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Electroconvulsive therapy: How modern techniques improve patient outcomes: Refinements have decreased memory loss, other adverse effects while retaining efficacy:

Refinements have decreased memory loss, other adverse effects while retaining efficacy

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Electroconvulsive therapy (ECT) has remained one of the most effective treatments for major depressive disorder (MDD) since it was introduced >70 years ago.[1] ECT's primary indication is severe, treatment-resistant MDD but sometimes is used to treat other disorders, including bipolar mania and schizophrenia. In ECT, electrical current is delivered to a patient's brain via electrodes placed on the scalp to induce a seizure while the patient is under anesthesia and a muscle relaxant. ECT's exact mechanism of action for MDD is unknown, but researchers believe it may relieve depressive symptoms by regulating functional disturbances in relevant neural circuits.[2]

Research has shown that 64% to 87% of patients with severe MDD respond to ECT, with response rates as high as 95% for patients with MDD with psychotic features.[3–5] Although patients may respond more quickly, 6 to 12 sessions typically are required to resolve a severe depressive episode.[2]

Despite ECT's proven effectiveness, several factors have limited its widespread use, including limited access and expertise, adverse cognitive effects such as memory

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Related Resources

- Leiknes KA, Jarosh-von Schweder L, Høie B. Contemporary use and practice of electroconvulsive therapy worldwide. Brain Behav. 2012;2(3):283-344.
- Manka MV, Beyer JL, Weiner RD, et al. Clinical manual of electroconvulsive therapy. Arlington, VA: American Psychiatric Publishing; 2010.

Drug Brand Names

Esmolol, Brevibloc, Etomidate, Amidate, Glycopyrrolate, Robinul, Ketorolac, Toradol, Labetalol, Normodyne, Trandate, Methohexital, Brevital, Nicardipine, Cardene, Succinylcholine, Anectine

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impairment, and negative public perception based on how ECT was administered decades ago.[2] This article describes current methods of administering ECT, and how these changes have helped minimize these concerns while retaining efficacy.

Modern ECT practices

Since ECT was first used in the 1930s, clinicians have made many modifications to improve its efficacy and safety. Refinements to how ECT is administered include changing waveform parameters, individualizing dosing to seizure threshold, and altering electrode placement.[6,7]

Pulse width

Most ECT devices used today feature a constant-current output stimulator[8] that allows continuous current regulation.[7] Total charge, in millicou-lombs (mC), is the common metric.[7] Pulse width is a commonly altered waveform parameter in ECT delivery. Most research supports administering repeated brief or ultra-brief pulses (0.5 to 2 milliseconds), which is associated with greater charge efficiency and fewer side effects than traditional sine wave ECT dosing.[8,9] Using a brief or ultra-brief pulse width increases clinical efficiency and decreases side effects because it focuses the stimulus on brain regions that regulate mood while limiting stimulation of brain regions involved in cognitive functioning.[7] With brief-pulse stimulus, a patient's cognitive performance may return to baseline levels within 3 days of treatment.[6] Increasing evidence demonstrates that using a larger number of pulses with a brief pulse width and amplitude enhances ECT's antide-pressant effects while reducing unwanted neurocognitive side effects.[7]

Dosing and duration

In terms of clinical efficacy, how much the electrical stimulus exceeds a patient's seizure threshold— the minimum amount of electrical charge that induces a generalized CNS seizure[10]—is more important than the absolute intensity of the stimulus.[1] The degree to which the stimulus should exceed the seizure threshold depends on electrode placement, which is described below. Acute therapy patients typically receive 2 to 3 treatments each week,[11,12] culminating in 12 to 18 treatments.[8,12] The optimum number of sessions administered is determined by the ratio of clinical improvement to the severity of cognitive adverse effects.[3]

Electrode placement

Spatial targeting of stimulus is crucial to maximize therapeutic benefits and minimize side effects. Concerns about cognitive side effects have led to variations in electrode placement to minimize the amount of brain parenchyma affected by electrical discharge (*Table*).[1,7,8] The most commonly used placements are:

- bitemporal (BT)—electrodes are placed midline between the eye and ear on both sides of the head
- right unilateral (RUL)—1 electrode is positioned just lateral to the vertex and the other at the right temple.[7]

When given in doses close to a patient's seizure threshold, RUL ECT offers only modest effects, but at suprathresh-old doses—eg, 6 times the seizure threshold—it is as effective as BT placement[1] but avoids cognitive disruption.[9] Patients who do not respond to several seizures with RUL placement often are switched to BT to enhance clinical response.[8] In BT ECT, stimulus is administered at 1.5 times the patient's threshold levels. Exceeding these values is unlikely to increase efficacy, but can contribute to adverse effects.[1]

Addressing safety concerns

In addition to changes to waveforms, dosing, and electrode placement, using anesthesia, muscle relaxants, and other medications has dramatically reduced adverse effects of ECT.[8,10,13] See the Box[10,14,15] for the specific agents used and their purposes. Before these medications and electroencephalography and electrocardiography (ECG) monitoring were used during ECT, the mortality rate was approximately 0.1%.[13] Today, ECT is considered a low-risk medical intervention, with a mortality rate of approximately 0.002%.[1,16] Before beginning an acute course of ECT, patients undergo laboratory testing, including a complete blood count, basic metabolic panel, and ECG. Spinal radiography and neuroimaging studies can be obtained to rule out preexisting vertebral injuries or neurologic disorders.[1,8]

