Chapter 36: Electroconvulsive Therapy and Other Brain Stimulation Techniques

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Electroconvulsive Therapy

Introduction

Electroconvulsive therapy (ECT) was first used by Ugo Cerletti and Lucio Bini in Italy in 1938 (Cerletti, 1950). Since then, it has been employed continuously for the treatment of a range of conditions, most importantly severe depression. ECT is perhaps the most controversial treatment in psychiatry. It is associated with varying degrees of misinformation, prejudice and stigma (with inaccurate portrayals in popular movies). However, at its core, the value of ECT as one of the principle therapeutic tools to treat severe mental illnesses has remained unchanged for the past 80 years. In recent decades, there have been many systematic refinements to the technique of ECT that retain clinical effectiveness while reducing adverse effects.

Indications

In contemporary practice, the primary indications for ECT (American Psychiatric Association, 2008) are as follows:

- Major Depressive Disorder in severe, melancholic and/or psychotic subtypes (see Chapter 16)
- Schizophrenia particularly catatonic subtype (see Chapter 15)
- Bipolar disorder- severe manic episode, mixed affective episode (see Chapter 17)

- Catatonia due to other causes

The criteria for ECT among these diagnostic conditions are *primary* when there is a need for the rapid resolution of symptoms. This occurs typically in clinical situations of acute or imminent suicide risk or severe self-neglect - not eating and drinking. The criteria for ECT are *secondary* when there is treatment resistance or intolerance with medications. The secondary indications for ECT are as follows:

- Treatment-resistant Major Depressive Disorder.
- Intolerance to antidepressant medication
- Treatment resistant schizophrenia.
- Treatment resistant severe manic episode, mixed affective episode.

Is ECT Effective?

ECT has the disadvantage of being a treatment that has been used for many decades when it comes to assembling the evidence of its effectiveness and safety as treatment practices and research methodology have varied over this period. Nevertheless, there is strong evidence for the effectiveness of ECT in the treatment of major depression when tested against sham ECT - in which participants were anaesthetised but not given ECT – with a standardised effect size (ES) of -0.91, (95% CI -1.27 to -0.54) and against antidepressant pharmacotherapy ES 0.80, (95% CI -1.29 to -0.29) (The UK ECT Review Group, 2003). There is evidence for its effectiveness in bipolar disorder, for both the treatment of the depressive phase of bipolar disorder (Bahji et al., 2019) and the manic phase (Elias et al., 2021). There is also clear evidence for the use of ECT as a treatment for schizophrenia both for the acute phase of the illness (Tharyan and Adams, 2009) and as an augmenting therapy with clozapine for treatment resistant schizophrenia (Lally et al., 2016).

Patient Selection

Conditions for which ECT are indicated are outlined above (Fink, 1993). Patient preference is important when considering ECT. Good prognostic indicators (van Diermen et al., 2018) of a response to a course of ECT include:

- elderly patients with severe delusional depression.
- a past history of response to ECT

Patients with a primary personality disorder or anxiety disorders including obsessive compulsive disorder are unlikely to benefit from ECT.

Contraindications

There are many *relative* contraindications to ECT (American Psychiatric Association, 2008). These carry a greater risk of harm to the patient, which precludes ECT as an immediate option until the risk is addressed. Some of the contraindications are as follows:

- acute myocardial infarction
- acute stroke
- raised intracranial pressure
- cardiac failure
- acute lower respiratory tract infection
- uncontrolled hypertension
- narrow angle glaucoma.

Ideally, management of these medical high-risk conditions should take place before ECT is commenced (Abrams, 2002). As an example, the commencement of ECT should be delayed for 3 months following a myocardial infarction. Similarly, commencement of ECT should be delayed until an acute lower respiratory infection is treated. Implicit in this discussion is the absence of *absolute* contraindications and that the choice of ECT is based on relative risks and benefits.

Mechanism of Action

The mechanisms of action of ECT in treating a myriad of seemingly different and contrasting disorders are complex and multimodal involving not only the plasticity of brain networks but also receptor systems, catecholamine-neurochemistry, brain peptides and genes. While the 'macro effects' can be studied at least partially in human subjects, the molecular effects are mostly limited to studies on rodent brains.

