002	0.0008	0.0001	NS
Retrograde Deficits						
Famous events recall	0.0001	0.0001	NS	0.0001	0.0001	NS
Famous faces recall	0.006	0.0001	NS	0.02	0.0001	NS
Personal memory recall	0.0001	0.0001	NS	0.0001	0.0001	NS
Global self-rating of memory function	NS	NS	NS	NS	NS	NS

effects for UL vs BL and P vs. S differences were present and, in addition, SUL, PBL, and SBL were more impaired than controls ($p < 0.03$, $p < 0.004$, $p < 0.0001$, respectively). In order to evaluate the role of guessing at the time of pre-ECT testing, the percent of baseline items not recalled at the second test session but later recalled at the third test session was determined. This measure showed similar relationships to that described above, suggesting that the results regarding acute effects are in fact valid. Use of baseline HDRS and IQ scores as covariates affected only the famous faces recall findings, for which the differences between UL and BL ECT groups disappeared. This may indicate that our famous faces recall test was not as sensitive as its famous events counterpart.

Overall, the objective data with respect to acute memory changes strongly implicate both bilateral electrode placement and sine-wave stimuli as potent risk factors, as do the EEG results reported elsewhere in this volume.[22] In terms of subjective memory function, however, a rather uniform tendency for self-perceived memory function to improve acutely following ECT was noted. No differences in terms

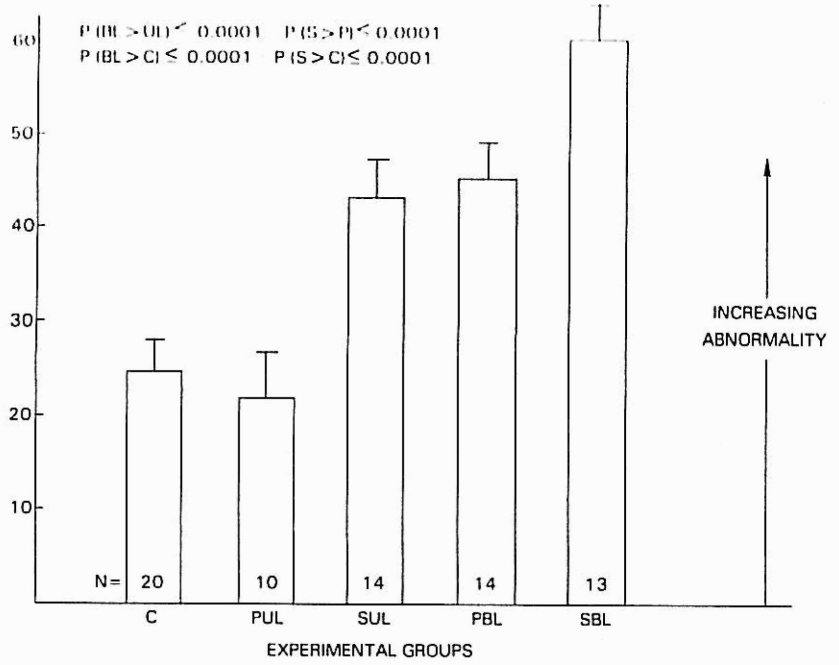

FIGURE 1. Acute personal memory impairment. Ordinate represents percent of baseline items not recalled two to three days post-ECT (+ standard error).

of post-ECT minus pre-ECT change scores, on either a total or an item-by-item basis, were observed as a function of ECT type or between controls and ECT subjects. Also interestingly, no appreciable relationship between subjective and objective memory measures was found, but, instead, acute measures of subjective memory function were significantly correlated with the respective differences in interviewer-rated and self-rated depression scales. While it is possible that the two to three day post-ECT rating time may not have allowed subjects sufficient opportunity to be aware of the extent of their deficits, this latter relationship suggests that self-rated memory changes with regard to a course of ECT may be more a function of the clinical response than of objectively demonstrable changes in memory function. Such a finding is compatible with available data reported by others,[34,35] but represents the first time this has been demonstrated in a systematic fashion.

Persistent ECT-associated effects upon memory function were investigated in a fashion identical to acute effects, except that baseline scores were compared to those obtained at six-month follow-up testing. In general, a return to at least pre-ECT level of function was found, with no evidence of intergroup differences for any of the measures of anterograde memory function. The famous events and famous faces recall tasks were likewise not productive of any long-term intergroup differences, although there was the suggestive finding that the three subjects with the largest long-term losses on the famous events task were all in the SBL group. The personal memory recall task, however, revealed a highly significant persistent intergroup difference favoring UL over BL ECT (FIGURE 2). The percentage of initial items not recalled at both the

two to three day post-ECT and six-month post-ECT test sessions revealed a greater impairment for BL subjects than either UL subjects ($p < 0.005$) or control subjects ($p < 0.002$). These differences were significant even when partitioning on the basis of stimulus waveform, and were not affected by the use of baseline HDRS or IQ as covariates. There was also suggestive evidence for a long-term toxicity of S with respect to control subjects ($p < 0.01$) on autobiographic memory, though no P vs. S differences were observed in this regard, and the latter difference disappeared with use of baseline IQ as a covariate. Again, no intergroup differences in long-term subjective memory function, as determined by either total or item-by-item change scores, were found.

