CURRENT PSYCHIATRIC THERAPY

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W. B. SAUNDERS COMPANY
Harcourt Brace Jovanovich, Inc.
Philadelphia, London, Toronto, Montreal, Sydney, Tokyo

1993

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ELECTROCONVULSIVE THERAPY

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Electroconvulsive therapy (ECT) continues to be one of the most effective treatments in psychiatry since its introduction over 50 years ago. Early clinicians recognized that psychotic patients who had spontaneous seizures often experienced a remission of symptoms. During the 1930s several attempts to induce seizures in psychiatric patients were made. Von Meduna in 1935 used camphor and subsequently metrazol to induce seizures. Cerletti and Bini in 1938 introduced ECT, which, because of its simplicity and ease of application, became the most common method of inducing seizure activity. Since then, research has clarified a great deal about the efficacy, side effects, optimal mode of administration, and mechanism of action of ECT.

EFFICACY OF ECT

Depression is by far the most common indication for ECT. It should be emphasized that depression is not simply sadness, but is a syndrome in which a persistent low mood is associated with altered sleep, altered appetite, weight change, agitation or retardation, poor concentration, decreased sex drive, low self-esteem, hopelessness, and suicidal ideation. Prior to the advent of ECT, depressive illness was associated with high death rates—10 to 15 per cent 1-year mortality rates in some studies. With the introduction of ECT, death rates decreased, both from suicide and nonsuicidal causes. Subsequent controlled studies of patients from the same era have confirmed the life-saving effect of ECT in depression. Several studies using sham ECT controls have demonstrated the efficacy of ECT.

With the introduction of antidepressant medication in the 1960s, numerous studies compared medication, both tricyclic antidepressants and monoamine oxidase inhibitors, with ECT. Most studies have shown ECT to be superior to antidepressant medication, some have shown the two treatments equal, but none have shown medication to be superior to ECT. Typically, these studies show 80 to 90 per cent response rates of hospitalized depressed patients to ECT compared to 60 to 80 per cent response rates with tricyclic antidepressants (even when given in dosages of 200 to 250 mg/day). Comparisons with monoamine oxidase inhibitors and tryptophan also support the superiority of ECT. The antidepressant effect of ECT may be faster than medication: the duration of hospitalization is shorter for patients treated with ECT. The response to ECT may also be more complete than with medication.

Depressive illness is associated with high suicide rates, with most suicides occurring within 8 months of hospitalization, and a person with a partially treated depression may be at increased risk. Suicide attempts in depressed patients are seen less frequently following treatment with ECT than with antidepressant medication. Treatment with ECT is associated with decreased suicide rates compared with depressed patients treated with neither ECT nor antidepressant medication. Because of the more complete, faster response seen with ECT compared with medication, ECT may be the treatment of choice in the suicidal depressed patient.

Psychotic depression often responds poorly to antidepressant medication alone, but has an 80 to 90 per cent response rate to ECT. Some recent data suggest that adding an antipsychotic to an antidepressant may improve the response to the ECT response rate, but replication is needed. Several investigators have found that the presence of psychosis in depressed patients is neither a good nor a poor prognostic sign for ECT response.

Many prognostic factors for ECT response have been studied. In general, endogenous depression has been found to have a better ECT response compared to neurotic or reactive depression. Bipolar and unipolar patients appear to respond equally well. Primary depressions respond better than depressions that are secondary to other psychiatric or medical problems. The presence of an Axis II personality disorder diagnosis in addition to the major depression diagnosis worsens the prognosis. Individual signs and symptoms of depression in general are poor predictors of response. Psychomotor agitation and a pyknic habitus are good prognostic factors. Guilt and a previous episode of depression may be good prognostic factors. Possible poor prognostic factors include a duration greater than 1 year, a fluctuating course in the episode, emotional lability, paranoia, and anxiety.

Electroconvulsive therapy continues to be an important treatment for depression in the elderly. Recently elderly patients referred for ECT were noted

to have a leukoencephalopathy when studied with magnetic resonance imaging: subcortical hyperintensity was more common compared to control group of normal elderly subjects. These patients responded well to ECT, and ECT caused no changes in the magnetic resonance image.

The natural history of depression is often associated with frequent relapses following recovery from an episode. Electroconvulsive therapy is clearly effective in treating the depressive episode, but does not decrease (or increase) the likelihood of a clinical relapse. Therefore, antidepressants, which are effective maintenance medications, are usually prescribed for 6 to 9 months after an ECT response. Some recent data indicate that relapse is much more likely following ECT in patients who had failed adequate antidepressant trials prior to the ECT than in patients who had not been determined to be medication resistant. For some patients with recurrent depression, maintenance ECT—single ECT sessions given every few weeks on an outpatient basis—may be helpful in preventing relapse.