A useful starting point is the clinical observation that eliciting a generalised seizure is a prerequisite for clinical improvement whereas 'sham ECT' with only anaesthesia will not produce a response (Ottosson, 1996). During an ECT treatment an ictal-electroencephalographic (ictal-EEG) typically shows an early phase of high frequency low amplitude activity followed by a mid-seizure phase of spike and slow wave activity. The EEG at the end of the seizure is characterised by post-ictal electrical silence or suppression. The degree of post-ictal suppression (Suppes et al., 1996) and the measurement of 'regularity' of the mid-seizure delta waves (Krystal et al., 1997) are predictive of antidepressant response. These changes to electrical activity of the brain are hypothetically linked to massive surges of GABA inter-neuron activity that has occurred due to electrical brain stimulation.

Positron Emission Tomography studies during ECT have shown that there are distinct increases in regional cerebral blood flow in basal ganglia, amygdala and frontal lobes compared to before ECT (Takano et al., 2007). The inter-ECT brain changes using PET studies indicate a reduction in cerebral metabolic rate of glucose in the frontal lobes and cingulate cortex and such changes are correlated with antidepressant responses (Nobler et al., 2001). More recent structural and functional magnetic resonance imaging studies have also identified a network of structures including the subgenual cingulate cortex, dorsolateral prefrontal cortex, ventromedial prefrontal cortex and hippocampus that are implicated in depression and the expression of emotion (Argyelan et al., 2023).

Electroshock (ECS) on rodent brains have revealed many distinct neurochemical effects on catecholamines (serotonin, norepinephrine and dopamine). The most studied effect is the sensitization of the post synaptic serotonin receptor and a consequent increase in serotonin transmission (Burnet et al., 1999). ECS may enhance post-synaptic noradrenaline neurotransmission and pre-synaptic dopamine neurotransmission and induces gene expression in frontal and hippocampal areas (Altar et al., 2004). The ECS-regulated genes - a notable gene being Brain Derived Neurotrophic Factor (BDNF) - are involved in a wide array of changes that essentially support neuroplastic changes in the brain through neurogenesis and altered neurotransmitter signalling.

ECT- Process and Technique

A course of ECT is composed of ECT sessions 2-3 times per week. The total number of sessions during an acute course can vary from shorter courses of 3-6 sessions to treat mania to 8-16 sessions to treat severe depression. Following an acute course, ECT may be administered less frequently for up to 6 months to prevent a relapse (continuation ECT) and beyond 6 months to prevent a new episode or prophylaxis (maintenance ECT).

ECT is typically administered using a short-acting anaesthesia (thiopentone, propofol) followed by a muscle relaxant (suxamethonium). Oxygenation (100% O_2 positive pressure) is maintained throughout the procedure from the onset of anaesthesia until spontaneous respiration, except during the period of electrical stimulation. Basic standards of ECT mandate routine monitoring of physiological parameters (EEG, ECG, pulse oximetry).

With each treatment (ECT session) an electrical stimulus is given via electrodes placed on the scalp to deliver a prescribed dose of electrical charge to the brain. The charge is delivered in brief pulses. The pulses vary in width (duration)

from 0.3 to 1 millisecond. Pulse widths shorter that 0.5 milliseconds are called 'ultra-brief' and have clinical benefit while minimising memory adverse effects. On contemporary ECT machines the dose of electrical charge delivered is determined by adjusting current (amplitude), width of the individual pulses, frequency of the pulses and the stimulus train length which typically varies from 0.5 to 8 seconds.

There are three commonly used electrode positions to deliver the stimulus dose: 1) bitemporal, 2) unilateral and 3) bifrontal. Bitemporal ECT is where the electrode is placed 1 inch above the midpoint of the line drawn between the tragus and the outer canthus of the eye. Unilateral ECT is where the electrode is placed 1inch lateral (right or left) to the intersection of the line connecting the auditory tragi and the line joining the nasion to the inion. Bifrontal ECT is where the electrode is placed 5cm above the outer canthus of the eye on a bony ridge at the lateral edge of the forehead where the forehead meets the temple.

