REVIEW

MAYUR PANDYA, DO
Psychiatric Neuromodulation Center, Cleveland Clinic

LEOPOLDO POZUELO, MD
Section Head, Consultation Liaison Psychiatry, Department of Psychiatry and Psychology, Cleveland Clinic

DONALD MALONE, MD*
Section Head, Adult Psychiatry, Medical Director, Psychiatric Neuromodulation Center, Cleveland Clinic

Electroconvulsive therapy: What the internist needs to know

ABSTRACT

Although electroconvulsive therapy (ECT) is widely used to treat a number of psychiatric disorders, many physicians are still unfamiliar with the procedure, its indications, and its contraindications. This article is an internist's guide to ECT, with particular focus on how commonly prescribed medications and medical conditions affect ECT.

KEY POINTS

ECT is safe and works rapidly, making it a primary therapy in situations requiring acute intervention. Another reason to consider ECT is a history of poor response to medications or of adverse effects with medications.

Although ECT was first used in patients with schizophrenia, it is most often used today for mood disorders, including unipolar depression, bipolar depression, and acute mania.

Before ECT is performed, patients require a medical evaluation to undergo anesthesia, and some may need special consultation.

Vagus nerve stimulation is the newest neuromodulatory technique to receive approval for adjunctive treatment of depression. Experimental treatments that show promise include deep brain stimulation and repetitive transcranial magnetic stimulation.

ELECTROCONVULSIVE THERAPY (ECT) has an undeservedly bad reputation. This is unfortunate. As currently performed, ECT is safe and is effective for treating a number of psychiatric disorders. For some patients, it is the only therapy that works.

The following article outlines the indications for and contraindications to ECT and special considerations for patients referred for it.

TREATING MENTAL ILLNESS BY INDUCING SEIZURES

In 1927, Wagner-Jauregg won the Nobel Prize for curing patients with "dementia paralytica" (tertiary syphilis) by infecting them with malaria. The concept that one illness could be treated by inducing another led von Meduna in 1934 to perform the first reported convulsive therapy in psychiatry.[1]

Von Meduna, a neuropathologist, had noted that patients with epilepsy had more glial cells than average, and patients with schizophrenia had fewer. He had also seen data that few patients had both schizophrenia and epilepsy (not true), and that when people with mental disorders suffered seizures, their mental condition often improved. He reasoned that if he could induce seizures in patients with schizophrenia by injecting camphor, their glial cells might increase, and their symptoms might improve. And in fact, in his initial work, symptoms of schizophrenia improved partially to completely.

In 1938, the Italians Bini and Cerletti performed the first documented electrical induction of seizures in humans.[2] One year later, ECT was introduced to the United States. Until effective antipsychotic drugs

*Dr. Malone has obtained research funding from and is a consultant for Medtronic, Inc.

were developed in the 1950s, the only effective alternatives to ECT were insulin shock therapy and lobotomy, which was falling out of favor.

In the early years, the lack of adequate anesthesia or muscle relaxation resulted in fractures or dislocations, often with negative recollection for the event. Lack of knowledge regarding the dose parameters of electrical stimulation led to more cognitive side effects.

Over the decades, the safety and efficacy of ECT have been improved and its indications have been defined. Today, it is usually done with the patient under general anesthesia, and with muscle relaxants and cardiopulmonary monitoring, which have reduced its complications. Nevertheless, ECT's historical beginnings, combined with its negative portrayal in the media,[3] have left some patients fearful and hesitant to undergo ECT if they need it.

How ECT works is unknown

Although many mechanisms have been proposed, how ECT works remains unknown. An attractive hypothesis to account for ECT's effects on depression is that it alters serotonin and dopamine activity.[4,5] Changes in gamma-aminobutyric acid (GABA) and noradrenaline levels have also been reported.[4,6] Most likely, the therapeutic effects of ECT are a result of a combination of neurotransmitter alterations.

ECT is far safer now than in the past

MOST OFTEN USED FOR MOOD DISORDERS

ECT was first used in patients with schizophrenia, and today, treatment-resistant psychosis is still considered an appropriate indication for it. Today, however, ECT is most often used for mood disorders, including unipolar depression, bipolar depression, and acute mania.

