

Chapter

Basic Concepts of ECT

Basic Concepts

Electroconvulsive therapy (ECT) is a safe and reliably effective procedure; it requires that the practitioner have a theoretical and practical background to perform it well. Our hope is that this book will assist the practitioner in the application of previously acquired knowledge of ECT. Our intent is that this book should complement the existing, comprehensive texts on ECT, including the report of the American Psychiatric Association (APA) Task Force on Electroconvulsive Therapy (2001) (American Psychiatric Association, 2001), *Electroconvulsive Therapy* by Richard Abrams (Abrams, 2002), *Electroconvulsive and Neuromodulation Therapies* by Conrad Swartz (Swartz, 2009), and *Electroconvulsive Therapy: A Guide for Professionals and Their Patients* by Max Fink (Fink, 2009).

Our belief is that ECT is a well-standardized procedure that can be learned quite easily. The body of knowledge that the practitioner must master is circumscribed and not overly complex. Of course, as in any clinical endeavor, situations arise that require expert judgment and some modification of standard technique. There is no substitute for clinical experience, and consultation with experts is recommended in difficult cases.

The goal of this text is to provide a practical and useful outline of the basics of the treatment and to assist the reader in developing a well-informed, commonsense attitude to approaching the patient who needs ECT. At all times, technical excellence and patient comfort should be foremost considerations.

Overview

ECT remains the most reliably effective treatment for serious depression. Its efficacy and speed of response compare favorably to those of antidepressant medications (Husain et al., 2004). For these reasons, it must be considered a mainstream treatment in modern psychiatric practice, not one that is optional or “on the fringe.” In the past two decades, there has been a steady increase in ECT research, as evidenced by the growing number of ECT-related citations in the scientific literature. In addition,

renewed clinical interest in ECT has led to the growth of professional societies dedicated to the advancement of ECT including the International Society for ECT and Neurostimulation (ISEN, formerly the Association for Convulsive Therapy [ACT]) and the European Forum for ECT (EFFECT), among others worldwide. Exciting developments include innovations in technique, such as the electrical dose titration method of estimating seizure threshold (Sackeim et al., 1987); the use of ultrabrief pulse stimuli (Sienaert et al., 2009); as well as new information about the use of ECT in catatonia (Fink & Taylor, 2003), autistic self-injury (D'Agati et al., 2017), and as a continuation/maintenance treatment for affective disorders (Kellner et al., 2006, 2016).

Despite the ongoing barrage of criticism of the treatment (based largely on either outdated or incorrect information), ECT has remained in continuous use since its introduction in Rome in 1938. But modern ECT is so far removed from that primitive procedure that it should hardly be considered the same treatment. Just as it would be unreasonable to equate surgery as performed in 1938 with surgery as performed in 2018, so old-fashioned ECT is now of purely historical interest. The remarkable popularity of the movie *One Flew Over the Cuckoo's Nest* (1975) is largely responsible for the continued public perception of ECT as a barbaric, coercive procedure. Several books for the lay public, including *Shock: The Healing Power of Electroconvulsive Therapy* by Kitty Dukakis and Larry Tye (Dukakis & Tye, 2006); *Shock Therapy: A History of Electroconvulsive Treatment in Mental Illness* by Edward Shorter and David Healy (Shorter & Healy, 2007); *Struck by Living: From Depression to Hope* by Julie Hersch (Hersch, 2010); and *Each Day I Like It Better: Autism, ECT, and the Treatment of Our Most Impaired Children* by Amy Lutz (Lutz, 2014), are both informative and factually accurate; they paint a realistic and positive picture of contemporary ECT.

Although ECT is an essential part of psychiatric practice, it remains a very small part. According to data from the National Institute of Mental Health (NIMH), in 1980, approximately 32,000 psychiatric inpatients received ECT in the United States; in 1986, the number increased to approximately 37,000 (Thompson et al., 1994). The current figure of patients who receive ECT annually in the United States is almost certainly greater, although, surprisingly, precise data are unavailable. Hermann et al. (1995) estimated that 100,000 patients received ECT in the United States in 1995; Abrams (2002) estimated that 1–2 million patients per year receive ECT worldwide. A recent large epidemiological study reported that only 1.5% of inpatients with mood disorders receive ECT in US psychiatric hospitals (Slade et al., 2017).

