

Electroconvulsive therapy: current status

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Abstract

Electroconvulsive therapy (ECT) can differ in its application in three ways: electrode placement, frequency of treatments and electrical waveform of the stimulus. Seizure threshold and dosing affects efficacy, speed of clinical response and cognitive deficits. Proposed mechanisms are psychological theories, structural theories, electrophysiology and neurophysiology, biochemical theories and molecular theories. In animal models, there is synaptic plasticity in hippocampus, mossy fibre sprouting, alterations in cytoskeletal structure, promotion of neurogenesis and suppression of apoptosis. Biochemical theories include the monoamine hypothesis, beyond monoamines, vascular endothelial growth factor and brain derived neurotrophic factor. It has generally low risk and one of the safest procedures performed under general anaesthesia. ECT can be given safely to patient with epilepsy; can be given in healed skull and brain trauma, neurologically stable patient after a cerebrovascular accident. Primary use is in rapid definitive response required on medical or psychiatric grounds, risks of alternative treatments outweigh benefits, past history of poor response to psychotropics or good response to ECT and patient preference. ECT is the most effective treatment in depression. Schizophrenia is the second most common diagnostic indication. Some individuals consider ECT to have been a beneficial and lifesaving treatment while others reported feelings of terror, shame and distress. Written, informed consent of the patient is important before ECT is administered. With the development of new techniques for application of ECT its public perception regarding its use has improved in a positive sense.

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Electroconvulsive therapy (ECT), formerly known as electroshock, is a psychiatric treatment in which seizures are electrically induced in anaesthetised patients for therapeutic effect. It was first introduced in 1938 by Italian neuropsychiatrists Ugo Cerletti and Lucio Bini. It was used as a form of treatment in the 1940s. ECT can differ in its application in three ways: electrode placement, frequency of treatments and electrical waveform of the stimulus.

Techniques

The techniques used for convulsive therapy administration are of two types. Direct ECT is given with the absence of muscular relaxation and general anaesthesia. Modified ECT is done by drug induced muscular relaxation and general anaesthesia given by an anaesthetist.

Electrode placement

Bifrontotemporal electrode placement is reliable in efficacy and easiness in use. Adverse effects are short and long term cognitive effects, restrict the dose to a moderately suprathreshold level, delirium may interrupt

the course of therapy, combination of ultrabrief pulse and bifrontotemporal electrode less effective.

Limitations of bifrontal placement are spreading of electrical stimuli and restrict possibilities for localisation of the stimuli, equally effective to bifrontotemporal and right unilateral electrode configuration. Advantages are sparing of cognitive deficits and seizure threshold are likely to be relatively higher.

Right unilateral has wider use, efficacy with adequate dosing 500% above the seizure threshold and better cognitive side effects.

Bilateral electroconvulsive therapy

This is standard form of ECT used most commonly. Each electrode is placed 2.5-4.0 cm above the midpoint on a line joining the tragus of the ear and the lateral canthus of the eye.

Unilateral electroconvulsive therapy

Here the electrodes are placed only on one side of head, usually the non dominant side, in the right handed. One electrode is in right frontotemporal position and the other right of the vertex.

Stimulus waveform

Sine wave with a wide pulse was the original ECT device (8.33 ms [60Hz]). Bipolar rectangular pulse is also known as brief pulse (0.5-2.0 ms). There are less cognitive deficits preserving efficacy. Ultra brief pulse is used in right unilateral ECT (0.3 ms). There is significantly less impairment in acute, subacute and long term cognitive deficits.

Seizure threshold and dosing

It affects efficacy, speed of clinical response and cognitive deficits. Higher the stimuli dose higher the response.

Determining stimulus dose—

1. Empirical determination of seizure threshold (titration): Approximation of the seizure threshold in first session. It is most precise method, by chance variation of threshold at least 50 fold and most safe.
2. Formula based dosing: Age, electrode placement, stimulus pulse width, gender and medications.
3. Fixed dosing: Same dose applied to all patients, easiest technically, maximises the chance of response. Increased cognitive deficits are reported.

Mechanisms of action

It is an active area of hypothesis and research. Proposed mechanisms are psychological theories, structural theories, electrophysiology and neurophysiology, biochemical theories and molecular theories.