The *Diagnostic and Statistical Manual of Mental Disorders* defines major depression as a constellation of symptoms, which may include depressed mood, anhedonia, sleep disturbance, psychomotor retardation or agitation, fatigue, guilt, poor concentration, and suicidality.[7] The symptoms result in marked social and occupational impairment, commonly resulting in interpersonal and financial distress. According to the Global Burden of Disease Study, depression ranks as the fourth-leading cause of disability worldwide.[8] Initial therapies consist of drugs and psychotherapy, alone or in combination. Patients with depression that is moderate to severe and resistant to drug treatment may be referred for ECT, which is often considered the gold standard antidepressant treatment.

Most patients should undergo an adequate trial of oral drug therapy before being referred for ECT. The actual number of drugs that should be tried and for how long are determined on a case-by-case basis; in general, one should try different classes of antidepressants and various augmentation techniques before turning to ECT. Poor response to medications or adverse effects with pharmacotherapy may be reasons to consider ECT.

On the other hand, ECT's safety and rapid efficacy make it a good primary treatment in situations requiring acute intervention, such as catatonia and psychiatric exacerbations during pregnancy.

All patients being considered for ECT should receive a general psychiatric evaluation. The psychiatrist will then proceed with referral for ECT if appropriate and recommend any necessary workup (discussed below).

ECT REQUIRES MEDICAL ASSESSMENT

Although no absolute contraindications to ECT exist, several conditions are associated with an increased risk of complications and even death (see below). The cardiovascular, central nervous, and pulmonary systems carry the highest risks from general anesthesia and the induction of generalized seizure activity.

In most routine cases, the patient undergoes routine clearance for anesthesia, but special considerations may necessitate consultation with medical specialists such as a cardiologist, neurologist, neurosurgeon, endocrinologist, anesthesiologist, or dentist. All cases referred for ECT require analysis of the medical risks of treatment (discussed below).

The pre-ECT evaluation includes basic tests such as a complete blood cell count, serum electrolyte levels, renal function tests,

and electrocardiography. Neuroimaging, chest radiography, and spine films are not routinely done unless clinically indicated. For example, spine films may be necessary in some patients who are elderly or who have osteoporosis. Compression fractures are not an absolute contraindication to ECT, but the physician performing ECT would want this information so that he or she can make sure to provide adequate paralysis. Careful attention should also be paid to the teeth, with dental consultation obtained if needed.

Before ECT, electrolyte levels should be stabilized and appropriate fluid status maintained.

SOME ECT PATIENTS NEED SPECIAL CONSIDERATION

According to the American Psychiatric Association's Task Force on Electroconvulsive Therapy,[9] patients with certain medical conditions may require more extensive workup and consideration during ECT (TABLE 1).

Patients with autonomic sensitivity

Seizure induction causes acute cardiopulmonary changes, including some initial parasympathetic bradycardia. This is followed by a sympathetic surge, causing transient tachycardia and hypertension. The sympathetic surge occurs only if a seizure is induced. Thus, patients at risk of bradycardia (eg, those on beta-blockers) may be particularly prone if stimulation is given but a seizure is not induced. To counteract the parasympathetic effect, some physicians give an anticholinergic drug—atropine or glycopyrrolate (Robinul)—although this is not routine or required.

These autonomic effects make patients with a number of cardiovascular and neurologic conditions particularly vulnerable to exacerbation and increased risk of death. These conditions include increased intracranial pressure, recent stroke, recent myocardial infarction, unstable angina, uncontrolled hypertension, severe valvular disease, decompensated congestive heart failure, fragile aneurysm, and significant arrhythmia. Recommended management for patients with many of these conditions includes functional cardiac testing before the procedure and giving an antihypertensive agent (eg, intravenous labetalol or esmolol) during the procedure to blunt the sympathetic response in patients at high risk.

Patients with chronic atrial fibrillation can undergo ECT safely. Therapeutic anticoagulation should be continued throughout the ECT course.