Electroconvulsive therapy is also an effective treatment for mania. One recent naturalistic study found a 78 per cent response rate to ECT, significantly better than the 62 per cent response rate in those receiving lithium. Bilateral electrode placement is superior to unilateral in treating mania. Even those patients who had had a poor response to lithium had a high response rate to ECT. Electroconvulsive therapy has stopped the rapid cycling in some bipolar patients, but ECT should not be considered the first line of treatment for this problem.

The possible role of ECT in the treatment of schizophrenia is obscured by diagnostic problems. "Schizophreniform" psychoses, although associated with hallucinations and delusions, will frequently respond well to ECT. Good prognostic signs for ECT response in atypical psychoses include the presence of symptoms of endogenous depression or mania, a relatively acute onset, a good premorbid personality, and a family history of affective disorder. Patients with catatonia often respond well. If the duration of illness is less than 1 year, the prognosis is favorable. Thus, patients with "acute schizophrenia" often respond well, whereas schizophrenics with chronic symptoms usually do not. In a well-controlled study of schizophrenics who were neither acutely ill nor extremely chronic, ECT was found to be equal to phenothiazines and superior to psychotherapy. The possible effectiveness of ECT in some schizophrenics takes on special significance in view of the concern over phenothiazine-induced tardive dyskinesia.

Electroconvulsive therapy has been used with some success in other disorders. Patients with neuroleptic malignant syndrome frequently respond to ECT. However, some of these patients may have been in the process of developing lethal catatonia and happened to have received neuroleptics. Electroconvulsive therapy is effective in some patients with Parkinson's disease, but the effect may be only temporary. Patients with chronic pain and patients with tardive dyskinesia have responded to ECT. Depressed patients with coexisting medical problems such as brain tumors, positive human immunodeficiency virus status, Down's syndrome, and mental retardation have responded well to ECT. While not routine, ECT has been effective in some depressed adolescents. There is no evidence that ECT is effective in treating personality disorders or autism.

ADMINISTRATION OF ECT

Before a patient is given ECT, a careful history, physical and neurological exam should be completed. Liver function tests, measures of creatinine, and electrolytes, a complete blood count, urinalysis, electrocardiogram, and radiographs of the chest and the thoracic and lumbar spine should be obtained. Any physical problems must be considered and evaluated appropriately. There are several relative contraindications for ECT: intracranial neoplasm, a recent cerebral vascular accident, subdural hematoma, a recent myocardial infarction, congestive heart failure, angina pectoris, and acute or chronic respiratory disease. As with any therapy, the risks of withholding treatment must be weighed against the risks of the treatment itself. For example, in a depressed patient who has postural hypotension, the possible hypotensive effects of tricyclic antidepressants might be avoided by giving ECT and carefully monitoring the electrocardiogram during treatment. Electroconvulsive therapy has been used successfully during pregnancy and can be an alternative to the possible teratogenic effects of antidepressant medication.

The patient should be informed of the risks and benefits of the treatment and a consent form should be signed. The patient should take no water or food by mouth for at least 8 hours prior to the treatment. The patient's temperature is taken in the morning before each treatment to rule out a febrile process. Some centers give atropine 1 mg IM 30 minutes prior to treatment to prevent the bradycardia that sometimes accompanies ECT. However, atropine has not been shown to be critical to successful ECT. The patient voids completely, and is placed on the treatment table in a supine position. Then the patient is given an anesthetic. In the past, thiopental or methohexital IV has been used, but in recent years etomidate has been used by some because it does not have significant anticonvulsant effects like the barbiturates.

Succinylcholine is injected to induce muscle relaxation and the patient is ventilated with oxygen. A rubber mouthpiece is inserted to prevent possible damage to the teeth. The electrodes are applied to the head. When relaxation is complete, the current is delivered. Depending on the degree of muscle relaxation induced, the tonic-clonic activity of the seizure may be seen, with the tonic phase lasting approxi-

mately 10 to 20 seconds and the clonic phase 30 to 60 seconds. An adequate seizure should have a duration of at least 25 seconds. Rarely, a seizure may continue for 120 seconds or more. Under these circumstances, the seizure may be stopped by administering IV diazepam. The patient is ventilated with oxygen and usually begins breathing spontaneously within a few minutes after the seizure ends. The patient is usually awake after 10 to 15 minutes. Most patients experience a transient postictal confusion and memory disturbance.

The seizure duration is monitored by using the blood pressure cuff technique. Inflating a blood pressure cuff on one arm to above systolic pressure prevents the muscle relaxant from reaching the muscles of that arm and allows the seizure activity to be observed. However, this technique underestimates the actual electroencephalographic (EEG) seizure duration. Many ECT machines now have the capability of EEG monitoring. Some preliminary data suggest that the effectiveness of the treatment may correlate with the total seizure duration up to 750 seconds of seizure activity.