Psychological theories: Patient expectation, placebo effects, fear, regression, medical attention and the contribution of retrograde amnesia to clinical response. Sham ECT is ineffective but these have been proved incorrect.

Structural explanation: Recently increased interest. In animal models, there is synaptic plasticity in hippocampus, mossy fibre sprouting, alterations in cytoskeletal structure, promotion of neurogenesis and suppression of apoptosis.

Biochemical theories: The monoamine hypothesis — Down regulates serotonin (5-HT₂) receptors in cortical regions,[1] increase in the function of neuronal system that use dopamine and noradrenaline,[2] increased dopamine (D₂, D₃) function after ECT (psychomotor activity, appetite), increased homovanillic acid in cerebrospinal fluid,[3] increased noradrenaline function (alertness, energy) and contradicts the function in schizophrenia, depression with psychosis.

Beyond monoamines — Concentration of gamma aminobutyric acid (GABA) in the occipital cortex almost

doubled after ECT in patients with major depression.[2] In responder of therapy, concentration of glutamate increased in prefrontal cortex (PFC) area.[4] In the left dorsolateral prefrontal cortex, N-acetyl aspartate levels were significantly decreased in responders to ECT compared with nonresponders.

Vascular endothelial growth factor (VEGF) — It is an angiogenic cytokine which induces vasopermeability and facilitates neurogenesis and synaptic plasticity in the adult brain. Expression studies in animal models have reported that brain VEGF is regulated by electroconvulsive seizures (ECS) which are used in an experimental paradigm similar to clinical ECT.

Brain derived neurotrophic factor — Helps in survival of existing neurons and encourages the growth and differentiation of new neurons mainly in hippocampus. The restoration of ordinary concentrations of this may be one mechanism of the long term effects of antidepressants.[2]

Neuroendocrine mechanism: Mid-hypothalamic regions displaying neuronal activation and endothelial cell proliferation in response to ECS treatment. Paraventricular nucleus and the neurons of the supraoptic nucleus produce the neuropeptide oxytocin (anxiolytic properties) and arginine vasopressin which acts in synergy with the corticotrophin-releasing hormone (CRH). CRH causes release of adrenocorticotrophin that in turn promotes secretion of cortisol.

Neurophysiology: It is known that large increases in global cerebral blood flow (CBF) and cerebral metabolic rate occur along with increased blood brain barrier permeability during a generalised seizure including those electrically induced. The magnitude of reductions in CBF in specific prefrontal regions is related to efficacy of ECT and slow wave activity on electroencephalography (EEG) in responder. Possibility of identifying specific functional networks and associating them with efficacy has improved like PFC, anterior cingulum, subcortical area like right medial thalamus, brain stem and midbrain tegmentum.

Physiology and adverse effects

It has generally low risk and one of the safest procedures performed under general anaesthesia (GA). Risk is similar to other minor medical procedure (1:1000). Risk of death is 1:10000.

Cardiovascular system: Results in parasympathetic outflow during and immediately after electrical stimulus; sinus bradycardia, asystole, supraventricular ectopic beats; arrhythmia (atrial, junctional, nodal), atrial flutter, atrial fibrillation.

Following sympathetic outflow mainly during the electrical stimulation and postictally (adrenal gland releases catecholamines) there is increased heart rate (HR) and blood pressure (BP). Increases peak immediately postictally and drop off within minute to preictal values. In above 50 years, normalisation takes up to one hour for BP and longer for HR.

In patients with cardiac diseases like pulmonary hypertension, subacute myocardial infarction, abdominal aneurysm and congestive heart failure, after stabilisation, 90% patients will be able to complete a course of ECT. It is administered without any complications in heart transplanted patients.

Respiratory system: Along with cardiac disease it is a leading cause of mortality and morbidity. Its effects are mostly associated with anaesthesia procedure rather than physiology. Muscle relaxant can cause cessation of breathing; there may be exaggeration of asthma or chronic obstructive pulmonary disease, increased secretion and aspiration and pulmonary oedema. Pseudocholinesterase deficiency leads to decreased metabolism of succinylcholine.

Central nervous system: Induces hypermetabolic state; increased blood flow, oxygen (O₂) and glucose consumption, blood-brain barrier permeability; least chance of brain injury at maximal output of a brief pulse device.