Other conditions that pose increased risk are clinically evident hyperthyroidism (in which ECT may result in thyroid storm), pheochromocytoma, and narrow-angle or closed-angle glaucoma. However, ECT has been successfully performed in all of the above conditions, and therefore the condition alone should not exclude appropriate patients from ECT.

A cardiology consultation is also recommended for patients with pacemakers or implantable cardioverter-defibrillators (ICDs); these patients can undergo ECT safely if the device has been checked recently. Depending on the type of pacemaker, it may have to be

TABLE 1

Conditions requiring special consideration before electroconvulsive therapy

Conditions associated with autonomic sensitivity
Clinically evident hyperthyroidism
Decompensated congestive heart failure
Elevated intracranial pressure
Fragile aneurysm
Narrow-angle or closed-angle glaucoma
Pheochromocytoma
Recent myocardial infarction
Recent stroke
Severe valvular disease
Significant arrhythmia
Uncontrolled hypertension
Unstable angina

Conditions associated with sensitivity to anesthesia
Amyotrophic lateral sclerosis
Genetic or acquired pseudocholinesterase deficiency
Myasthenia gravis
Neuroleptic malignant syndrome
Porphyria
Pregnancy

Conditions associated with cognitive sensitivity
Dementia
Traumatic brain injury

TABLE 2

Medications requiring special consideration before electroconvulsive therapy

MEDICATION	POSSIBLE UNDESIRED EFFECT
Lidocaine	Seizure inhibition
Diabetic agents	Hypoglycemia
Theophylline	Prolonged seizures, status epilepticus
Antidepressants, mood stabilizers	
Carbamazepine (Carbatrol, Tegretol)	Seizure inhibition (major effect)
Gabapentin (Neurontin)	Seizure inhibition (major effect)
Lamotrigine (Lamictal)	Seizure inhibition (minor effect)
Lithium	Delirium, prolonged seizures
Monoamine oxidase inhibitors	Hypertensive crisis
Tricyclic antidepressants	Cardiotoxicity
Topiramate (Topamax)	Seizure inhibition (minor effect)
Valproic acid (Depakene)	Seizure inhibition (major effect)
Benzodiazepines	Seizure inhibition, reduced efficacy, cognitive effects
Anticholinesterases	Prolonged anesthesia effect
Herbal supplements	
Ginkgo biloba	Increased intracranial pressure, cerebral hemorrhage
Ginseng	Parasympathetically mediated bradycardia
St. John's wort	Prolonged anesthesia effect, cardiovascular collapse

Most patients should have an adequate trial of drug therapy before trying ECT

adjusted, especially if the patient is pacemaker-dependent. ICDs must be turned off immediately before the procedure, during which the patient must be monitored electrocardiographically. The ICD is turned back on when the treatment is complete.[10]

Patients with anesthesia sensitivity

A pre-anesthesia consultation is indicated to address any cardiac, pulmonary, or other medical risk factors that affect the risk of anesthesia and to determine whether the patient's medication regimen or the anesthetic technique need to be modified.

The depolarizing muscle relaxants that are commonly used, such as succinylcholine, may pose risks of adverse effects in patients with certain conditions, eg, myasthenia gravis, amyotrophic lateral sclerosis, genetic or acquired pseudocholinesterase deficiency, and neuroleptic malignant syndrome. In such conditions, a substitute nondepolarizing agent may be indicated. Barbiturates are considered unsafe in patients with porphyria, who should receive alternative anesthetics.

During pregnancy, the risk of teratogenesis with many oral psychotropic agents makes ECT invaluable for the treatment of decompensated psychiatric conditions. Although ECT does pose risks (greatest during the first trimester) and should be avoided if possible,[11] it can be safe and effective with proper preparation and monitoring, including a pelvic examination, uterine tocodynamometry, intravenous hydration, fetal cardiac monitoring, and avoidance of excessive hyperventilation.[12] The risk to the fetus is low because the anesthetic doses are small, the patient receives the anesthetic for only a short time, and little of it crosses the placenta. Similarly, breastfeeding can continue during courses of ECT, since the concentrations of anesthetics in breast milk are low.