The above results represent provocative evidence for what amounts to objective personal memory losses lasting at least six months with BL but *not* with UL ECT, and represents the first time such a differential effect has been reported. While analysis of personal memory data with respect to recency effects has not been completed, a preliminary assessment indicates that items dealing with the year immediately preceding the ECT may have been most affected.[36] At the same time, however, it does appear that the described period of retrograde amnesia is greater than, say, a few weeks.

Unfortunately, the study of autobiographic memory function, as carried out in the present protocol, is confounded by the possibility that some personal memory information given at the time of baseline testing may have been incorrect. In an attempt to partially compensate for such a potential bias all subjects were asked, immediately

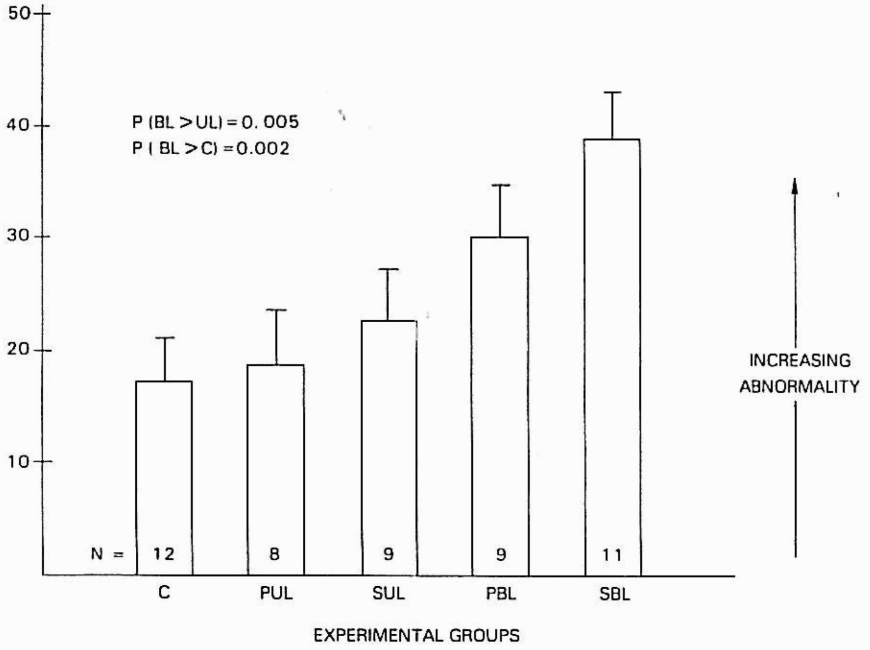

FIGURE 2. Long-term personal memory impairment. Ordinate represents percent of baseline items not recalled at both two to three day and six-month post-ECT test sessions (+ standard error).

following completion of the six-month follow-up personal memory questionnaire, to respond to a series of recognition trials. These consisted of questions based upon all items where both acute and follow-up responses differed from those given at baseline testing. In every case, subjects were given three choices: baseline response correct, six-month follow-up response correct, or unclear which of the two responses was correct. This procedure, in effect, approximated an attempt at "self-corroboration" of baseline items. Choices of the response that was given at baseline would suggest that responses given at the time of six-month follow-up testing may have been based upon incorrect recall, but that recognition of the correct response was still intact. Similarly, choices of the "unclear" alternative would suggest that both recall and recognition might be deficient.

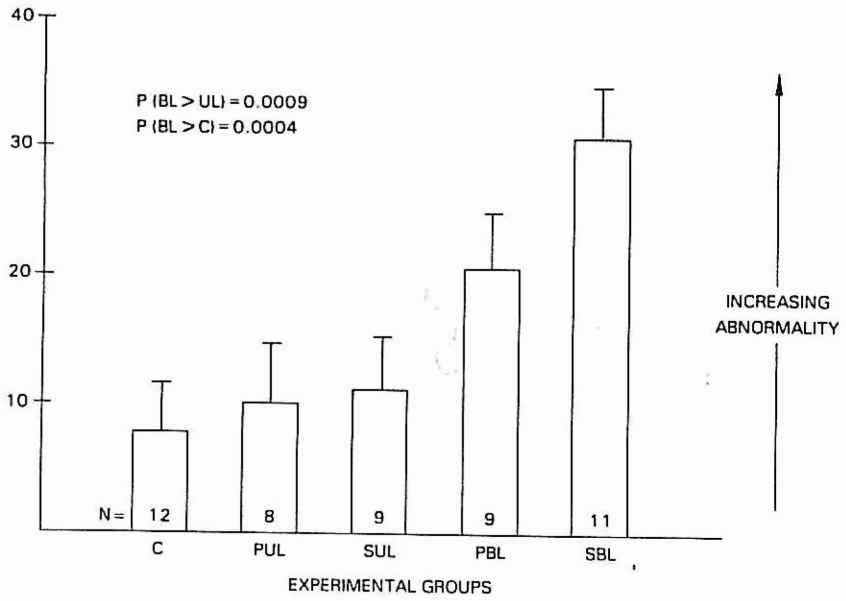

FIGURE 3. Long-term personal memory impairment adjusted using self-corroborative technique (see text for details). Ordinate represents percent of baseline items not recalled at both two to three day and six-month post-ECT test sessions (+ standard error.) Corrected to include only items with "session I" and "uncertain" self-corroborative responses.

