Marshall, T.J., and Dobbs, D. Treatment technique and apnea in electroshock. *Dis. Nerv. Syst.*, 20(12):582-583, 1959.

Small, J.G., Small, I.F., and Milstein, V. Electrophysiology of EST. In: Lipton, M.A., DiMascio, A., Killam, K.F. (eds.), *Psychopharmacology: A Generation of Progress*. New York:Raven Press, 1978, pp. 759-769.

Staton, R.D., Hass, P.J., and Brumback, R.A. Electroencephalographic recording during bitemporal and unilateral nondominant hemisphere (Lancaster position) electroconvulsive therapy. *J. Clin. Psychiatry*, 42(7):264-269, 1981.

Weiner, R.D. ECT and seizure threshold: Effects of stimulus wave form and electrode placement. *Biol. Psychiatry*, 15(2):225-241, 1980a.

Weiner, R.D. The persistence of electroconvulsive therapy-induced changes in the electroencephalogram. *J. Nerv. Ment. Dis.*, 168(4):224-228, 1980b.

Weiner, R.D., Rogers, H.J., Davidson, J., and Miller, R.D. Evaluation of the central nervous system risks of ECT. *Psychopharmacol. Bull.* 18(1):29-31, 1982.

Short- and Long-Term Cognitive Effects of ECT: Part I—Effects on Memory

Trevor R.P. Price, M.D.[1]

Introduction

In this article and the one that follows, the effects of electroconvulsive therapy (ECT) on various cognitive functions, both short- and long-term, will be reviewed. In the interest of simplification and clarity, they will be discussed in two separate sections: one dealing with the effects of ECT on memory function and the other with the effects of ECT on nonmemory-associated cognitive function. Obviously this is a heuristically useful though somewhat artificial distinction, since memory capacity is an important underlying component of at least some so-called nonmemory-associated cognitive functions.

In attempting to understand the effects of ECT on neuropsychological and cognitive functions, it is crucial to bear in mind that the diseases for which it is most frequently used, i.e., major depressive disorder and schizophrenia, may themselves cause significant changes in these functions. It is therefore important, but at the same time often difficult, in patients receiving ECT to separate out the extent to which observed cognitive changes are due to the treatment as opposed to the underlying disease. The article by Nasrallah in this series speaks to this issue in greater detail.

[1]Department of Psychiatry, Dartmouth Medical School, Hanover, NH 03755.

Memory Dysfunction Associated with Depression

Patients with depression may have impaired concentrating ability and experience difficulty in focusing attention (Wexler, 1980). Depression may also cause impaired memory function (Sternberg & Jarvik, 1976) of a particular type. It has been shown that short-term memory, which is dependent on registration, is impaired, while long-term memory, which is dependent on retention and recall, is not (Cronholm & Ottosson, 1961). Further, it is thought that impaired registration is a result of concentration and attention deficits, so-called "prograde effects" (Reichert, Benjamin, Neufeldt, & Marjerrison, 1976). It has been shown that when patients are treated, improvement in depression and short-term memory function are highly correlated and tend to be proportional in magnitude. In general, as will be detailed below, the memory impairments resulting from ECT tend to be just the reverse of those associated with depression. There may be uncertainty in some cases as to whether observed memory problems are due to depression or to the effects of ECT. Squire, Wetzel, and Slater (1979) have developed a self-rating instrument which may allow for differentiation between them. Using this scale, they showed that the patterns of memory complaints 1 week and 6 months post-bilateral ECT were qualitatively similar to each other, though quantitatively different, with the memory impairment at 1 week, as expected, being greater. In comparison to the pattern obtained before treatment, however, the two post-treatment scores differed both qualitatively and quantitatively, allowing for clear differentiation between them.

Methodological and Technical Issues

In reading the literature on the cognitive effects of ECT, one must be aware that much of the work

done in the past on the effects of ECT on memory and cognition has suffered from inadequate research methodology. There has been a great need evident in earlier studies, which has only in recent years begun to be met, for more standardized and sophisticated assessments of memory function (Harper & Wiens, 1975).

One must also bear in mind that conclusions regarding ECT's effect on memory depend to a great extent on how one measures memory function (Squire & Miller, 1974) and what one is measuring. Thus the experimental methodology employed; the sensory modality that is mediating memory, be it auditory, visual, or tactile; the content of the material administered, whether verbal or nonverbal; and whether one is measuring recognition, recall, relearning, or forgetting (the differences between immediate and delayed reproduction scores) are all important in interpreting and comparing the results of studies of the effects of ECT on memory function.

One should also be aware that while much is now known with a reasonably high degree of certainty about the effects of differential electrode placement on certain cognitive and memory functions, so-called laterality effects, their relationship to the type of stimulus waveform, and the frequency and intensity of stimuli and seizures have not thus far been adequately investigated.

The Effects of ECT on Memory Function

Memory impairment is a frequent and distressing, though for the most part, reversible, consequence of ECT. It occurs in a variety of forms which will be discussed below, and its nature and severity depend to an important degree on where and how the electric stimulus is delivered. While over the years this has been a subject of considerable debate, there is now widespread agreement that memory deficits are neither correlated with nor necessary for clinical improvement with ECT (Korin, Fink, & Kwalwasser, 1956; Fink, 1974; Squire, 1977; Dornbush & Williams, 1974). They are thus considered undesirable and often largely avoidable side effects of ECT.

General Aspects of ECT-Induced Memory Dysfunction

ECT can induce both retrograde and anterograde amnesia and has deleterious, though generally variable and transient, effects on immediate, intermediate, and remote memory (Fink, 1977). It has relatively little effect on short-term memory; its major impact is therefore on long-term memory (Dornbush & Williams, 1974; McGaugh & Williams, 1974).