Patients with cognitive sensitivity

Transient cognitive effects are a common side effect of ECT. Although this can occur in patients with normal cognitive function, the risk is higher in patients with a history of brain trauma or dementia. Cognitive effects include

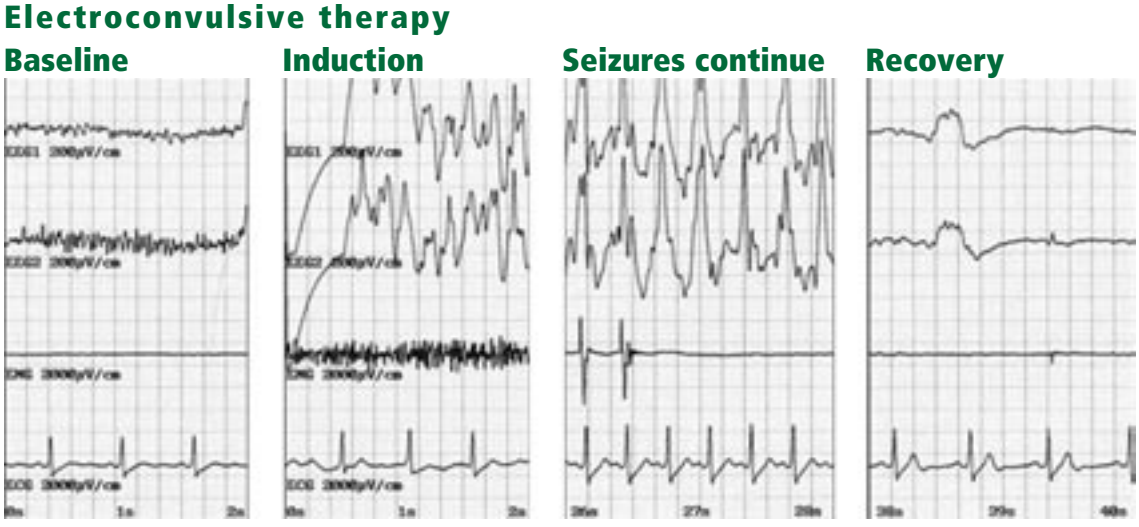

FIGURE 1. Electroencephalographic (EEG, top two lines); electromyelographic (EMG, foot lead, third line), and electrocardiographic (ECG, bottom line) monitoring during electroconvulsive therapy.
At baseline, notice the EEG activity.
At induction (time 0 seconds), the immediate spike of EEG activity documents seizures. EMG activity in the foot lead documents motor seizures. The heart rate is unchanged from baseline.
As seizures continue, EEG activity continues, while motor seizures terminate at 26 seconds on the EMG lead. Tachycardia is evident on the ECG tracing.
On recovery, EEG activity returns to baseline, indicating that the seizure is over, and the heart rate returns to baseline.

short-term retrograde and anterograde amnesia around the time of the procedure.

The risk is less if the electrodes are placed unilaterally instead of on both sides of the head. Because the response to unilateral treatment is believed to be correlated with the dosage of stimulation above threshold, we recommend dose titration to determine the seizure threshold level and to assure appropriate but not excessive stimulation dosage. For bilateral treatment, this dose-response relationship above threshold may be less critical.

Another strategy to reduce cognitive impairment may be to place the electrodes on both sides, but over the frontal lobes instead of the temporal lobes. Research on bifrontal placement is ongoing to determine if it minimizes cognitive impact and if it is as effective as bitemporal placement.[13,14]

Cognitive impairment can also be reduced by scheduling longer intervals between treatments.

DRUG INTERACTIONS

The pre-ECT evaluation includes a CBC count, electrolytes, renal function tests, and ECG

Several classes of medications need to be reduced in dosage or completely stopped before ECT. Some medications suppress seizure activity; others have synergistic effects with ECT that can lead to serious complications such as cardiotoxicity or prolonged seizures. For this reason, all cardioprotective agents are usually continued during the course of ECT.