Prolonged seizure — Greater than three minutes by motor or EEG measurement, risk in adolescent and young adults, in case of greater than 30 minutes there may be structural brain injury even at adequate preoxygenation, more common in presence of proconvulsant medicine like theophylline or lithium or trazodone, greater than one seizure induced in single session, electrolyte imbalance and epilepsy.

ECT can be given safely to patient with epilepsy; can be given in healed skull and brain trauma, neurologically stable patient after a cerebrovascular accident. Patient of dementia with depression are at risk for greater adverse cognitive effects, delirium and confusion.

Dental: Due to direct stimulation of jaw muscle, patient bite down; unstable teeth may be broken and dislodged.

Musculoskeletal: Fracture of long bone and spine are common. In modified they are less common. Precautions should be taken in elderly patient, osteoporotic patient and temporomandibular joint problem. Myalgia is common in first session.

Neurocognitive: It is a major limitation mostly in depressed patients. There are disorientation, decreased anterograde and retrograde memory and errors in visual-

spatial function and word finding. Cognitive affects generally returns to pre ECT baseline or better after completion of course especially in right unilateral ECT. Several factors are involved for it.

Retrograde amnesia — It is most marked for events occurring in the weeks or months before treatment with one study showing that although some people lose memories from years prior to treatment, recovery of such memories was “virtually complete” by seven months post treatment with the only enduring loss being memories in the weeks and months prior to the treatment.

Anterograde amnesia — It is usually limited to the time of treatment itself or shortly afterwards. In the weeks and months following ECT these memory problems gradually improve but some people have persistent losses especially with bilateral ECT.

Treatment factor	Technique Associated with Fewer Adverse Cognitive Effects
Electrode placement	Right unilateral
Stimulus waveform	Brief pulse
Stimulus intensity	Threshold determination; dosage closer to threshold
Number of treatments	Fewest necessary to achieve remission or plateau of target symptoms
Frequency of treatment sessions	Less frequent e.g. twice weekly for acute treatment
Number of seizures per session	One
Simultaneous use of psychotropics	Discontinue lithium, sedatives; reduce dose of neuroleptics
Dosage of anaesthetic medications	Adjust dosage to produce light anaesthesia

Other adverse effects

Post ictal agitation: Associated with bilateral electrode placement, lower anaesthetic dose, concomitant use of medications and anxiety or pre ECT agitation. Short acting benzodiazepine, ECT anaesthetics and restraints are helpful.

Headache: Up to 50% cases; unknown etiology; may be throbbing, migraineous quality. Nonsteroidal antiinflammatory drug and tryptans are helpful.

Nausea: Maybe associated with headache or alone. Ondansetron are helpful.

Indications of ECT

Experts disagree on whether ECT is an appropriate first line treatment or if it should be reserved for patients who have not responded to other interventions such as medication and psychotherapy. The decision to use ECT depends on severity and chronicity of the depression, alternative treatments would be effective, patient's preference and capacity to consent, weighing of the risks and benefits.

Diagnoses for which ECT may be indicated

Major diagnostic indications: Major depression, unipolar and bipolar and psychotic depression in particular; mania including mixed episodes; schizophrenia with acute exacerbation, catatonic subtype particularly and schizoaffective disorder; other diagnostic indications include Parkinson's disease, neuroleptic malignant syndrome and intractable seizure disorder.

Clinical indications: Primary use – Rapid definitive response required on medical or psychiatric grounds, risks of alternative treatments outweigh benefits, past history of poor response to psychotropics or good response to ECT and patient preference.

Secondary use – Failure to respond to pharmacotherapy in the current episode, intolerance of pharmacotherapy in the current episode and rapid definitive response necessitated by deterioration of patient's condition.

ECT in depressed patients

First line treatment (American Psychiatric Association [APA] 2001) in high suicidal risk, rapid definitive response is needed, severe psychomotor retardation, problems of eating and drinking, physical deterioration, treatment resistant depression and responded in previous episode and pregnant women.

Second line in treatment resistant depression, severe side effects from medication limiting effective treatment, medical and psychiatric condition deteriorated to an extent that raises concern. National Institute of Clinical Excellence (NICE) guidelines recommend the use of ECT as a maintenance therapy in depressive illness as “the long-term benefits and risks had not been clearly established.” Maintenance ECT is also an option.