Bilateral ECT seems to accelerate the process of normal forgetting (Squire, Wetzel, & Slater, 1978). Immediately following each treatment it induces a global anterograde amnesia which by 30 to 45 minutes later has become a well-circumscribed deficit characterized by good immediate memory, rapid forgetting, and temporally graded retrograde amnesia occurring in the absence of confusion or intellectual impairment (Squire et al., 1978; Squire, 1977). After ECT, memory performance is best on recognition testing and worst on recall testing, with relearning intermediate but tending to be more similar to recall than recognition (Dornbush & Williams, 1974). Evaluation of the ability to retain information following ECT is most sensitivity accomplished by the use of recall or relearning rather than recognition testing paradigms. While the ability to recall information is generally more important to patients than simple recognition, it is also considerably more difficult to test.

With ECT there is amnesia (of variable duration) for the seizure itself as well as for immediate pre- and posttreatment periods (Fink, 1977). While memory impairment is typically seen immediately after a treatment is over, its onset may occasionally be delayed for up to 24 hours (Hargreaves, Fischer, Elashoff, & Blacker, 1972). In general terms, Ottosson (1968) has described ECT as transforming the memory disturbance associated with depression from one characterized by poor learning with normal retention to one characterized by normal learning with poor retention.

It is believed that the severity and duration of ECT-induced memory impairments are positively correlated with the number, frequency (Squire & Miller, 1974; Korin et al., 1956; Dornbush, Abrams, & Fink, 1971; Fromholt, Christensen, & Stromgren, 1973), and intensity (Fink, Kahn, & Green, 1958; Ottosson, 1960; McGaugh &

Alpern, 1966) of the electrical stimuli given as well as of the seizures experienced (Laurell, 1970; Ottosson, 1960; Small & Small, 1972).

While increased frequency of treatments may have important implications with bilateral ECT, this may not be the case with unilateral nondominant ECT. Thus, Stromgren, Christensen, and Fromholt (1976) found that four unilateral nondominant treatments per week, as opposed to two, resulted in greater improvement in memory due presumably to more rapid improvement in the underlying depression. Likewise, Abrams (1967) found no greater memory impairment when unilateral nondominant ECT was given on a daily basis as opposed to three times a week.

While early studies suggested that alternating current sine wave stimuli caused more severe cognitive effects than other types of stimulus waveforms (Lieberson, 1953; Valentine, Keddie, & Dunne, 1968), more recent work has indicated that differences between brief pulse and sinusoidal waveform are not likely to be major factors in determining the degree of memory dysfunction associated with ECT (Weaver, Ives, Williams, & Nies, 1977; Weiner, Rogers, Davidson, & Miller, 1981; Spanis & Squire, 1981).

Some work with multiple monitored ECT has reported that it causes both anterograde and retrograde memory disturbances no greater in extent and severity than those seen after a single conventional treatment of the same type and of lesser proportions than if the same number of seizures had been induced individually on an alternate day schedule (Abrams & Fink, 1972).

Giving ECT via unilateral as opposed to standard bilateral administration substantially decreases the extent of memory impairment. Treating unilaterally over the nondominant or dominant hemispheres will also result in major differences in the kinds of memory impairment that occur. These differences will be discussed in detail in a later part of this review.

Administering ECT via anterior bifrontal (Inglis, 1970; Abrams & Taylor, 1973) as opposed to standard bitemporal electrode placement has been reported to lead to a reduction in memory dysfunction while achieving therapeutic efficacy intermediate between unilateral and bilateral ECT.

Stimulating unilaterally over various combinations of anatomic areas seems to have relatively little effect on memory dysfunction. Thus, there is no difference in the impact on memory between nondominant unilateral fronto-parietal and temporo-parietal lead placements (d'Elia & Widepalm, 1974). The findings are somewhat more complex in regard to comparison between fronto-frontal and temporo-parietal lead placements. While two earlier studies reported no difference in anterograde memory function between them both for verbal as well as nonverbal material (d'Elia, 1976; d'Elia, Frederiksen, Raotma, & Widepalm, 1977), a later study reported less retrograde amnesia with fronto-frontal as compared to temporo-parietal stimulation (d'Elia, 1981).

One study has indicated that the degree of immediate memory dysfunction following ECT is highly correlated with the rise in systolic blood pressure that occurs during treatment (Hamilton, Stocker, & Spencer, 1979).

Memory research in animals has shown that material ordinarily not affected by ECT may be forgotten if a reminder of it is presented just before a treatment is given (Schneider & Sherman, 1968; Misanin, Miller, & Lewis, 1968; Lewis, Bregman, & Mahan, 1972). This is known as the "reinstatement phenomenon." The evidence available (Squire, Slater, & Chace, 1976) suggests that this phenomenon does not occur in humans given ECT.

ECT-Induced Anterograde Amnesia

Both bilateral and unilateral ECT can cause anterograde amnesia which is the inability to incorporate material newly learned after ECT into long-term memory storage (Squire & Miller, 1974; Squire et al., 1976; Fleminger, Horne, Nair, & Nott, 1970a; d'Elia, 1974; Halliday, Davison, Browne, & Kreeger, 1968). Adequate investigation of ECT-induced anterograde amnesia requires the use of both immediate and delayed recall assessment devices. This is because tests of delayed reproduction which predominantly reflect retention are generally more sensitive to the deleterious effects of ECT than are tests of immediate reproduction which predominantly reflect new learning ability (Squire & Miller, 1974). Over the course of several treatments new learning ability may actually be improved. Sub-

tracting delayed from immediate reproduction scores yields a highly useful direct measure of memory function, the so-called "forgetting score" (Harper & Wiens, 1975).

The severity of ECT-induced anterograde amnesia depends on the temporal distance from ECT of the new learning. Thus, in a study by Squire et al. (1976), recognition memory for material learned 3 hours after bilateral ECT was significantly better than for that learned 1 hour or less after ECT. Furthermore, the ability to retain material over a short (e.g., 30-minute) period recovers rapidly after ECT, being nearly normal by 3 hours after treatment. There is no cumulative impairment in this short-term measure over the first four treatments. However, the ability to retain new material over longer periods such as 24 hours appears to be much more vulnerable to the effects of ECT. Thus impairment in 24-hour retention was more severe than that seen with short-term retention given comparable amounts of ECT, and the effects of ECT were cumulative. Based on these observations, the theories that ECT causes anterograde amnesia by disrupting the ability to transfer material from short-term memory to long-term memory or to recall material from long-term memory have been advanced.