Box

Medications used during electroconvulsive therapy

Anesthesia increases patients' comfort during electroconvulsive therapy (ECT) by making them unaware of and unable to recall the procedure. The most commonly used anesthetic for ECT is methohexital, 0.5 to 1 mg/kg.[14] Etomidate can be used in patients with contraindications to methohexital[15]; however, this medication can lengthen ictal duration.[14] After the initial ECT treatment, clinicians can adjust the anesthetic dose based on the patient's previous response.[14]

Using muscle relaxants during ECT has virtually eliminated bone fractures resulting from the procedure.[10] The most common muscle relaxant is succinylcholine,[15] which also reduces delirium in patients with post-ECT agitation.[14] Mask ventilation and standard, noninvasive monitoring of cardiac parameters and oxygen saturation are necessary.[14]

Tachycardia and hypertension associated with ECT can be countered with beta blockers such as esmolol or labetalol as well as calcium channel blockers such as nicardipine.[14] In addition, most patients are treated with the anticholinergic glycopyrrolate before the procedure to avoid bradycardia[14] and reduce secretions, which may cause aspiration.[15] Patients who experience headache or muscle pain after ECT can be treated with ibuprofen or acetaminophen before ECT sessions; patients with more severe complaints can be treated with intravenous ketorolac, 15 to 30 mg, before stimulus administration.[15]

Hemodynamic changes in response to ECT-induced seizures can exacerbate pre-existing cardiac conditions. Normal physiologic response to ECT consists of a brief parasympathetic outflow, inducing bradycardia for 10 to 15 seconds, followed by a prominent sympathetic response characterized by hypertension and tachycardia for approximately 5 minutes. Although these changes can induce myocardial ischemia or infarction,[14] the most common

cardiac disturbances caused by ECT are ar-rhythmias, primarily in patients with pre-existing cardiac abnormalities.[17]

Memory impairment

The most prevalent adverse reaction to ECT is memory loss, although not all aspects of recall are impaired to the same degree.[18] Memory impairment varies based on factors such as electrode placement,[9] stimulus waveform,[19] site of seizure initiation, and pattern of activation.[20] The risk of experiencing memory loss or other cognitive side effects following ECT can be decreased by using RUL electrode placement, brief pulses, and lower stimulus charge relative to seizure threshold.[21] Memory deficits incurred by ECT usually are transient. In a study of 21 patients who received BT ECT for severe MDD, Meeter et al[22] found that memory was stable and possibly improved at 3-month follow-up.

Subsets of memory function are impaired to differing degrees after ECT. For example, after treatment, autobiographical memory generally is less impaired than impersonal data.[12,23] Weiner et al[9] found that autobiographical information was more significantly impaired in patients treated with bilateral sine wave ECT than in those who underwent RUL ECT.

Procedural memory—memories of learned motor skills or mechanical tasks—often are left intact compared with semantic memory, which is general, declarative information recalled without context.[18] The subsets of memory collectively regarded as declarative memory—the recollection of facts and events—may be most severely affected because this type of memory relies upon median temporal lobe structures, which are affected by ECT.[21]

Anterograde amnesia—the inability to form new memories—often is limited to the immediate posttreatment period and has been shown to become less pronounced at follow-up visits.[22] Many clinicians and patients consider retrograde amnesia—forgetting memories that were formed before ECT—to be the most serious adverse effect of ECT. However, Mini-Mental State Examination scores tend to improve for patients who undergo ECT.[1,16] Retrograde amnesia usually improves within weeks to months after ECT.[12] Evidence suggests that retrograde amnesia mostly lifts during the recovery period and typically is not evident after 3 months.[22] The best indicators of possible retrograde amnesic effects are preexisting cognitive deficits[12] and duration of disorientation after ECT.[1] Therefore, retrograde amnesia is more common among older adults, in whom age-related changes predispose patients to ECT's adverse effects.[24]

The conventionally accepted mechanism for memory deficits after ECT is excito-toxic damage in the pyramidal cell layer of neurons in the hippocampus that induces calcium influx, which damages cells and causes neuronal atrophy.[12] However, in animal studies, Dwork et al[25] found an absence of neuronal or glial loss in regions subserving memory or cognitive functions (ie, the hippocampus or frontal cortex). Even in regions exquisitely sensitive to neuronal damage—such as CA1 of the hippocampus—neither cell number or volume or density of neuronal or glial cells were detected at statistically significant levels.[25] Therefore, it is unlikely that ECT causes cell damage or atrophy in hippocampal neurons.

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Table

ECT electrodes: Bitemporal vs right unilateral placement

Placement	Location	Comments
BT	Electrodes are placed midline between the eye and ear on both sides of the head	Stimulus is administered at 1.5 times a patient's seizure threshold. Often used for patients who do not respond to several seizures with RUL
RUL	1 electrode positioned just lateral to the vertex and the other at the right temple	When stimulus is administered in doses 6 times a patient's seizure threshold, RUL is as effective as BT but avoids cognitive disruption. Offers only modest effects when stimulus is administered in doses close to a patient's seizure threshold

BT: bitemporal; ECT: electroconvulsive therapy; RUL: right unilateral

Source: References 1,7,8