Health care reform has led to a greater emphasis on the ability to offer the treatment to outpatients. Because ECT is likely to be more effective than antidepressant medications for many patients (Janicak et al., 1985), it stands to reason that it would be viewed favorably in an increasingly cost- and efficiency-conscious environment.

The old assumption that a course of ECT necessitates being in the hospital is no longer valid. Of course, some patients will be so severely psychiatrically or

medically ill as to require hospitalization. Many, however, with adequate family support and close attention to the logistics of treatment (e.g., explicit written instructions about concurrent medications, nothing by mouth [NPO] status, prohibition of driving) can be safely and comfortably treated as outpatients (Fink et al., 1996; Jaffe et al., 1990).

Because ECT requires specialized knowledge and technical skill, it is likely to be performed by only a small minority of psychiatrists. Thus, local ECT experts, to whom other practitioners refer patients, may be the norm.

Although there may be some controversy about what level of ECT expertise should be required of all psychiatric residents, there can be little disagreement that all psychiatrists should know enough about ECT to make informed referrals to ECT practitioners (Kellner & Li, 2016). Furthermore, the report of the APA Task Force on Electroconvulsive Therapy (American Psychiatric Association, 2001, pp. 225–231, 242) makes specific recommendations about minimum didactic and practical experiences for psychiatric residents and practitioners who want to be privileged by a hospital to perform ECT.

ECT should be performed only by qualified personnel in an appropriate setting. This setting has traditionally been a hospital or hospital-based clinic where access to the equipment and personnel necessary to handle cardiopulmonary emergencies is available. In the United States, the fact that ECT is not reimbursed by Medicare or most private insurances unless it is performed in a hospital has likely limited its availability. However, there is no good reason why ECT could not be safely administered in a properly equipped and staffed surgicenter or outpatient practice. Close cooperation with the staff who provide anesthesia support is essential for optimal ECT. As in all medicine, the goal of scientific and technical advancement remains improved patient care.

Theories of Mechanism of Action

ECT has multiple, profound effects on brain systems, and we continue to add to our understanding of how it works to alleviate psychiatric illness. Patients and practitioners, understandably, would be reassured to know exactly how ECT exerts its therapeutic effects. While we are not yet able to explain this in an accurate and comprehensive way, rather than settle for a stark “we don’t know,” it is more reasonable to invoke one of the better-supported theories of mechanism of action (see below). In truth, we know nearly as much about how ECT works as we do about how antidepressant medications work. A full understanding of how ECT (and other antidepressant treatments) works may need to await a more thorough understanding of the etiology of the major psychiatric illnesses.

Research over the last several decades has provided a wealth of information about specific changes in neurobiology induced by ECT (Mann, 1998; Sackeim, 1989; Swartz, 2009). The classic research of Ottosson (Ottosson, 1960, 1962) using lidocaine-modified ECT helped to establish the seizure as crucial to the efficacy of ECT. From time to time, this facet of ECT dogma is challenged (Regenold et al., 2015). The finding that low-dose right unilateral

ECT may produce suboptimal clinical outcomes despite adequate seizure duration confirmed that not all ECT seizures are equivalent (Sackeim et al., 1987). It appears that both the anatomic location of seizure initiation as well as intensity of the electrical stimulus affect both therapeutic efficacy and cognitive effects (Nobler & Sackeim, 2008; Nobler et al., 2000). The search continues for more sophisticated measures of seizure therapeutic adequacy other than seizure duration (e.g., postictal electroencephalographic [EEG] suppression) (Krystal & Weiner, 1994; Minelli et al., 2016; Nobler et al., 1993). It is generally accepted that more robust EEG seizure expression (perhaps best characterized by a combination of morphological features and other physiological characteristics) is associated with better clinical outcomes.

The main theories are summarized below.

Neurotrophic Theory

The most exciting progress in the elucidation of ECT's mechanism of action has been the rapid accumulation of evidence for its neurotrophic effects. It is now quite clear that the effects of ECT, in contradistinction to those of prolonged depression, may be beneficial for the brain. In fact, it appears that ECT reverses many of the structural abnormalities seen in severely depressed individuals.