On the other hand, Squire et al. (1976) postulated that anterograde amnesia results from an ECT-induced impairment of acquisition and consolidation of new information, rather than an impairment of the ability to call upon and use information that has already been stored. Others (Cronholm & Ottosson, 1961, 1963) have suggested that ECT interferes with the memory function, retention, while concomitantly improving new learning, i.e., acquisition and consolidation, to the extent that it reverses the patient's depression. Thus, ECT may have a mixed effect on various aspects of memory function.

ECT-induced anterograde amnesia does not appear to depend on the presence of intellectual dysfunction, confusion, or disorientation following ECT. In general, it gradually recedes after each individual treatment but may be cumulative over a series of treatments (Squire & Miller, 1974).

In 1958, Lancaster, Steinert, and Frost first reported that memory and cognitive impairment due to ECT could be reduced without a major diminution in therapeutic efficacy by using unilateral rather than bilateral stimulation. Subsequently, a variety of studies clearly documented that bilateral ECT produced greater amounts of anterograde amnesia than did either unilateral nondominant (Halliday et al., 1968; Fleminger et al., 1970a; d'Elia, 1970, 1974) or unilateral dominant ECT (Jackson, 1968).

In the mid- to late sixties evidence began to accumulate that there was a differential effect of unilateral dominant and nondominant ECT on verbal and nonverbal visuospatial anterograde memory. This was based on ECT studies that employed assessment batteries which specifically tapped verbal and nonverbal memory function.

Zamora and Kaelbling (1965), using Form One of the Wechsler Memory Scale, found that unilateral dominant ECT caused deterioration in verbal memory performance whereas unilateral nondominant ECT enhanced it, an effect they attributed to ECT-induced improvement in depression in the patients they studied. However, since the instrument they used did not include delayed reproduction subtests, it is more likely that they were measuring differences in new verbal learning ability rather than true verbal memory function.

Subsequently, a study by Jackson (1968) comparing verbal and nonverbal memory effects of right and left unilateral as well as bilateral ECT showed that patients treated with right unilateral ECT had the least verbal memory impairment; those treated with left unilateral, the least nonverbal visuospatial impairment; and those treated with bilateral the greatest degree of both. Similar findings were also reported by Halliday et al. (1968), Cohen, Noblin, Silverman, and Penick (1968); and Zinkin and Birtchnell (1968).
chnell (1968).

Kozma and Galbraith (1968) reported similar results in that they noted improvement in memory with unilateral nondominant ECT, some deterioration with unilateral dominant, and marked deterioration with bilateral ECT.

Sutherland, Oliver, and Knight (1969), in a double-blind study comparing the effects of unilateral dominant, unilateral nondominant, and bilateral ECT on memory function, found that all three types of treatment improved it, and attributed this to the indirect beneficial effect of improvement in depression on cognitive and

memory function. They, like others, found that the greatest degree of improvement occurred with unilateral nondominant ECT.

Two years later Cronin, Bodley, Potts, et al. (1970) showed that impairment of anterograde verbal memory as assessed by word learning and the Wechsler Memory Scale was less marked with unilateral nondominant than with either unilateral dominant or bilateral ECT. Also in 1970, Fleminger, Horne, and Nott, (1970b) reported anterograde verbal memory to be more impaired after left unilateral than right unilateral ECT.

Two more recent well-designed and executed studies (Squire & Slater, 1978; Robertson & Inglis, 1978) have provided further confirmation of the differential effects of various types of ECT on verbal and nonverbal memory. The first study, using a before and after five-treatment design, showed that right unilateral ECT impaired delayed retention of nonverbal material in the form of faces, designs, and spatial relations, without affecting delayed retention of verbal material in the form of a paragraph. In this study, as in earlier ones, bilateral ECT caused greater impairment of both verbal and nonverbal memory than right unilateral ECT. The second study, using more sophisticated dimensions of symbolism and imagery in addition to the usual verbal and nonverbal dimensions in memory testing, further confirmed the differential effects of unilateral nondominant and bilateral ECT on verbal and nonverbal memory function. Unlike earlier studies, neither of these studies directly assessed the effects of unilateral dominant ECT on verbal and nonverbal memory.

Several of the studies that showed clear-cut differential effects of various forms of ECT on memory function reported virtually identical degrees of therapeutic efficacy (Fleminger et al., 1970a; d'Elia, 1974; Halliday et al., 1968; d'Elia & Raotma, 1975). Other studies have disputed the notion that unilateral and bilateral ECT are equipotent (Abrams, Fink, Dornbush, et al., 1972; Abrams, Taylor, Faber, et al., 1981; Price, 1980). Thus, whether or not the risk-benefit ratio (Fink, 1978, 1979) with respect to potential memory effects clearly favors unilateral nondominant over bilateral ECT in all cases is at present unclear and is an issue the APA Task Force on ECT felt should be left up to the clinical judgment of individual practitioners (APA Task Force Report on ECT, 1978).

Relatively few studies have attempted to establish the duration of ECT-induced anterograde amnesia. Halliday et al. (1968) reported that verbal memory impairment persisted over at least a 3-month period after unilateral dominant ECT. This study also indicated that nonverbal memory impairment persists longer after bilateral than unilateral nondominant ECT. Bidder, Strain, and Brunschwig (1970) found verbal memory as assessed by a paired-associate learning test to have returned to baseline within 30 days of the end of courses of both unilateral and bilateral ECT. At the followup assessment, memory was better than it had been before treatment in both groups. Finally, Cronin et al. (1970) showed that differences in anterograde verbal memory resulting from unilateral dominant, unilateral nondominant, or bilateral ECT persisted for 4 to 6 weeks following a course of eight treatments.