For most patients, an adequate course of ECT consists of 6 to 12 treatments; usually three treatments are given per week. The number of treatments is determined by the clinical improvement of the patient. Many clinicians believe that one or two additional treatments are necessary after clinical remission has occurred to prevent early relapse. Some have advocated the use of multiple monitored ECT, giving several seizures in a single session, and have claimed that fewer sessions are necessary. However, controlled studies have not yet supported this claim.

The administration of lithium to patients undergoing ECT is associated with a clear increase in cognitive dysfunction and is contraindicated. The administration of antidepressant medication during ECT treatment offers no increased efficacy and may be associated with increased memory disturbance. Concomitant benzodiazepine use may interfere with the induction of the seizure or shorten the seizure. One study has even demonstrated reduced ECT efficacy associated with concomitant benzodiazepine use. Sometimes it is difficult to induce seizures, or the seizures are short even in patients not taking benzodiazepines or barbiturates. Recently, intravenous administration of caffeine has been successfully used in such patients.

Very rarely, the patient may have prolonged apnea because of decreased metabolism of the succinylcholine. Succinylcholine is metabolized by plasma pseudocholinesterase. Decreased pseudocholinesterase activity may be associated with decreased liver function and severe anemia, as well as certain medications, including amitriptyline and some antibiotics.

Succinylcholine, a depolarizing muscle relaxant, has been shown to release large amounts of potassium from skeletal muscle in patients with burns, muscle trauma, central nervous system trauma, peripheral nerve injury, spinal cord injury, and muscle changes due to prolonged inactivity. Since a rapid rise in potassium may cause ventricular arrhythmia and cardiac arrest, patients with these conditions may require the use of a nondepolarizing muscle relaxant such as atracurium.

A low dose of succinylcholine (about 0.7 mg/kg) has been associated with post-ECT agitation; no agitation was noted in these patients after increasing the succinylcholine dose to a mean of about 1.0 mg/kg. It has been hypothesized that a low dose of succinylcholine might allow enough muscle activity to produce high lactate levels and thus create a situation analogous to a lactate infusion–induced panic attack.

The use of brief-pulse ECT can reduce the postictal memory disturbance relative to the traditional sinusoidal wave form.

Some investigators have advocated titrating the dose of electricity to assess the seizure threshold. For example, one might begin with pulse frequency of 20 Hz, a pulse width of 1.5 msec, and a duration of 1 second. If there is no seizure elicited, the next stimulus might be given after a 40-second waiting period with a higher dose (e.g., 40 Hz, 1.5-msec pulse width, and 1 second duration). Subsequent doses might be 70 Hz, 1.5 msec, and 1.0 second, and 70 Hz, 1.5 msec, and 2.0 seconds. Using the lowest threshold that elicits a seizure might decrease the memory disturbance. The seizure thresholds may vary as much as 12-fold among patients with higher thresholds, which are seen among men and older patients and with bilateral placement. As patients recover with ECT, the seizure threshold increases.

Unilateral (both electrodes over the same hemisphere) and bifrontal ECT clearly cause less of the transient memory disturbance than the traditional bilateral (bitemporal) treatments. When unilateral treatments are used, right unilateral placement is usually used since its effects on verbal memory are less than with left unilateral treatment. However, controversy continues over whether unilateral treatments are as efficacious as bilateral treatments. Some studies show the two treatments to be equal; others show bilateral treatments to be superior. Unilateral ECT failures will usually respond to bilateral treatments. Unilateral treatments often yield shorter seizures. Even when seizure duration is controlled, bilateral treatments appear to have a greater physiological effect, as measured by prolactin secretion and heart rate increase, compared to unilateral treatments. Some clinicians begin with bilateral treatments and, if the patient experiences significant memory disturbance, switch to right unilateral treatments.

ADVERSE EFFECTS OF ECT

The risk of death during ECT is estimated at about 1:10,000 patients treated. The most common cause

of death is cardiovascular problems. Since the modification of the ECT technique with muscle relaxants, anesthesia, and hyperoxygenation, there have been no reports of structural neurological damage in patients given ECT. Magnetic resonance imaging and cerebral computed tomography performed before and after ECT show no changes. Furthermore, studies of animals given ECT have revealed no neuropathological changes, even with electron microscopic tissue examination.

Memory disturbance has long been associated with ECT use. Both retrograde memory (memory of past events) and anterograde memory (capacity to remember newly acquired material) are impaired during the days following ECT. Within 6 to 9 months after a course of ECT, the capacity to learn new material returns to normal. In addition, the ability to remember past events returns except for the days prior to and during the course of treatment.

As with other antidepressant treatments, ECT can precipitate mania. Those who experience ECT-induced mania have an earlier age of onset and a longer duration of illness compared to those who do not experience this. Mania should be distinguished from organic euphoric states, which are more brief and usually associated with more severe cognitive impairment and silly, inappropriate laughter.