Animal studies show that ECS (electroconvulsive shock, the animal analog of ECT) results in increased neurogenesis and mossy fiber sprouting in the dentate gyrus of the hippocampus (Bolwig & Madsen, 2007; Lamont et al., 2005; Madsen et al., 2000). This line of research continues rapidly, with frequent additions to the literature both replicating previous work and providing a more nuanced understanding of the neurogenesis process (Olesen et al., 2017; Otabe et al., 2014; Schloesser et al., 2015; Smitha et al., 2014; Svensson et al., 2016). It is possible that advanced neuroimaging techniques, such as magnetic resonance spectroscopy (MRS), may soon be able to provide evidence for neurogenesis in humans after ECT. Evidence now shows that ECT leads to increases in neurotrophic factors such as brain-derived neurotrophic factor (BDNF) in depressed patients (Piccinni et al., 2009; Rocha et al., 2016).

Whether neurogenesis is a principal part of the process by which ECT induces structural brain changes is not yet clear; what is clear is that we now have MRI evidence that ECT leads to increased volume in cortical and subcortical structures. Dukart et al. (2014) showed gray matter volume increases in hippocampus and subgenual cortex in a group of unipolar and bipolar patients. Joshi et al. (2016) showed increases in hippocampus and amygdala volume in depressed adult patients; Bouckaert et al. (2016) showed increased hippocampal volume with ECT in a large group of geriatric depressed patients, with return to baseline volumes after 6 months. Redlich et al. (2016) also demonstrated increases in hippocampal volume with ECT, as well as a correlation between baseline subgenual cingulate gyrus volume and ECT response. Preliminary evidence shows that other basal ganglia structures are also increased in volume with ECT (Wade et al., 2016). A meta-analysis reviewed the body of evidence (nine

studies, $n = 174$) that ECT is associated with volume increases of hippocampus (Wilkinson et al., 2017). It has recently been suggested that the increase in hippocampal volume may be associated with temporary cognitive effects as well as antidepressant effects (van Oostrom et al., 2018).

Taken together, the above MRI data indicate that ECT has profound restorative effects on the brain. Given the rapid pace of discovery in this field, future research will likely soon elucidate which component of the procedure (stimulus, electrode placement, current density, seizure, or other component) is responsible for these structural changes; it may also soon be possible to better predict who will respond to ECT and to which specific technique.

Classical (Monoamine) Neurotransmitter Theory

This theory suggests that ECT works in a way similar to that of antidepressant medications – that it enhances deficient neurotransmission in relevant brain systems. This is a corollary of the classical monoamine depletion theory of depression, a theory that has been updated to include the possibility of a modulatory role for monoamine systems, rather than a simple deficit-adequacy model (Heninger et al., 1996). Specifically, ECT is known to enhance dopaminergic, serotonergic, and adrenergic neurotransmission. Animal studies using ECS have demonstrated increases in dopamine-related behaviors (Fochtmann, 1994). The exact mechanism for this dopaminergic enhancement is as yet unclear; however, it may involve increased dopamine release, receptor changes, and/or changes in the blood–brain barrier (Fall et al., 2000). The fact that ECT has clear antiparkinsonian effects argues strongly for dopaminergic enhancement (Cumper et al., 2014; Popeo & Kellner, 2009). That ECT also has profoundly antipsychotic effects (and we would expect decreases in dopamine function to be associated with antipsychotic effects) argues against a single theory of increased dopamine availability throughout the brain (Rosenquist et al., 2014).

Numerous studies of the serotonin system in both animals (ECS) and humans (ECT) have revealed a complex pattern of changes to pre- and post-synaptic receptors, the serotonin transporter and serotonin metabolites in the cerebrospinal fluid, not all of which are consistent with a simple theory of serotonin enhancement with ECT (Swartz, 2009). For many years, based on animal studies, the serotonin system was believed to be the only monoaminergic system in which ECT had opposite effects from most antidepressant drugs. ECS increases 5-HT₂ receptor number, whereas antidepressant drugs decrease 5-HT₂ receptor number (Mann & Kapur, 1992). A positron emission tomography (PET) scan investigation found, in contrast to the ECS studies, that ECT reduces brain 5-HT₂ receptors in depressed patients (Yatham et al., 2010). These authors speculated that “the ability of ECT to further down-regulate brain 5-HT₂ receptors in antidepressant non-responsive individuals may explain its efficacy in those people with antidepressant refractory depression.” Rudorfer et al. (1988) demonstrated that 5-hydroxyindoleacetic acid (5HIAA), the major