ECT-Induced Retrograde Amnesia

As mentioned previously, retrograde amnesia, which is a lack of ability to recall events occurring prior to ECT, also occurs as a result of both bilateral and unilateral ECT though to a significantly lesser extent with the latter (Cohen et al., 1968). It is more severe with increased number and frequency of bilateral ECTs and is thought by some to increase in severity with increasing patient age (Squire, 1974; Fink, 1977), though not all researchers agree on this (Fink, 1979). It often occurs in association with confusion, disorientation, or impairment on the verbal portion of the Wechsler Adult Intelligence Scale (WAIS) (Squire, 1974), but can also be present as an isolated defect.

ECT-induced retrograde amnesia occurs for both public and autobiographical events both temporally close in occurrence to (Harper & Wiens, 1975; Dornbush & Williams, 1974; and Dornbush, 1972), as well as many years (even up to 20) prior to treatment (Squire, 1977; Squire et al., 1975; Squire, 1975; Squire, Chace, and Slater, 1976; Brody, 1944; Squire, 1974; Janis, 1950). In the past the standard explanation for retrograde amnesia due to ECT had been the

"consolidation hypothesis," which held that ECT somehow disrupted neural mechanisms and processes underlying the consolidation of memory traces (Zinkin & Birtchnell, 1968; McGaugh & Williams, 1974). Current theories, however, focus more on ECT-induced interference with the "retrieval process" as the underlying mechanism (Patterson, Lawler, & Rochester, 1978).

There is a temporal gradient in retrograde amnesia induced by ECT (Squire, 1975; Squire, 1976). Thus it was shown that following five bilateral ECTs, television programs broadcasted 1 to 3 years before ECT were forgotten, whereas those broadcasted 4 to 17 years before ECT were not.

Long-term memory for temporal order, which depends on recall not just recognition, appears to be more sensitive to bilateral ECT than other aspects of memory and is, like other forms of retrograde amnesia, associated with a temporal gradient of impairment (Squire et al., 1976). Thus temporal sequencing of events occurring from 4 to 7 years before ECT was impaired, whereas it was not impaired for events 8 to 16 years before. This temporal sequencing impairment persisted unchanged for 1 to 3 weeks after the end of treatment.

d'Elia (1970) reported that unilateral nondominant ECT caused less retrograde amnesia than bilateral ECT with unilateral dominant intermediate between them.

Cohen et al. (1968) showed that five unilateral dominant ECTs selectively impaired retrograde verbal memory, while five unilateral nondominant ECTs selectively impaired retrograde nonverbal, visuospatial memory. They also showed that both verbal and nonverbal memory were more profoundly impaired by five bilateral ECTs than with a comparable number of administrations of either form of unilateral treatment.

Berent, Cohen, and Silverman (1975) replicated the findings of Cohen et al. (1968) after one unilateral nondominant, unilateral dominant, or bilateral ECT, using words or visual forms learned 24-48 hours before and tested 5 hours after ECT. Based on their observation that verbal memory impairment after five unilateral dominant ECTs was much greater than after one, whereas visuospatial memory impairment was nearly identical after both five and one unilateral nondominant treatments, they suggested that the left hemisphere and verbal memory might be more susceptible to the cumulative effects of a series of ECTs than the right hemisphere and visuospatial memory.

Clearing of retrograde amnesia following ECT occurs as a result of spontaneous recovery not via relearning or "prompting" (though this may indeed help). As would be expected from Ribot's Law of Regression (Ribot, 1885), there is greater recovery of more remote events, months to years before ECT, than of very recent events, within days of treatment, for which loss of memory may be permanent (APA Task Force Report on ECT, 1978). Ease of restitution of retrograde memory loss is directly related to the patient's motivation to remember forgotten material, the degree of personal importance and hence presumably the amount of attention paid to it, the amount of affect associated with it, the degree of familiarity with it, and the ease with which it was originally assimilated into memory storage (Williams, 1975).

Recovery from ECT-induced retrograde amnesia occurs over a variable and, thus far, not definitely determined period of time. Various studies have demonstrated persistence of retrograde amnesia over periods ranging from 24 hours (Squire, 1975) to 10 to 14 weeks (Janis, 1950), to as much as 1 year or more following ECT (Brody, 1944). The last was an early study which was uncontrolled, and assessed memory function with respect to familiar, long-known names of persons and places as well as habits of work. Several more recent studies have indicated that the recovery of memory for remote events may be substantially complete in as little as 1 to 2 weeks (Squire, 1975, 1976) or as much as 6 to 9 months post-ECT (Squire & Chace, 1975; APA Task Force Report on ECT, 1978; Squire, 1980; Squire et al., 1980). The latter two studies indicated that memory impairment for events occurring more than 2 years before ECT, as well as new learning capacity, return to normal by 6 months post-ECT. While impaired memory for events occurring during the 1- to 2-year period before ECT substantially improves over the 6 months following ECT, there may be permanent loss of memory for some of them. Most of these permanent memory "gaps" are irritating but not functionally incapacitating to the patient (Freeman, Weeks, & Kendell, 1980).

Followup Studies of Long-Term Effects of ECT on Memory

Assessing the long-term effects of ECT on memory function is difficult because, as was first described nearly 20 years ago (Cronholm & Ottosson, 1963), and more recently confirmed (Squire & Chace, 1975), patients' subjective experience of their memory function is often at odds with the results of objective testing. In general, a patient's subjective assessment of the adequacy of his or her memory function post-ECT is directly related to verbal but not visuospatial performance, the degree of affective improvement from ECT, and the adequacy of immediate reproduction capacity, i.e., learning, more than delayed reproduction capacity, i.e., retention (Cronholm & Ottosson, 1963). Given the numerous and potentially complex interactions that may occur between these variables, it is not surprising that subjective and objective assessments of memory are often at variance with each other.

Squire and Chace (1975) found no objective difference in new learning, retention memory scores, remote memory, or self-rating of memory function 6 to 9 months after unilateral nondominant or bilateral ECT or inpatient psychiatric treatment without ECT. Despite the lack of objective differences, 63% of prior bilateral ECT patients felt their memory was not as good as it had been before treatment, while only 30% of unilateral ECT patients and 17% of non-ECT-treated patients felt similarly.