Upon applying this self-corroborative technique and rejecting all equivocal items (i.e., where subjects felt that their follow-up response, rather than their initial response, was correct), the level of difference between BL and both UL and C groups was indeed found to increase (FIGURE 3). This strengthens the likelihood that the observed findings represent a true persistent deficit with BL ECT. Still, it must be pointed out that any such self-corroboration would be even more useful when supplemented by external corroboration using significant others or other relevant sources. For this reason, attempts to provide this modification were begun in the latter portion of the study. This allowed a comparison of long-term effects of ECT between C (four subjects) and SBL (three subjects) groups, using externally corroborated items.

It was, in fact, found that corroborated items, which constituted around three-fourths of the entire data set for those subjects, showed at least as much persistent forgetting (35% of baseline items for SBL vs. 13% for C subjects) as was observed based upon analysis without the use of external corroboration.

Given that both acute and persistent memory deficits were present, a further series of points can be made with respect to their possible correlates. First, even though HDRS scores were highly correlated with subjective memory ratings, no such relationship was established between HDRS scores and results on objective memory testing for either acute or long-term effects. This suggests that the findings are in fact organic rather than functional, and is supported by a number of highly significant correlations between acute objective memory test changes and acute EEG abnormalities. Second, the presence and amount of ongoing psychotropic medications presumably could affect memory performance. Analyses of medication effects are pending, though preliminary consideration of these factors indicates that BL subjects, for example, were no more likely to be medicated at the final test session than UL subjects. Next, the possibility that memory changes might be related to number of ECT treatments or EEG seizure parameters was considered. No significant correlations were observed, though the range of available values could have precluded relationships from appearing.

Finally, the effects of stimulus intensity per se (energy, current, and charge) upon objectively assessed memory function were evaluated. Here it was determined that stimulus intensity, especially energy, was correlated significantly with a variety of measures of memory function, particularly both acute and long-term personal memory performance ($p < 0.0002$, $p < 0.0009$, respectively). While at first this was felt to represent perhaps a reflection of S vs. P differences, these relationships were found to be present only with S ECT and *not* with P ECT, despite the existence of wide parameter ranges in each case. This suggests that, as long as stimuli are only slightly suprathreshold, the relatively low-energy stimuli present with the pulse waveform may lie below a cutoff for intensity-related effects upon memory performance with ECT and, furthermore, that only the higher energy sine-wave stimulus is able to exceed this cutoff in an appreciable number of cases.

DISCUSSION AND CONCLUSIONS

This study has provided a number of findings that are both new and potentially pertinent to clinical practice. Evidence presented suggests that unilateral nondominant electrode placement and brief-pulse stimuli may each provide significantly fewer acute CNS adverse effects while remaining equally effective. Given the present widespread clinical reluctance to use such ECT modifications, the finding of long-term personal memory impairment with bilateral electrode placement is particularly important.

The bases for why electrode placement and stimulus waveform should each exert independent and additive differential effects upon memory systems are poorly understood.[6] UL nondominant ECT appears to be associated with less intracerebral current flow, less generalization of the seizure discharge, and less postictal suppression in the dominant, contralateral hemisphere. It has even been proposed that seizures produced by UL and BL ECT differ in their onset, i.e., focal cortical initiation with the former and generalized diencephalic onset with the latter.[37] Certainly, such electrophysiologic differences could well account for the relative sparing of at least verbal memory function with UL nondominant ECT.

The basis of stimulus waveform effects on cognitive performance could be

secondary to the direct electrical effects of a higher mean current or charge distribution within the cerebral structures subserving memory function with S ECT. Alternatively, the apparently more intensely generalized seizures produced by the higher energy stimuli, as discussed in a companion paper in this volume,[22] may be involved. The former possibility, when combined with the reported significant relationship between sine wave stimulus intensity and extent of both acute and long-term memory deficits, raises a concern about the use of grossly suprathreshold stimuli,[38] something that was not dealt with in the present study.

At present, we are involved in an attempt to replicate and extend the findings described above. It is felt that such work is crucial, not only to the understanding of how ECT produces both its beneficial and adverse effects, but also in the optimization of a beleaguered and maligned treatment modality which has time and time again proven too clinically valuable to consign to the halls of oblivion.

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