During the first ECT session, an essential step is the determination of seizure threshold, which is the minimum stimulus dose that is required to produce a generalised seizure of at least 20 seconds. Thereafter, from the second ECT session, the stimulus dose is administered at a higher stimulus intensity, usually a multiple of the seizure threshold. The determination of this multiple varies with the electrode position to deliver the stimulus. The multiple is smaller (Letemendia et al., 1993; Sackeim et al., 2000) (1.5-2.5 times threshold) for bitemporal and bifrontal electrode position and larger (Sackeim et al., 2000) (5-6 times threshold) for a unilateral electrode position. A higher stimulus intensity above the threshold has demonstrated a better clinical efficacy particularly in unilateral ECT (Sackeim et al., 2000).

Preparing the Patient

ECT is a medical procedure. Similar to other medical procedures, patients will need to be prepared for their sessions. Written consent is sought from the patient. In circumstances where ECT is considered essential and the patient does not have the capacity to provide consent, or if they are an involuntary patient, then an order for involuntary treatment with ECT can be made under the appropriate Mental Health Act.

A focused clinical examination is a basic requirement. At a minimum, a bed side clinical examination of the chest, a neurological examination, examination of blood pressure and an examination of the state of the dentition to make sure that there are no loose teeth are required. A chest X ray and an ECG are routinely ordered. Brain imaging is not typically required. Patients are instructed to fast for at least 6 hours before the procedure. Most medications except anti-hypertensive

medications are withheld before the commencement of ECT and given following the completion of the procedure. An anaesthetic review is recommended particularly in patients who are medically high-risk.

Is ECT Safe?

Modern ECT as described above is safe. Death due to ECT is extremely rare (one in 30000 treatments) and is more often related to anaesthetic events (e.g. aspiration) than the ECT stimulus itself. On the other hand, adverse effects such as headache or muscle aches (related to muscle relaxant) are commonly encountered during ECT.

Memory effects are the most clinically significant adverse effect associated with ECT. Memory effects are more pronounced with bitemporal ECT compared to unilateral ECT (Squire, 1977). There are broadly two types of memory disturbances: anterograde amnesia and retrograde amnesia. Anterograde amnesia is almost always seen in varying degrees with ECT. It could be mild in the form of forgetting some of what the doctors discussed with the patient to severe post ECT confusion or delirium. Anterograde amnesia is fully reversible within 2-4 weeks after the completion of the course of ECT (Semkovska and McLoughlin, 2010). Retrograde amnesia is sometimes seen during ECT. Retrograde amnesia is of two types: non-personal memory (memory of public events) and personal or autobiographical memory. It is important to note that ECT produces less personal memory loss compared to non-personal memory loss. Personal memory when affected is usually restricted to memories formed over the past 6 months to 2 years (Lisanby et al., 2000). Unfortunately, personal memory loss can be permanent.

Legal and Ethical Issues

The administration of ECT may sometimes pose difficult ethical dilemmas. They are encountered typically when a patient is incapable of providing consent for the treatment due to their severe mental illness. Some examples are a severely depressed patient may seek (to avoid) ECT so that he or she could die or experience hell, a catatonic patient may not be able to discuss the pros and cons of ECT because he is mute and unresponsive. In such situations, beneficence and non-maleficence direct one to prescribe the most effective form of ECT with the least number of adverse effects. One should not forget the *moral* underpinnings of the treatment that should afford the patient the right to be treated with respect and dignity, right for a second opinion and the right to have ones next of kin treated with consideration.

Many patients voluntarily consent to have ECT when ECT is recommended. The question of 'mental competence' may arise even in such

situations. The prescriber should then ask whether the patients understands the nature of his condition, understand and *appreciate* the nature of ECT and consequences of accepting or refusing ECT (Clark, 1985).