Squire et al. (1979), using a self-report memory assessment scale, found that subjective complaints of memory impairment persist in a gradually diminishing fashion for up to 6 months after ECT. The complaints present 6 months after ECT differ qualitatively from the depression-associated complaints present prior to ECT and are similar to, but less marked than, those present 1 week following ECT. Thus, while their etiology is unclear, the authors suggested that they are unlikely to be due to such commonly advanced explanations as persistent low self-esteem, a general tendency to complain about memory capacity, or recurrent depression-associated memory dysfunction.

Freeman, Weeks, and Kendel, (1980) retrospectively studied patients who had had ECT (mainly bilateral) from 2.6 to 12.8 years (mean = 10 years) previously and who complained of permanent unwanted effects secondary to the ECT. They found these patients to be more depressed and anxious and to be taking more psychotropic medications than the noncomplainers. Nonetheless, even after partialling out the effects of these factors, they still found more impairment in the patients than in volunteer, nonpatient controls on 3 out of 19 wide-ranging cognitive and memory tests. In fact, a few of the patients scored in the organically-impaired range on some of the tests. The authors concluded that: ECT may induce permanent memory impairment in a very small proportion of patients who receive it; this memory loss is, for the most part, irritating but not incapacitating; and that ECT does not normally produce persistent memory defects in most patients.

In a related study, Weeks, Freeman, and Kendell (1980) studied unilateral nondominant and bilateral ECT patients as well as normal and non-ECT-treated patient controls with a battery of tests that assessed both memory and non-memory associated cognitive function. These tests assessed recall, relearning, and recognition functions in auditory, verbal, and visuospatial modes. They also tested immediate and delayed retrieval, short and long-term memory, as well as remote (long-term) memory for both personal and impersonal material. They found that unilateral nondominant ECT patients scored close to normal controls on many of the tests after 1 week of treatment; whereas, bilateral ECT patients showed significantly greater impairment after 1 week. At 3-month followup, however, unilateral nondominant and bilateral ECT patient performances were identical. At 4- and 7-month followups both ECT patients and non-ECT patient controls showed deficits on some tests when compared to the normal controls. They also complained subjectively of memory deficits which were attributed to the effects of residual depression, medication, and/or persistent ECT-induced memory impairment.

While there have been several anecdotal reports of patients who have received very large numbers of ECT with no apparent cognitive or memory impairment, such as that of Perlson's (1945) male patient who had received 248 bilateral ECTs, other reports (Templer, Ruff, & Armstrong, 1973; Goldman, Gomer, & Templer, 1972; Teuber, Corkin, & Twitchell, submitted) have raised the possibility

that large numbers of bilateral ECT (more than 50 treatments per patient) may be associated with impairment on a variety of memory tests not present in controls on followup testing many years later. The conclusion of these studies that ECT is responsible for the observed persistent impairment must be viewed with caution since, given their design and retrospective nature, the effects of underlying chronic schizophrenia, depression, and/or associated organic lesions such as cingulotomy cannot be separated from the effects of ECT.

Summary

From this review a variety of reasonably firm conclusions about the effects of ECT on memory can be drawn. These include:

1. ECT causes both retrograde and anterograde amnesia.
2. Bilateral ECT causes greater anterograde amnesia than unilateral nondominant or dominant ECT, both for nonverbal and verbal memory.
3. Anterograde amnesia severity depends on the temporal distance from ECT of the new learning in question.
4. Anterograde amnesia recedes gradually after each individual treatment, but is cumulative over a series of treatments.
5. The early time course of recovery of anterograde amnesia due to ECT is not clear but is substantially complete by at least 6-9 months post-ECT.
6. Bilateral ECT causes greater retrograde amnesia than unilateral dominant and nondominant ECT, both for verbal and nonverbal memory.
7. Retrograde amnesia is characterized by a temporal gradient, and recall of when events occurred intime is more sensitive to impairment than other aspects of retrograde memory.
8. Unilateral nondominant ECT selectively impairs nonverbal retrograde memory, while unilateral dominant ECT selectively impairs verbal retrograde memory.
9. Recovery from retrograde amnesia following ECT is substantially complete by 6-9 months; however, some events during the 1-2 years before ECT and events during the course of treatment may be lost permanently.
10. ECT-induced memory dysfunction appears to be qualitatively different than depression-related memory dysfunction, at least as assessed by self-report scales.
11. Despite lack of objective evidence of memory dysfunction several months post-ECT, patients will often complain of subjective memory impairment following treatment. These complaints are more frequent following bilateral than unilateral ECT.
12. ECT, in a small number of patients, may cause permanent memory impairment; the functional significance of this memory loss is unclear at present.
13. ECT does not normally cause enduring memory deficits, and with unilateral nondominant ECT there is generally relatively little clinically apparent memory disturbance even immediately following ECT.

Areas for Future Research

Despite the extensive investigation of the effects of ECT on memory function over the past two decades and despite the fact that, as this review indicates, much is known about this area with a reasonable degree of certainty, many questions remain, and these indicate important directions for future research.

For example, what is the true incidence of permanent memory dysfunction from bilateral ECT? Does it ever occur in patients treated with unilateral ECT? If so, how often, and is the type of dysfunction different than that seen with bilateral ECT? Is it possible to identify, prior to treatment, through biological markers or clinical profiles, that small but finite number of patients who will be prone to experience permanent ECT-induced memory impairment? Can the nature and functional significance of such deficits be better characterized, especially with respect to the kinds of impact they have on the patient's life and work?

How long do subjective memory deficits persist post-ECT and what relationship do they bear to permanent memory impairments on objective memory tests?

How do ECT, particularly unilateral nondominant ECT, and various commonly used drug treatments for depression compare in regard to causing cognitive or memory disturbances in the short-run, but even more importantly over extended followup periods after acute treatment?

