

Options for treatment-resistant depression

Why electroconvulsive therapy may be the best alternative to medication.

Although medications and psychotherapy are usually the first treatments offered to patients with major depression, they don't work for everyone. As we reported in August 2008, the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study found that about one-third of patients were unable to achieve full relief of symptoms (remission) even after trying four different strategies.

But the STAR*D data on relapse rates suggest that treatment-resistant depression may be even more common than remission rates might indicate. Relapse was a significant problem at each treatment level. By the end of the study, 50% of the patients who were able to achieve remission after trying a fourth treatment ended up relapsing within an average of 2.5 months.

By taking both relapse and remission rates into account for the entire study, Dr. J. Craig Nelson, an expert in treatment-resistant depression at the University of California, San Francisco, estimated that only 43% of patients enrolled in STAR*D were able to sustain their recovery. Other commentators have estimated that recovery rates may be even lower.

Thus, for treatment-resistant depression, clinicians remain interested in nonpharmacological ways to change brain function. Two FDA-approved options now exist: electroconvulsive therapy (ECT) and vagus nerve stimulation (VNS). In October 2008 the FDA also approved transcranial magnetic stimulation (TMS) for patients with depression who have not benefited from one antidepressant, but not for those who haven't responded to multiple drugs.

Insurers have balked at paying for VNS because it has not proven any more effective than ECT — and they may also refuse to pay for TMS. Therefore, ECT remains the most practical alternative because it is effective, covered by health insurance, and readily available.

ECT at a glance

Although ECT is often regarded as a treatment of last resort, it is probably the most powerful tool available to treat depression. Misconceptions and stigma about ECT may explain why it is not used more often. Here's a brief review of current ECT practice and several remaining challenges.

Who might benefit. ECT is an option for any patient whose depression has not been relieved after trying three or more distinct drugs; for patients at risk for suicide (ECT works faster and more reliably than drugs); for women who are pregnant or have just given birth who don't want to take antidepressants; and for elderly patients who either don't respond to drugs as well as they used to, or who, with age, have become more sensitive to side effects.

Although ECT has been used in children and adolescents, the technique has not been well studied in this population. The American Academy of Child and Adolescent Psychiatry has produced guidelines for ECT treatment of adolescents, recommending that it be considered after a patient does not respond to two or more medications, or when symptoms are so severe that fast treatment is necessary.

How it works. Before each treatment, the patient receives a short-acting anesthetic to prevent awareness of the procedure and to reduce discomfort. Other drugs are given to relax the muscles. While the patient is sleeping, the psychiatrist uses a special device to deliver an electrical impulse that stimulates the brain and causes a seizure. There are no outward signs of this seizure, but the doctor can watch it on a monitor (similar to an electroencephalogram) that measures electrical activity of the brain.

The mechanism of ECT action is not understood, but the seizure seems to restore the brain's ability to regulate mood. It may enhance the transmission of chemical signals or improve blood flow to the brain; animal studies suggest it may stimulate the creation of new brain cells. It is the seizure (not the electrical stimulus) that generates improvement.

Duration. Therapy usually consists of three ECT sessions a week, for a total of six to 12 treatments.

Side effects. The most bothersome side effects are memory problems and difficulty concentrating, although certain ECT techniques may help reduce risk. Other side effects — partly from the anesthetic — include headache and nausea.

ECT remission and relapse rates

Study	Patients achieving remission with ECT	Relapse rates at 6 months, with various maintenance therapies	
Consortium for Research in ECT (CORE)	86%	Nortriptyline (Aventyl, Pamelor) and lithium	32%
ECT	37%		
Columbia University Consortium (CUC)	55%	Placebo	84%
Nortriptyline	60%		
Nortriptyline and lithium	39%		

Sources: Sackeim HA, et al., *Journal of the American Medical Association* (March 14, 2001), Vol. 285, No. 10, pp. 1,299–307; and Kellner CH, et al., *Archives of General Psychiatry* (Dec. 2006), Vol. 63, No. 12, pp. 1,337–44.

Challenges in remission and relapse

The Consortium for Research in ECT (CORE) and the Columbia University Consortium (CUC) concluded that ECT produced remission rates of 86% and 55%, respectively — higher than those achieved with medication in the STAR*D trial. (The CUC study had stringent remission criteria.) An analysis of 18 studies also found that ECT was more effective than drug therapy — although some studies may not have used optimal drug doses. Remission usually occurs relatively quickly with ECT, in an average of one to three weeks, compared with four to 12 weeks or longer with drug treatment.