metabolite of serotonin, was increased in the spinal fluid of patients after ECT. A review in the special issue of the *Journal of ECT* dedicated to “Mechanisms in ECT” (Volume 30, #2, 2014) contained a review of serotonin and dopamine neurotransmission in ECT (Baldinger et al., 2014).

The adrenergic system is also affected by ECT; here, too, numerous pre-clinical, as well as clinical studies have yielded complex, sometimes contradictory findings. As with other antidepressant drugs, down regulation of beta-adrenergic receptors has been a consistent finding in ECS studies. Some studies suggest that ECS results in increased cortical norepinephrine transmission as a result of postsynaptic effects (Newman et al., 1998). However, human studies have failed to find consistent alterations in norepinephrine turnover with ECT (Rudorfer et al., 1988).

Other neurotransmitter systems, including glutamate and gamma-aminobutyric acid (GABA), have been implicated in the mechanism of action of ECT. Studies of glutamate, in both animals and human subjects, have yielded conflicting results. Pfleiderer et al. (2003) showed reduced glutamate with MRS in the anterior cingulate of depressed patients; glutamate levels normalized with successful ECT. A more recent study showed the opposite in the rat hippocampus, with glutamate levels decreasing after ECS (Dong et al., 2010). Glutamate may be involved in both the antidepressant and the cognitive effects of ECT.

The GABA system has been implicated in the antidepressant and anticonvulsant properties of ECT (Swartz, 2009). Both animal (Ferraro et al., 1990) and human studies (Esel et al., 2008) have demonstrated increases in GABA levels after ECS or ECT. As a major inhibitory neurotransmitter that is measurable in human serum, GABA is likely to be the focus of further investigations of ECT’s mechanism of action in the future.

Neuroendocrine Theory

This theory suggests that ECT-induced release of hypothalamic or pituitary hormones results in antidepressant effects (see Haskett, 2014, for a review). The specific hormone(s) responsible for this therapeutic effect has yet to be isolated. ECT results in release of prolactin, thyroid-stimulating hormone (TSH), adrenocorticotrophic hormone (ACTH), and endorphins, among other neurohumoral substances (Kamil & Joffe, 1991). A putative antidepressant neuropeptide, “antidepressin” or “euthymesin,” has been theorized to be released from the hypothalamus during the ECT seizure, exerting beneficial effects on mood disorders in a way similar to the diabetes/insulin model (Fink & Nemeroff, 1989).

Many investigations have confirmed both the dysregulation of the hypothalamic-pituitary-adrenal (HPA) in melancholic depression and the correction of this abnormality with successful antidepressant treatment, most notably, ECT (Carroll, 1986). The dexamethasone suppression test (DST), the endocrine test that identifies the HPA abnormality, has also been used as a marker of the adequacy of continuation ECT; failure to normalize has been shown to be an indication of the need for ongoing continuation ECT (for review, see Bourgon and Kellner, 2000).

Anticonvulsant Theory

This theory suggests that the antidepressant effect of ECT is related to the fact that ECT itself exerts a profound anticonvulsant effect on the brain. Several lines of evidence indicate that this is so, including the facts that seizure threshold rises (and seizure duration decreases) over a course of ECT and that some patients with epilepsy have fewer seizures after ECT (Griesemer et al., 1997; Sackeim, 1999). ECT has even been used to treat resistant status epilepticus (Lisanby et al., 2001; Miras Veiga et al., 2017). Neurohormones have been postulated to mediate this anticonvulsant effect. The cerebrospinal fluid of animals receiving ECS is anticonvulsant when given intraventricularly to recipient animals, possibly as a result of endogenous opioids (Holaday et al., 1986). GABA has also been proposed as a key mediator of ECT's anticonvulsant effect (see above).