Does ECT have differential effects on memory function in different diagnostic groups, for example, in patients with schizophrenia as opposed to patients with major depressive disorders? Some early studies suggested that there might be such differences but this issue has not been adequately examined with studies using rigorous experimental designs in patient populations carefully defined by current research diagnostic criteria.

Studies of the latter type, as well as rigorously designed, prospective controlled studies with long-term followups involving large enough numbers of patients so that solid statistical inferences, regarding observed differences can be drawn, are badly needed. Multicenter, collaborative studies, despite their obvious drawbacks, lend themselves uniquely well to the need to collect large numbers of experimental subjects. Carefully done, large-scale, longitudinal, studies of the incidence, nature, and natural history of various types of ECT-induced memory dysfunction are also sorely needed. Additional rigorously designed and executed studies of the relationship between ECT-induced memory changes and the electrical characteristics (waveform, intensity, duration, frequency, etc.) of the stimulus; the number, frequency, and duration of induced seizures; and various ECT-induced neurophysiological and neuroendocrinological changes would also be important additions to the literature.

Research aimed at developing means of further attenuating, or even preventing altogether, ECT-induced memory loss via additional technical modifications of ECT or pharmacological interventions with, for example, peptide hormone fragments, should also have a high priority. Efforts aimed at identifying the basic mechanisms underlying ECT's therapeutic effects should be encouraged, as these may make it possible to develop an alternate form of treatment that will have comparable therapeutic efficacy without memory impairment.

References

Abrams, R. Daily administration of unilateral ECT. *Am. J. Psychiatry,* 124:384-386, 1967.

Abrams, R., and Fink, M. Clinical experience with multiple electroconvulsive treatments. *Compr. Psychiatry,* 13:115-121, 1972.

Abrams, R., Fink, M., Dornbush, R.L., et al. Unilateral and bilateral electroconvulsive therapy. *Arch. Gen. Psychiatry,* 27:88-91, 1972.

Abrams, R., and Taylor, M. Anterior bifrontal ECT: A clinical trial. *Br. J. Psychiatry,* 122:587-590, 1973.

Abrams, R., Taylor, M., Faber, R., et al. Bilateral vs. unilateral ECT: Efficacy in melancholia. *Am. J. Psychiatry.* (In press)

American Psychiatric Association Task Force Report on Electroconvulsive Therapy, Washington, D.C., 1978.

Berent, S., Cohen, B.D., and Silverman, A.J. Changes in verbal and nonverbal learning following a single left or right unilateral electroconvulsive treatment. *Biol. Psychiatry,* 10:95-100, 1975.

Bidder, T.G., Strain, J.J., and Brunschwig, L. Bilateral and unilateral ECT: Followup study and critique. *Am. J. Psychiatry,* 127:737-745, 1970.

Brody, M.B. Prolonged memory defects following electrotherapy. *J. Ment. Sci.,* 90:777-779, 1944.

Cohen, B.D., Noblin, C.D., Silverman, A.J., and Penick, S.B. Functional asymmetry of the human brain. *Science,* 162:475-476, 1968.

Cronholm, B., and Ottosson, J.O. Memory functions in endogenous depression: Before and after electroconvulsive therapy. *Arch. Gen. Psychiatry,* 5:193-199, 1961.

Cronholm, B., and Ottosson, J.O. The experience of memory function after electroconvulsive therapy. *Br. J. Psychiatry,* 109:251-258, 1963.

Cronin, D., Bodley, P., Potts, L., et al. Unilateral and bilateral ECT: A study of memory disturbance and relief from depression. *J. Neurol. Neurosurg. Psychiatry,* 33:705-713, 1970.

d'Elia, G. Unilateral ECT. *Acta Psychiatr. Scand. (Suppl.),* 215:5-98, 1970.

d'Elia, G. Unilateral electroconvulsive therapy. In: Fink, M., Kety, S., McGaugh, J., et al. (eds.), *Psychobiology of Convulsive Therapy.* Washington, D.C.: V.H. Winston and Sons, 1974, pp. 21-34.

d'Elia, G. Memory changes after unilateral electroconvulsive therapy with different electrode positions. *Cortex,* 7:280-289, 1976.

d'Elia, G. The effect of fronto-frontal and temporo-parietal unilateral ECT on retrograde memory. *Biol. Psychiatry,* 16:55-59, 1981.

d'Elia, G., Fredericksen, S.-O., Raotma, H., and Widepalm, K. Comparison of fronto-frontal and temporo-parietal unilateral ECT. *Acta Psychiatr. Scand.,* 56:233-239, 1977.

d'Elia, G., and Raotma, H. Is unilateral ECT less effective than bilateral ECT? *Br. J. Psychiatry,* 126:83-89, 1975.

d'Elia, G., and Widepalm, K. Comparison of fronto-parietal and temporo-parietal unilateral ECT. *Acta Psychiatr. Scand.,* 50:225-232, 1974.

Dornbush, R. Memory and induced ECT convulsions. *Semin. Psychiatry,* 4:47-54, 1972.

Dornbush, R.L., Abrams, R., and Fink, M. Memory changes after unilateral and bilateral convulsive therapy. *Br. J. Psychiatry,* 119:75-78, 1971.

Dornbush, R.L., and Williams, M. Memory and ECT. In: Fink, M., Kety, S., McGaugh, J., et al. (eds.), *Psychobiology of Convulsive Therapy.* Washington, D.C.: V.H. Winston and Sons, 1974, pp. 199-207.

Fink, M. Induced seizures and human behavior. In: Fink, M., Kety, S., McGaugh, J., et al. (eds.), *Psychobiology of Convulsive Therapy.* Washington, D.C.: V.H. Winston and Sons, 1974, pp. 1-171.

Fink, M. CNS sequelae of electroseizure therapy: Risks of therapy and their prophylaxis. In: Shagass, C., Gershon, S., and Friedhoff, A.J. (eds.), *Psychopathology and Brain Dysfunction.* New York: Raven Press, 1977, pp. 223-240.