Transcranial Magnetic Stimulation

Introduction

Transcranial magnetic stimulation (TMS) is the induction of small currents in the superficial layers of the brain through applying rapidly alternating magnetic fields to the head. An electromagnetic coil, which emits pulsed magnetic fields is held on the scalp, which induces electrical current in the brain. TMS stimulation paradigms include single pulse TMS where stimulation is one pulse at a time and repetitive pulse TMS (rTMS) where stimulation is repeated at regular intervals ranging from 1-25Hz. In contrast to ECT, TMS delivers a more focal electrical stimulation of the brain. In addition, a course of TMS can be entirely administered as an outpatient procedure in contrast to a typical acute course of ECT.

Indications

TMS is indicated in the treatment of Major Depressive Disorders. There have been trials conducted over a number of decades which have showed a modest effect size comparable to that of antidepressants but less than that of ECT (Bares et al., 2009). The role of TMS in the treatment of schizophrenia is uncertain. While little benefit appears to be gained in using TMS for the treatment of positive symptoms of schizophrenia, in particular auditory hallucinations (Marzouk et al., 2019), more benefit has been seen in the use of TMS for the treatment of negative symptoms (Lorentzen et al., 2022). More experience is needed before the indications of TMS in schizophrenia are clear.

Contraindications

Presence of metal particles in the head, cochlear implants, implanted neural stimulators or medical pumps are absolute contraindications. Risk of seizures although rare should be considered during the administration of TMS.

Patient selection

TMS is generally administered to less severely depressed patients and those who are relatively less medication-resistant in contrast to ECT. Patient choice is also a factor in decisions to commence ECT or TMS.

Mechanism of Action

TMS generates electrical currents oriented perpendicular to the magnetic field called 'eddy currents' in the superficial areas of the cortex. This can trigger functional neural circuits and cause observable behavioural effects. At a single motor neuron level, when stimulus is applied over the motor cortex area of the scalp at sufficient intensity, there is a twitch of contralateral hand muscles. In single-pulse stimulation, the twitch is instantaneous and short lasting. In rTMS stimulation, functional neural circuits are stimulated to produce lasting changes in cortical excitability at the site of the stimulation and increased connectivity and plasticity in the stimulated areas (Jannati et al., 2023). Thus, alteration or correction of focal abnormalities in cortical excitability, posited in psychiatric conditions such as depression, is considered to be a mechanism of action of rTMS.

TMS - Process and Technique in Depression

TMS is given to an awake patient and does not require anaesthesia. It is therefore a non-invasive form of brain stimulation. Screening for metal particles in the head, past seizures or head injuries should occur before commencement of TMS. TMS is administered under medical supervision. At the beginning the resting motor threshold (RMT) is determined by single pulse stimulation of the motor cortex that will produce twitching of the contralateral thumb muscles. Determination of RMT allows the determination of the stimulus intensity generally below the RMT (80-90%) or above the RMT (110-120%). In the treatment of depression, stimulation is given with either left sided high frequency (10Hz) stimulation or right sided low frequency (1Hz) stimulation. A scalp position 5 cm forward from the motor site in the sagittal plane allows for the determination of the coil position over the dorsolateral prefrontal cortex. One session will generally involve multiple trains of stimulation, a typical recommendation is 75 trains in a session (Fitzgerald and Daskalakis, 2013). Each train duration should be limited to 4 seconds if the intensity is at 120% to avoid provoking a seizure. Newer treatment techniques are personalising placement of the coil on the basis of functional and structural brain anatomy.

Clinical recommendation of first line rTMS treatment for depression should involve a course of 4 weeks of rTMS (at least 5 sessions a week) with left sided high frequency stimulation at 110-120% stimulus intensity (Fitzgerald and Daskalakis, 2013).

Is rTMS safe?

rTMS is generally well tolerated. Syncope or seizure can rarely occur during stimulation. During stimulation, ear plugs are recommended to minimise

impact on hearing. There is no evidence to suggest that rTMS administered through standard protocols produces cognitive impairment. This is a major difference with respect to that of ECT.