- Lidocaine should be continued only in life-threatening situations due to its anticonvulsant effects.
- On the day of the procedure, hypoglycemic medications should be reduced or withheld until after the procedure, since patients must fast before ECT.
- Theophylline should be decreased in dose or discontinued, if possible, as it has been associated with prolonged seizures and status epilepticus.

- Mood stabilizers and sedative agents may interfere with seizure activity, owing to agonist effects on GABA.
- Anticholinesterases and popular common alternative and complementary medications may carry risks as well (TABLE 2).[15]

THE PROCEDURE

The ECT procedure involves coordinated care between the anesthesiologist and psychiatrist. The goal of ECT is to produce a controlled and monitored seizure. It is most often performed in a postanesthesia care unit, with anesthesia and cardiac, hemodynamic, and respiratory monitoring.

General anesthesia is commonly achieved with methohexital or etomidate. Once the patient is completely asleep, he or she is given a muscle relaxant (almost always succinylcholine). The goal is to cause significant muscle relaxation, especially if the patient has osteoporosis or a history of spinal injury. Direct electrical stimulation of the masseter muscles will bypass succinylcholine's effect, so a bite block is inserted to avoid oral injury. The anesthetist ventilates the patient with 100% oxygen under positive pressure.

Antidepressant drug therapy should resume immediately after ECT to maintain remission

Once anesthesia and muscle relaxation are achieved, the electrical stimulus is given. Depending on the institution or physician, the stimulus is delivered either unilaterally or bilaterally. The induced seizure usually lasts 30 to 90 seconds (FIGURE 1). Seizures lasting more than 120 seconds are commonly terminated with intravenous benzodiazepines. After the seizure is over, the patient usually recovers in 5 to 15 minutes and does not remember the treatment episode. Once cleared to leave the recovery area, the patient is taken back to his or her ward if an inpatient or sent home if an outpatient. (Many patients receive ECT on an outpatient basis and can be sent home approximately 1 hour after the procedure without complications.)

Common adverse effects include myalgias, headache, nausea, and transient cognitive effects. Tardive seizures have been reported but are extremely rare.

A COURSE OF ECT IS SIX TO 10 TREATMENTS

A typical course of ECT consists of six to 10 treatments, scheduled at intervals of two or three times per week. The patient should start to experience some improvement in psychiatric symptoms by the second or third treatment, with a full response by the fifth to 10th treatment. How many treatments are ultimately given is based upon clinical improvement; treatments are stopped when the patient no longer improves with successive treatments.

Many patients with severe refractory depression begin ECT treatment while hospitalized. Those who have significant improvement quickly may be able to complete the ECT series on an outpatient basis.

The series of six to 10 treatments is known as the acute index series and typically is all that is needed to lift the patient out of depression. In contrast, 2 to 3 months are needed to achieve remission with standard antidepressant therapy. Treatment with antidepressants, mood stabilizers, or both should be resumed immediately after the ECT series is done, as relapse rates greater than 80% have been reported within 6 months in those not receiving treatment (compared with 60% with nortriptyline [Pamelor] and 39% with nortriptyline and lithium in combination).[16]

A subset of patients who have more refractory mood disorders may need to continue their ECT treatments in combination with maintenance medication. These are patients who had relapses on medication alone and needed another series of ECT as rescue therapy. After a response is achieved with ECT, the treatments are tapered in frequency over the next few weeks until they are given every month.

THE FUTURE

Although ECT has been an effective treatment for mood disorders, the search continues for better long-term psychiatric neuromodulatory techniques. The most promising treatments on the horizon include vagus nerve stimulation, deep brain stimulation, and repetitive transcranial magnetic stimulation.

Vagus nerve stimulation (by means of an implanted pacemaker-type device) is the most recent neuromodulatory technique to receive US Food and Drug Administration (FDA) approval for adjunctive treatment of depression. Its current indications require failure of treatment with four or more antidepressants. Symptoms improve gradually with time. Unlike ECT, vagus nerve stimulation is not indicated for acute or emergency treatment.