Fink, M. Convulsive therapy: A risk-benefit analysis. Abstracted from *Convulsive Therapy: Theory and Practice.* New York: Raven Press, 1979, p. 304, and presented, in part, at the ECT: Efficacy and Impact Conference, New Orleans, LA, February 1978.

Fink, M., Kahn, R.L., and Green, M. Experimental studies of the electroshock process. *Dis. Nerv. Syst.,* 19:113-118, 1958.

Fleminger, J.J., Horne, D.J. deL., Mair, N.P.V., and Nott, P.N. Differential effect of unilateral and bilateral ECT. *Am. J. Psychiatry,* 127:430-436, 1970a.

Fleminger, J.J., Horne, D.J. deL., and Nott, P.N. Unilateral electroconvulsive therapy and cerebral dominance: Effect of right and left-sided electrode placement on verbal memory. *J. Neurol. Neurosurg. Psychiatry,* 33:408-411, 1970b.

Freeman, C.P.L., Weeks, D., and Kendell, R.E. ECT: II: Patients who complain. *Br. J. Psychiatry,* 137:17-25, 1980.

Fromholt, T.P., Christensen, A., and Stromgren, L.S. The effects of unilateral and bilateral electroconvulsive therapy on memory. *Acta Psychiatr. Scand.,* 49:466-478, 1973.

Goldman, H., Gomer, F.E., and Templer, D.I. Long-term effects of electroconvulsive therapy upon memory and perceptual motor performance. *J. Clin. Psychol.,* 28:32-34, 1972.

Halliday, A.M., Davison, K., Browne, M.W., and Kreeger, I.L. A comparison of the effects on depression and memory of bilateral ECT and unilateral ECT to the dominant and nondominant hemispheres. *Br. J. Psychiatry,* 114:997-1012, 1968.

Hamilton, M., Stocker, M.J., and Spencer, C.M. Post-ECT cognitive defect and elevation of blood pressure. *Br. J. Psychiatry,* 135:77-78, 1979.

Hargreaves, W.A, Fischer, A., Elashoff, R.M., and Blacker, K.H. Delayed onset of impairment following electrically induced convulsions. *Acta Psychiatr. Scand.,* 48:69-77, 1972.

Harper, R.G., and Wiens, A.N. Electroconvulsive therapy and memory. *J. Nerv. Ment. Dis.,* 161:245-254, 1975.

Inglis, J. Shock, surgery, and cerebral asymmetry. *Br. J. Psychiatry,* 117:143-148, 1970.

Jackson, B. The effects of unilateral and bilateral ECT on verbal and visual spatial memory. *J. Clin. Psychol.,* 34:4-13, 1978.

Janis, I.L. Psychologic effects of electric convulsive treatments. *J. Nerv. Ment. Dis.,* 3:359-382, 1950.

Korin, H., Fink, M., and Kwalwasser, S. Relation of changes in memory and learning to improvement in electroshock. *Confin. Neurol.,* 16:88-96, 1956.

Kozma, A., and Galbraith, D. The effects of unilateral dominant and non-dominant and bilateral ECT on changes in depression and memory. Paper read at Canadian Psychological Association meeting, Calgary, Alberta, June 1968.

Lancaster, N.P., Steinert, R.R., and Frost, I. Unilateral electroconvulsive therapy. *J. Ment. Sci.,* 104:221-227, 1958.

Laurell, B. Fluothyl convulsive therapy. *Acta Psychiatr. Scand. (Suppl.),* 213:5-79, 1970.

Lewis, J., Bregman, N.J., and Mahan, J.J. Cue dependent amnesia in the K-maze. *J. Comp. Physiol. Psychol.,* 81:243-247, 1972.

Lieberson, W.T. Current evaluation of electric convulsive therapies. In: *Psychiatric Treatment.* Baltimore, MD: Williams and Wilkins, 1953, pp. 199-231.

McGaugh, J.L., and Alpern, H.P. Effects of electroshock on memory: Amnesia without convulsions. *Science,* 152:665-666, 1966.

McGaugh, J.L., and Williams, T.A. Neurophysiological and behavioral effects of convulsive phenomena. In: Fink, M., Kety, S., McGaugh, J.L., and Williams, T.A. (eds.), *Psychobiology of Convulsive Therapy.* Washington, D.C.: V.H. Winston and Sons, 1974, pp. 279-283.

Misanin, J.R., Miller, R.E., and Lewis, D.J. Retrograde amnesia produced by electroconvulsive shock after reactivation of a consolidated memory trace. *Science,* 160:554-555, 1968.

Ottosson, J.O. Experimental studies of memory impairment after electroconvulsive therapy. *Acta Psychiatr. Scand. (Suppl.),* 145(35):103-127, 1960.

Ottosson, J.O. Psychological or physiological theories of ECT. *Int. J. Psychiatry,* 5:170-174, 1968.

Patterson, K.E., Lawler, E., and Rochester, S.R. Retrograde amnesia from electroconvulsive therapy. *Neuropsychologia,* 16:91-97, 1978.

Perlson, J. Psychologic studies on a patient who received two hundred and forty-eight shock treatments. *Arch. Neurol. Psychiatr.,* 54:409-411, 1945.

Price, T.R.P. Unilateral electroconvulsive therapy for depression. *N. Engl. J. Med.,* 304:53, 1980.

Reichert, H., Benjamin, J., Neufeldt, A.H., and Marjerrison, G. Bilateral and non-dominant unilateral ECT: Part II: Development of prograde effects. *Can Psychiatr. Assoc. J.,* 21:79-86, 1976.

Ribot, T. (ed.). *Diseases of Memory.* London: Kegan Paul, 1885.

Robertson, A.D., and Inglis, J. Memory deficits after electroconvulsive therapy: Cerebral asymmetry and dual-encoding. *Neuropsychologia,* 16:179-187, 1978.

Schneider, A.M., and Sherman, W. Amnesia: A function of the temporal relation of footshock to electroconvulsive shock. *Science,* 159:219-221, 1968.

Small, J.G., and Small, I.F. Clinical results: Indoklon versus ECT. *Semin. Psychiatry,* 4:13-16, 1972.