Connectivity Theory

Preliminary data suggest that abnormal baseline neural network connectivity in patients with depression or schizophrenia is re-regulated by ECT. The significance of this finding for explaining the mechanism of action of ECT remains to be elaborated (Argyelan et al., 2016; Li et al., 2017; Mulders et al., 2016).

Basics of Electricity

The ECT practitioner should know the following basic facts about electricity in ECT.

Stimulus Characteristics

Modern ECT devices use alternating current that delivers a stimulus in the form of a series of bidirectional square-wave pulses. This is referred to as a brief pulse or ultra-brief pulse (when the pulse width is below 0.5 ms) stimulus. Older ECT devices delivered a sine-wave stimulus. The brief pulse or ultra-brief pulse stimulus is more efficient at inducing seizures and consequently can produce seizures with a lower “dose” of electricity. This results in less cognitive impairment. Emerging data are promising that ultra-brief pulse stimuli will be much less cognitively impairing, yet preserve efficacy (Kellner et al., 2016; Sienaert et al., 2010; Tor et al., 2015; Verwijk et al., 2012).

Charge

Charge refers to the total number of electrons flowing through a conductor. Many ECT experts agree that the dose of electricity used in ECT should be expressed in terms of charge. The setting dials on some ECT devices vary the charge (by increasing stimulus duration), although they are labeled “energy.” The equation for charge is

$$\text{charge} = \text{current} \times \text{time}$$

Charge is expressed in millicoulombs (mC).

Energy

Energy adds a term for voltage to the equation for charge. Thus,

$$\text{energy} = \text{voltage} \times \text{current} \times \text{time}$$

Voltage can be thought of as the pressure with which the electrons are “pushed” through the conductor.

By rearranging the above equation with the substitution of an expanded term for voltage

$$(\text{voltage} = \text{current} \times \text{resistance} [\text{Ohm's law}])$$

we arrive at

$$\text{energy} = \text{current}^2 \times \text{resistance} \times \text{time}$$

Thus, as resistance increases, if current and time are kept constant, energy also increases. Because modern ECT devices are mostly of the constant-current type, a patient with a higher resistance will have more energy delivered than a patient with lower resistance treated at the same setting. The constant-current ECT device is designed to increase the voltage automatically (up to a predetermined safe maximum limit) to deliver the desired charge despite high resistance. Because a patient's resistance (impedance) during the delivery of a stimulus is unknown until the stimulus is delivered, settings on an ECT device in terms of joules (J) must necessarily be estimates based on an arbitrary fixed “standard” impedance (e.g., 200 or 220 Ω). Remember that the dial on the ECT device that controls the length of the stimulus is actually setting the charge and only indirectly setting the energy.

Energy is expressed in terms of joules. Note that the number of joules used in ECT is generally considerably smaller than that used in cardiac defibrillation. ECT devices available in the United States deliver an allowable maximum of 101.4 J. Joules may be converted to millicoulombs by multiplying by 5.7 (assuming fixed impedance of 220 Ω and current of 0.8 A).

Impedance may be highly variable between individual patients. The primary contributor to the impedance of the electrical circuit is not the brain, but rather the skin, the underlying scalp soft tissues, and the skull. The contribution of these elements to the inter-individual variability of seizure threshold for ECT requires further research (Beale et al., 1994; Coffey et al., 1995; Petrides et al., 2009; Sackeim et al., 1994).

Electrical Safety

The risk of injury to the patient or the practitioner from being shocked is very small. Theoretically, if the patient's impedance is too high, a skin burn at the electrode site can occur. This possibility is virtually eliminated by the provision of electrical self-test features in modern ECT devices, which allow the psychiatrist to check impedance before delivering the stimulus (see section “Electrode Site Preparation” in Chapter 3). The person delivering the stimulus is at no risk

for getting shocked unless he or she actually touches the metal or the conducting surface of one of the stimulus electrodes. The patient's scalp may be touched (e.g., to provide counter pressure on the left side of the forehead during a right unilateral treatment) during the delivery of the stimulus without fear of being shocked. Calls of "Stand clear!" are unnecessary. However, it is prudent to ensure that anesthesia personnel or other personnel do not touch the electrodes during the delivery of the stimulus.