Other Brain Stimulations

There are several other brain stimulation techniques including transcranial Direct Current Stimulation (tDCS), Vagal Nerve Stimulation (VNS), and Deep Brain Stimulation (DBS). Direct current stimulation using tDCS (applied to the scalp using saline soaked electrodes) is based on polarization of tissue thereby affecting the firing rate of neurons. It is a neuromodulation technique that has experimental value in the treatment of depression. The technique delivers 1-3 mA of DC current to the scalp, is safe and well tolerated. It is also purported to be a technique to enhance cognition although this remains to be proven.

Vagal Nerve Stimulation is the stimulation of the left cervical vagal nerve by a subcutaneously implanted pulse stimulator. This technique has been approved by the Food and Drug Administration (FDA) in the United States for the treatment of treatment-resistant chronic depression although only two randomised controlled trials have been conducted (Bottomley et al., 2020).

Deep Brain Stimulation using implantable electrodes to stimulate specific areas of the brain has promise to treat intractable depression, OCD and Tourette syndrome (Williams and Okun, 2013).

Conclusion and Future Directions

The field of brain stimulation contains established treatments such as ECT and rTMS and emerging treatments such as transcranial Direct Current Stimulation, Vagal Nerve Stimulation and Deep Brain Stimulation. The evolving application of these techniques to a range of psychiatric conditions offers exciting possibilities that have the potential to enhance the biological treatment toolbox for psychiatric conditions. It is likely that even if they are not stand-alone treatments, they have the potential to be integrated with existing pharmacological and psychological approaches to treat chronic and medication-resistant conditions in psychiatry.

Further Reading

Abrams, R. (2002). *Electroconvulsive therapy*. Oxford University Press.

Weiss, A., Hussain, S., Ng, B., Sarma, S., Tiller, J., Waite, S., & Loo, C. (2019). Royal Australian and New Zealand College of Psychiatrists professional practice guidelines for the administration of electroconvulsive therapy. *Australian & New Zealand Journal of Psychiatry*, *53*(7), 609-623.

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References

Abrams R (2002) *Electroconvulsive therapy.* Oxford University Press.

Altar CA, Laeng P, Jurata LW, et al. (2004) Electroconvulsive seizures regulate gene expression of distinct neurotrophic signaling pathways. *Journal of Neuroscience* 24(11): 2667-2677.

American Psychiatric Association (2008) *The practice of electroconvulsive therapy: recommendations for treatment, training, and privileging (A task force report of the American Psychiatric Association).* American Psychiatric Pub.

Argyelan M, Deng Z-D, Ousdal OT, et al. (2023) Electroconvulsive therapy-induced volumetric brain changes converge on a common causal circuit in depression. *Molecular psychiatry*. DOI: 10.1038/s41380-023-02318-2.

Bahji A, Hawken ER, Sepehry AA, et al. (2019) ECT beyond unipolar major depression: systematic review and meta-analysis of electroconvulsive therapy in bipolar depression. *Acta Psychiatrica Scandinavica* 139(3): 214-226.

Bares M, Kopecek M, Novak T, et al. (2009) Low frequency (1-Hz), right prefrontal repetitive transcranial magnetic stimulation (rTMS) compared with venlafaxine ER in the treatment of resistant depression: a double-blind, single-centre, randomized study. *Journal of Affective Disorders* 118(1-3): 94-100.

Bottomley JM, LeReun C, Diamantopoulos A, et al. (2020) Vagus nerve stimulation (VNS) therapy in patients with treatment resistant depression: A systematic review and meta-analysis. *Comprehensive Psychiatry* 98: 152156.

Burnet PW, Sharp T, LeCorre SM, et al. (1999) Expression of 5-HT receptors and the 5-HT transporter in rat brain after electroconvulsive shock. *Neuroscience letters* 277(2): 79-82.

Cerletti U (1950) Old and new information about electroshock. *American Journal of Psychiatry* 107(2): 87-94.

Clark C (1985) Report of the electro-convulsive therapy review committee. Toronto: Ontario Ministry of Health.