Spanis, C.W., and Squire, L.R. Memory and convulsive

stimulation: Effects of stimulus waveform. *Am. J. Psychiatry,* 138:1177-1181, 1981.

Squire, L.R. Amnesia for remote events following electroconvulsive therapy. *Behav. Biol.*, 12:119-125, 1974.

Squire, L.R. A stable impairment in remote memory following electroconvulsive therapy. *Neuropsychologia,* 13:51-58, 1975.

Squire, L.R. ECT and memory loss. *Am. J. Psychiatry,* 134: 997-1001, 1977.

Squire, L.R. Memory dysfunction and memory complaint: Long-term followup studies. In: Autry, J., Squire, L.R., Shagass, C., and Cole, J.O. (eds.), *ECT: Impact and Efficacy.* New York: Grune & Stratton, 1980.

Squire, L.R., and Chace, P.M. Memory functions six to nine months after electroconvulsive therapy. *Arch. Gen. Psychiatry,* 32:1557-1564, 1975.

Squire, L.R., Chace, P.M., and Slater, P.C. Retrograde amnesia following electroconvulsive therapy. *Nature,* 260: 775-777, 1976.

Squire, L.R., and Miller, P.L. Diminution of anterograde amnesia following electroconvulsive therapy. *Br. J. Psychiatry,* 125:490-495, 1974.

Squire, L.R., and Slater, P.C. Bilateral and unilateral ECT: Effects on verbal and nonverbal memory. *Am. J. Psychiatry,* 135:1316-1320, 1978.

Squire, L.R., Slater, P.C., and Chace, P.M. Retrograde amnesia: Temporal gradient in very long-term memory following electroconvulsive therapy. *Science,* 187:77-79, 1975.

Squire, L.R., Slater, P.C., and Chace, P.M. Anterograde amnesia following electroconvulsive therapy: No evidence for state-dependent learning. *Behav. Biol.,* 17:31-41, 1976a.

Squire, L.R., Slater, P.C., and Chace, P.M. Reactivation of recent or remote memory before electroconvulsive therapy does not produce retrograde amnesia. *Behav. Biol.,* 18:333-343, 1976b.

Squire, L.R., Slater, P.C., and Miller, P.L. Retrograde amnesia and bilateral electroconvulsive therapy: Long-term followup. *Arch. Gen. Psychiatry,* 38:89-95, 1980.

Squire, L.R., Wetzel, C.D., and Slater, P.C. Anterograde amnesia following ECT: An analysis of the beneficial effects of partial information. *Neuropsychologia,* 16:339-348, 1978.

Squire, L.R., Wetzel, C.D., and Slater, P.C. Memory complaint after electroconvulsive therapy: Assessment with a new self-rating instrument. *Biol. Psychiatry,* 14:791-801, 1979.

Sternberg, D.E., and Jarvik, M.E. Memory function in depression. *Arch. Gen. Psychiatry,* 33:219-224, 1976.

Stromgren, L.S., Christensen, A.L., and Fromholt, P. The effects of unilateral brief-interval ECT on memory. *Acta Psychiatr. Scand.,* 54:336-346, 1976.

Sutherland, E.M., Oliver, J.E., and Knight, D.R. EEG, memory, and confusion in dominant, non-dominant, and bi-temporal ECT. *Br. J. Psychiatry,* 115:1059-1064, 1969.

Templer, D.I., Ruff, C.F., and Armstrong, G. Cognitive functioning and degree of psychosis in schizophrenics given many electroconvulsive treatments. *Br. J. Psychiatry,* 123:441-443, 1973.

Teuber, H.L., Corkin, S., and Twitchell, T.E. A study of cingulotomy in man. Report submitted to the National Committee for the Protection of Human Subjects of Biomedical and Behavioral Research.

Valentine, M., Keddie, K.M.G., and Dunne, D. A comparison of techniques in electroconvulsive therapy. *Br. J. Psychiatry,* 114:989-996, 1968.

Weaver, L.A., Ives, J.O., Williams, R., and Nies, A. A comparison on standard alternating current and low energy brief-pulse electrotherapy. *Biol. Psychiatry,* 12:525-543, 1977.

Weeks, D., Freeman, C.P.L., and Kendell, R.E. ECT: III. Enduring cognitive deficits. *Br. J. Psychiatry,* 137:26-37, 1980.

Weiner, R.D., Rogers, H.J., Davidson, J., and Miller, R.D. Evaluation of the central nervous system risks of ECT. *Psychopharmacol. Bull.,* 18(1):29-31, 1982.

Wexler, B.E. Cerebral laterality and psychiatry: A review of the literature. *Am. J. Psychiatry,* 137:279-291, 1980.

Williams, M. Retrograde amnesia. In: Kennedy, A., and Wilkes, A. (eds.), *Studies in Long-Term Memory.* London: John Wiley & Sons, 1975, pp.323-326.

Zamora, E.N., and Kaelbling, R. Memory and electroconvulsive therapy. *Am. J. Psychiatry,* 122:546-554, 1965.

Zinkin, S., and Birtchnell, J. Unilateral electroconvulsive therapy: Its effect on memory and its therapeutic efficacy. *Br. J. Psychiatry,* 114:973-998, 1968.

Short- and Long-Term Cognitive Effects of ECT: Part II—Effects On Nonmemory Associated Cognitive Functions.

Trevor R.P. Price, M.D.[1]

In addition to the multiple effects that electroconvulsive therapy (ECT) has on memory function, which were reviewed in the preceding article (Price, 1982), it likewise has a variety of effects on cognitive functions which are largely independent of memory. The range of cognitive domains affected include, for example, perceptual function, psychomotor speed, visuomotor ability, simple and complex sensory capacity, complex discrimination ability, and synthesizing and abstracting ability (Fink, 1979). This article will review these effects of ECT.

To understand ECT's effects on memory function or nonmemory-associated cognitive and neuropsychological function, it is important to

[1]Department of Psychiatry, Dartmouth Medical School, Hanover, NH 03755.