In some medical centers, however, remission rates may not be as high as those achieved in university-based research studies, where the selection criteria for participation are carefully applied. A study of seven community hospitals, for example, reported that only 30% to 47% of patients achieve remission after ECT.

A persistent challenge is relapse after successful ECT treatment. Several options help reduce this risk. First, ECT can be tapered gradually once remission is achieved, by decreasing sessions from three times a week to once or twice a week, and then to once a month, rather than stopping abruptly. Other options include maintenance ECT therapy, maintenance drug treatment, or some combination of the two.

Although maintenance ECT is usually delivered on a fixed calendar basis (such as once or twice a month), researchers are now trying to find ways to better tailor the treatment schedule to each patient's symptoms.

Remission, relapse, and recovery

STAR*D investigators collected data about both remission rates (those listed below are based upon self-report after 14 weeks of treatment) and relapses that occurred at some point during follow-up. If patients did not adequately respond at one level, they progressed to the next.

Memory and thinking problems

ECT can cause three types of memory and thinking problems: retrograde amnesia (problems recalling events in the past), anterograde amnesia (reduced ability to retain new information), and postictal delirium (confusion following ECT). Studies have consistently found such deficits tend to be temporary, and many patients either don't find them bothersome or find ways to cope. But others find them wrenching. Indeed, ECT-related memory problems are the main reason that patients refuse to consider ECT or decide to end treatment early. Several strategies may help reduce risk of ECT-related memory problems.

Electrode placement. During an ECT session, electrodes can be placed on one side of the skull (unilateral placement) or on each temple (bilateral placement). Studies have found that unilateral ECT is less likely to cause cognitive problems than bilateral ECT, yet may be just as effective. For this reason, patients usually initially undergo unilateral ECT, and then progress to bilateral ECT only if they don't receive sufficient benefit from the unilateral treatments.

But unilateral treatments may not be appropriate for all patients. In order to work, ECT must overcome a patient's "seizure threshold," an individualized set point that determines what amount of electrical stimulation is necessary to induce a seizure. Unilateral ECT requires a stronger electrical stimulus to overcome a patient's seizure threshold than bilateral ECT does. The ECT devices approved for use in the United States may not produce the energy levels necessary for unilateral placement of electrodes, especially in older patients, because seizure threshold increases with age.

Patients may also need to undergo more sessions of unilateral than bilateral ECT to achieve remission. In the CUC study, patients received an average of seven unilateral treatments followed by an average of three bilateral treatments — or a total of 10 treatments on average — to achieve remission. In contrast, the CORE study, which involved only bilateral treatment, found that patients required an average of seven sessions to achieve remission. For this reason, some clinicians advise starting with bilateral treatments.

Pulse width. Electricity is produced in waves. In ECT, the longer the pulse width (the space between peaks in the wave), the greater the chance of cognitive side effects. In the past, ECT devices used relatively long "sine wave" pulses. Today, most devices use shorter pulse widths that may also help prevent memory loss and other cognitive problems.

Under investigation. Researchers are investigating whether particular drugs or dietary supplements might help protect memory during ECT treatments. Researchers at Massachusetts General Hospital and McLean Hospital, for example, have conducted pilot studies with galantamine (Razadyne, Reminyl), a medication that modestly improves cognitive deficits in patients with Alzheimer's disease. But the research is still in the early stages.

Although ECT is not a perfect treatment (and none is, after all), it remains the best alternative for patients who continue to struggle with disabling symptoms of depression even after taking several different medications. It works relatively quickly, it's effective for most patients, and for some it may be life-saving.

-Harvard Mental Health Letter, 2008

How to get ECT in Winston-Salem

Call the psychiatry department at Baptist Hospital, 716-4551, and ask for an evaluation for ECT. Even if you decide not to go forth with it, it is helpful to get that consultation and the psychiatrist there may have other ideas to help your depression. Ask them what their fax number is for us to send records to and call us back with that and we'll fax them to them.

How to get TMS in North Carolina

The closest provider to Winston-Salem is:

Irving A. Lugo, M.D., P.A.
2006 New Garden Road Unit 202
Greensboro, NC27410
Phone: (336) 288-6440

Other providers are listed at
<http://www.neuronetics.com/Contact-Find-Provider.aspx>