Repetitive transcranial magnetic stimulation and deep brain stimulation have not yet received FDA approval, but they appeared promising in initial trials.[17,18] Repetitive transcranial magnetic stimulation is delivered via an induction coil, in brief daily sessions over a course of days to weeks. It has an advantage over ECT in that it does not induce convulsions, so it does not necessitate anesthesia and therefore causes fewer side effects. However, it does not appear to work as well as ECT.

Deep brain stimulation is delivered via electrodes implanted in precise areas of the brain, which are connected to an implanted pacemaker-type device. It is also used in Parkinson disease, but with the electrodes in different areas of the brain. Studies of its use in several psychiatric disorders were prompted by observations in studies in which lesions were surgically created in the brain. Of the experimental treatments, deep brain stimulation may hold the most promise because it is directed at precise targets in the brain and it has been successful in severe, refractory cases. However, its use remains investigational, and the results seen so far are highly preliminary.

REFERENCES

1. **Fink M.** Meduna and the origins of convulsive therapy. Am J Psychiatry 1984; 141:1034–1041.
2. **Bini L.** Professor Bini's notes on the first electro-shock experiment. Convuls Ther 1995; 11:260–261.
3. **McDonald A, Walter G.** The portrayal of ECT in American movies. J ECT 2001; 17:264–274.
4. **Ishihara K, Sasa M.** Mechanism underlying the therapeutic effects of electroconvulsive therapy (ECT) on depression. Jpn J Pharmacol 1999; 80:185–189.
5. **McGarvey KA, Zis AP, Brown EE, Nomikos GG, Fibiger HC.** ECS-induced dopamine release: effects of electrode placement, anticonvulsant treatment, and stimulus intensity. Biol Psychiatry 1993; 34:152–157.
6. **Sanacora G, Mason G, Rothman D, et al.** Increased cortical GABA concentrations in depressed patients receiving ECT. Am J Psychiatry 2003; 160:577–579.
7. Diagnostic and Statistical Manual of Mental Disorders. 4th edition, Text revision. Washington, DC; American Psychiatric Association, 2000.
8. **Murray CJ, Lopez AD.** Global mortality, disability, and the contribution of risk factors: Global Burden of Disease Study. Lancet 1997; 349:1436–1442.
9. The Practice of Electroconvulsive Therapy: Recommendations for Treatment, Training, and Privileging. 2nd edition. Washington, DC: American Psychiatric Association, 2001.
10. **Dolenc TJ, Barnes RD, Hayes DL, Rasmussen KG.** Electroconvulsive therapy in patients with cardiac pacemakers and implantable cardioverter defibrillators. Pacing Clin Electrophysiol 2004; 27:1257–1263.
11. **Echevarria M, Martin M, Sanchez V, Vazquez G.** Electroconvulsive therapy in the first trimester of pregnancy. J ECT 1998; 14:251–254.
12. **Miller LJ.** Use of electroconvulsive therapy during pregnancy. Hosp Community Psychiatry 1994; 45:444–450.
13. **Bailine SH, Rifkin A, Kayne E, et al.** Comparison of bifrontal and bitemporal ECT for major depression. Am J Psychiatry 2000; 157:121–123.
14. **Loo CK, Schweitzer I, Pratt C.** Recent advances in optimizing electroconvulsive therapy. Aust N Z J Psychiatry 2006; 40:632–638.
15. **Patra KK, Coffey CE.** Implications of herbal alternative medicine for electroconvulsive therapy. J ECT 2004; 20:186–194.
16. **Sackeim HA, Haskett RF, Mulsant BH, et al.** Continuation pharmacotherapy in the prevention of relapse following electroconvulsive therapy: a randomized controlled trial. JAMA 2001; 285:1299–1307.
17. **Lisanby SH, Schlaepfer TE, Fisch H, et al.** Magnetic seizure therapy of major depression. Arch Gen Psychiatry 2001; 58:303–304.
18. **Mayberg HS, Lozano AM, Voon V, et al.** Deep brain stimulation for treatment-resistant depression. Neuron 2005; 45:651–660.

ADDRESS: *Donald Malone, MD, Department of Psychiatry, P57, Cleveland Clinic, 9500 Euclid Avenue, Cleveland, OH 44195; e-mail malonep@ccf.org.*