Elias A, Thomas N and Sackeim HA (2021) Electroconvulsive Therapy in Mania: A Review of 80 Years of Clinical Experience. *American Journal of Psychiatry* 178(3): 229-239.

Fink M (1993) Who should get ECT? The Clinical Science of Electroconvulsive Therapy. Washington DC: American Psychiatric Press.

Fitzgerald PB and Daskalakis ZJ (2013) *Repetitive transcranial magnetic stimulation treatment for depressive disorders: a practical guide.* Springer Science & Business Media.

Jannati A, Oberman LM, Rotenberg A, et al. (2023) Assessing the mechanisms of brain plasticity by transcranial magnetic stimulation. *Neuropsychopharmacology* 48(1): 191-208.

Krystal AD, Zaidman C, Greenside HS, et al. (1997) The largest Lyapunov exponent of the EEG during ECT seizures as a measure of ECT seizure adequacy. *Electroencephalography and clinical neurophysiology* 103(6): 599-606.

Lally J, Tully J, Robertson D, et al. (2016) Augmentation of clozapine with electroconvulsive therapy in treatment resistant schizophrenia: A systematic review and meta-analysis. *Schizophrenia research* 171: 215-224.

Letemendia F, Delva N, Rodenburg M, et al. (1993) Therapeutic advantage of bifrontal electrode placement in ECT. *Psychological medicine* 23(2): 349-360.

Lisanby SH, Maddox JH, Prudic J, et al. (2000) The effects of electroconvulsive therapy on memory of autobiographical and public events. *Archives of general psychiatry* 57(6): 581-590.

Lorentzen R, Nguyen TD, McGirr A, et al. (2022) The efficacy of transcranial magnetic stimulation (TMS) for negative symptoms in schizophrenia: a systematic review and meta-analysis. *Schizophrenia* 8(1): 35.

Marzouk T, Winkelbeiner S, Azizi H, et al. (2019) Transcranial Magnetic Stimulation for Positive Symptoms in Schizophrenia: A Systematic Review. *Neuropsychobiology* 79(6): 384-396.

Nobler MS, Oquendo MA, Kegeles LS, et al. (2001) Decreased regional brain metabolism after ECT. *American Journal of Psychiatry* 158(2): 305-308.

Ottosson J-O (1996) Experimental studies of the mode of action of electroconvulsive therapy. *The Journal of ECT* 12(3): 172-194.

Sackeim HA, Prudic J, Devanand D, et al. (2000) A prospective, randomized, double-blind comparison of bilateral and right unilateral electroconvulsive therapy at different stimulus intensities. *Archives of general psychiatry* 57(5): 425-434.

Semkovska M and McLoughlin DM (2010) Objective cognitive performance associated with electroconvulsive therapy for depression: a systematic review and meta-analysis. *Biological Psychiatry* 68(6): 568-577.

Squire LR (1977) ECT and memory loss. *The American Journal of Psychiatry* 134(9): 997-1001.

Suppes T, Webb A, Carmody T, et al. (1996) Is postictal electrical silence a predictor of response to electroconvulsive therapy? *Journal of Affective Disorders* 41(1): 55-58.

Takano H, Motohashi N, Uema T, et al. (2007) Changes in regional cerebral blood flow during acute electroconvulsive therapy in patients with depression: positron emission tomographic study. *The British Journal of Psychiatry* 190(1): 63-68.

Tharyan P and Adams CE (2009) Electroconvulsive therapy for schizophrenia. *Cochrane Database of Systematic Reviews* 4.

The UK ECT Review Group (2003) Efficacy and safety of electroconvulsive therapy in depressive disorders: a systematic review and meta-analysis. *Lancet* 361: 799-808.

van Diermen L, van den Ameele S, Kamperman AM, et al. (2018) Prediction of electroconvulsive therapy response and remission in major depression: meta-analysis. *The British Journal of Psychiatry* 212(2): 71-80.

Williams NR and Okun MS (2013) Deep brain stimulation (DBS) at the interface of neurology and psychiatry. *The Journal of clinical investigation* 123(11): 4546-4556.