Medical Physiology

Of greatest importance to the clinician are the physiological effects of ECT on the central nervous and cardiovascular systems. As described in later sections, modifications in ECT technique may be required in patients with neurological or cardiovascular disease.

Cerebral Physiology of ECT

Seizure Induction

ECT involves the use of an electrical stimulus to depolarize cerebral neurons and thereby produce a generalized seizure. The more completely generalized the seizure, the more powerful the antidepressant effect is thought to be. The mechanism by which ECT seizures are propagated is not well understood (Enev et al., 2007). However, important differences in efficacy and cognitive effects between bilateral and unilateral electrode placements may result from differing routes of seizure generalization in the brain (Staton et al., 1981) and different regional current density (Lee et al., 2016).

Ictal EEG

During the initial phase of the induced seizure, EEG activity is variable, consisting of patterns of low-voltage fast activity and polyspike rhythms. These patterns correlate with tonic or irregular clonic motor movements. With seizure progression, EEG activity evolves into a pattern of hypersynchronous polyspikes and waves that characterize the clonic motor phase. These regular patterns begin to slow and eventually disintegrate as the seizure ends, sometimes terminating abruptly in a "flat" EEG (Weiner et al., 1991) (see Figure 3.8a–c in Chapter 3).

Interictal EEG

Transient, cumulative changes also occur in the interictal EEG in response to a course of ECT. Increased predominance of delta activity on interictal EEG is seen as a function of the number of ECT treatments given in a course of ECT and their rate of administration (Fink, 1979). The interictal EEG typically returns to baseline by approximately 1 month following the ECT course in most patients. Generalized EEG slowing has been associated with a positive outcome after ECT (Sackeim et al., 1996). Farzan et al. (2014) have suggested that EEG changes with ECT may reflect resetting of aberrant functional connectivity between brain regions.

Other Neurophysiological Effects of ECT

The ECT seizure is also associated with a variety of transient and benign changes in cerebral physiology, including increases in cerebral blood flow, cerebral blood volume (resulting in a transient rise in intracranial pressure), and cerebral metabolism. The brief rise in intracranial pressure is rarely of clinical consequence, but it is the reason for the historical proscription of ECT in patients with space-occupying mass lesions. Postictally, cerebral blood flow and metabolism are decreased, often for several days after the seizure, and then return to normal levels. Transient disruption of the blood–brain barrier also occurs, possibly related to the hypertensive surge, but the significance of this is unclear (Andrade & Bolwig, 2014; Bolwig et al., 1977).

Cardiovascular Physiology

Cardiac Rate and Rhythm

ECT results in a marked activation of the autonomic nervous system, and the relative balance of parasympathetic and sympathetic nervous system activity determines the observed cardiovascular effects. Vagal (parasympathetic) tone is increased during and immediately after administration of the electrical stimulus; it may be manifested by bradycardia or even a brief period of asystole. This is generally benign and often resolves spontaneously without intervention (Burd & Kettl, 1998). With development of the seizure, activation of the sympathetic nervous system occurs, resulting in a marked increase in heart rate, blood pressure, and cardiac workload. Peripheral stigmata of sympathetic activation may also be observed; they include piloerection and gooseflesh. The tachycardia and hypertension continue through the ictus and generally end along with the seizure. Shortly after the seizure, there may be a second period of increased vagal tone, which may be manifested by bradycardia and various dysrhythmias, including the appearance of ectopic beats. As the patient awakens from anesthesia, there may be an additional period of increased heart rate and blood pressure as a result of arousal and further sympathetic outflow (Welch & Drop, 1989).

Cardiac Workload

The cardiovascular responses during ECT combine to produce an increase in myocardial oxygen demand and a decrease in coronary artery diastolic filling time. Transient electrocardiographic (ECG) changes in the ST segment and T waves are seen in some patients during and shortly following the procedure, although it is unclear whether these findings are related to myocardial ischemia. A direct effect of brain stimulation on cardiac repolarization has been proposed as an alternative mechanism (Welch & Drop, 1989). No corresponding rise in cardiac enzymes has been found to accompany these ECG changes (Braasch & Demaso, 1980; Dec et al., 1985). An echocardiographic study done during and after ECT treatments found transient regional wall motion abnormalities more often in patients with ST segment/T wave changes in ECG, suggesting a period