MECHANISM OF ACTION OF ECT

Theories of ECT's mechanism of action have changed as the theories of the etiology of depression have changed. Some have believed that depression represents "introjected anger" and that ECT worked by satisfying the persons's needs for self-punishment. However, the effectiveness of the modified technique, during which the patient is unconscious, speaks against this theory. It has also been hypothesized that ECT works by interfering with the memory of stressful events. However, there is no association between clinical effectiveness and memory disturbance.

The *sine qua non* for an effective treatment appears to be seizure activity. Chemically-induced seizures are efficacious. When electrically-induced seizures are prevented with lidocaine, the electrical stimuli are not effective in relieving the depression.

Some evidence suggests that deficiencies of neurotransmitters are associated with the depressed state; some animal studies show increased release of serotonin and norepinephrine during seizures. Like many antidepressant medications, repeated seizures may decrease postsynaptic β-adrenergic sensitivity.

Affective disorders may be associated with desynchronization of circadian rhythms; ECT has been hypothesized as a *Zeitgeber* that resynchronizes these rhythms. Electroconvulsive therapy may work in a way analogous to cardiac defibrillation, resetting desynchronous clocks back to time zero. One catatonic patient who responded to ECT was noted to have a high temperature (38.3°C) and no 24-hour rhythm prior to ECT. With the ECT treatments, a circadian rhythm developed and the 24-hour temperature amplitude and mean gradually returned to normal. During the second week of treatment, the timing of the minimum of the temperature rhythm corresponded with the time of ECT administration even on non-ECT days.

Electroconvulsive therapy has also been hypothesized to work as an anticonvulsant in a manner analogous to carbamazepine. Electroconvulsive therapy has been proposed to work by restoration of the equilibrium between the cerebral hemispheres. The "nonphysiological" depolarizations may be important for the restoration of aberrant intravesicular transmitter ratios.

Response to ECT is associated with normalization of a variety of physiological functions that have been found to be abnormal in depression: dexamethasone nonsuppression, short rapid eye movement sleep latency, reduced slow wave sleep, and high nocturnal temperature.

Electrophysiological evidence indicates that centrocephalic structures are implicated in the mechanism of the ECT process. As with antidepressant medication, it is too early to formulate a definite model for the mechanism of action of ECT. However, the lack of a theoretical construct does not diminish the empirical evidence for its efficacy and relative safety.

LEGISLATION OF ECT

Controversy concerning ECT has led to legislative changes restricting its use, particularly in the United States. After passage of such legislation in California, the rate of ECT use was approximately 6:100,000 persons per year; in Great Britain, Denmark, and Sweden, the rate is approximately seven to 15 times greater. The use and availability of ECT is particularly low in public hospitals in the United States. In California, minorities are probably untreated, with whites accounting for 92 per cent of the ECT use.

In spite of the controversy, ECT remains the most effective treatment for severe endogenous depressions, especially psychotic depressions.

ACKNOWLEDGMENT

This work was supported in part by Research Scientist Development Award 5 KO MH00493-04.

SUGGESTED READINGS

Abrams R: Electroconvulsive Therapy. New York: Oxford University Press, 1988.

American Psychiatric Association Task Force Report on Electroconvulsive Therapy. Report no. 14. Washington, DC: American Psychiatric Association Press, 1978.

American Psychiatric Association Task Force Report on Electroconvulsive Therapy. "The Practice of Electroconvulsive Therapy: Recommendations for Treatment, Training, and Privileging." Washington, DC: American Psychiatric Association Press, 1990.

Avery DH, Mills M: Electroconvulsive therapy and antidepressants in the treatment of depression. *In* Ayd F, Taylor IJ, eds. Mood Disorders: The World's Major Public Health Problem. Baltimore: Ayd Medical Communications, 1978:138–153.

Avery DH, Winokur G: Mortality in depressed patients treated with electroconvulsive therapy and antidepressants. Arch Gen Psychiatry 33:1029–1037, 1976.

Coffey CE, Figiel GS, Weiner RD, Saunders WB: Caffeine augmentation of ECT. Am J Psychiatry 147(5):579–585, 1990.

Fink M: Convulsive Therapy: Theory and Practice. New York: Raven Press, 1979.

King BH, Liston EH: Proposals for the mechanism of action of convulsive therapy: A synthesis. Biol Psychiatry 27:76–94, 1990.

Sackeim HA, Decina P, Portnoy S, Neeley P, Malitz S: Studies of dosage, seizure threshold, and seizure duration in ECT. Biol Psychiatry 22:249–268, 1987.

Squire LR: ECT and memory loss. Am J Psychiatry 134(9):997–1001, 1977.

Squire LR, Zouzounis JA: ECT and memory: Brief pulse versus sine wave. Am J Psychiatry 143(5):596–601, 1986.