ECT is the most effective treatment. It decreased chronicity, morbidity and mortality. ECT is effective for all type of depression, unipolar, bipolar, melancholia and psychotic depression. It is used safely in all population including at special risk: elderly, medically ill, pregnant women and adolescents. In elderly patients, it is safe and effective. Special attention should be given to underlying physical illnesses and anaesthesia risk.

Regular assessment of cognition function is to be carried out.

Pregnant women – Very few complications from the use of ECT in all trimester. Only anticholinergic should be in use. Following attention should be given at the time of administration: obstetric consultation before referral, foetal heart monitoring before and after and case by case consideration of intubation because risk of regurgitation.

Children and adolescents – Used with caution. First line use is very rare. In less than 16 years two independent opinion should be taken and in 16-17 years one psychiatrist's opinion. Stop all nonessential medicine to reduce prolonged seizure.

ECT in mania

It was first line treatment before lithium, anticonvulsants and atypical antipsychotics were introduced. In modern era its use is reserved for patients who are resistant or intolerant to usual medications including mixed states or rapid cycling or with severe symptomatology like manic delirium. It is assigned to second line status (APA, World Federation of Societies of Biological Psychiatry, Canadian Network for Mood and Anxiety Treatments). As per NICE guideline it is third line for acute episodes. APA recommends its use as maintenance treatment for bipolar disorder. Response rate is 75-80%.

An eight week study found ECT treated patients improved more than those treated with lithium carbonate.[5] In treatment resistant patients, it is found that 59% were responders compared with patients receiving pharmacotherapy. No difference in outcome in unilateral versus bilateral ECT.[6] Sikdar *et al.*[7] found that combination of ECT and moderate dose of neuroleptic is extremely effective in aborting an acute episode of mania.

ECT in schizophrenia

It is the second most common diagnostic indication. Atypical antipsychotics remain the first choice. ECT was equivalent to neuroleptics in short term efficacy. In long term follow up, patients who received ECT had superior outcomes. Combination treatment showed good outcome. In treatment of schizophrenia ECT is reserved for patients who are nonresponsive or intolerant to clozapine. There is inconsistent response to support the presence of affective symptoms improves better. ECT also responds in extrapyramidal syndrome induced by neuroleptics. ECT may protect against the development of tardive dyskinesia in neuroleptic treated patients.

Other diagnostic indications

Psychiatric: Acute response in obsessive-compulsive disorder but patients soon relapsed and ECT is not recommended for this disorder. No study of the effects of ECT on panic disorder. Dysthymia is more difficult to ameliorate with ECT even in the setting of comorbid major depression. ECT is not considered to be a treatment for any personality disorder.

Neurological: Disorder comorbid with psychiatric disorder like resistant catatonia. In neuroleptic syndrome, ECT has the advantage of being a treatment for the comorbid psychiatric syndrome for which neuroleptic must be discontinued. In Parkinson's disease, motor symptoms of rigidity and bradykinesia may respond. Comorbid depression is also improved. In epilepsy, no demonstrated superiority is observed over anticonvulsants. There are some case reports about the use of ECT in Tourette's syndrome, post stroke depression, mood disorder with dementia, mental retardation, head trauma and brain tumour.

Public opinion

The APA ECT taskforce guidelines report findings that most patients find ECT no worse than going to the dentist and many found it less stressful than the dentist. Some individuals consider ECT to have been a beneficial and lifesaving treatment while others reported feelings of terror, shame and distress. Curtis Hartmann, a lawyer in western Massachusetts, stated: "ECT, a treatment of last resort for severe, debilitating depression, is all that has ever worked for me. I awaken about 20 minutes later and although I am still groggy with anaesthesia, much of the hellish depression is gone. It is a disease that for me, literally steals me from myself—a disease that executes me and then forces me to stand and look down at my corpse. Thankfully ECT has kept my monster at bay, my hope intact." "Well, what is the sense of ruining my head and erasing my memory which is my capital and putting me out of business? It was a brilliant cure but we lost the patient."

Ethical issues

The Union Health Ministry of India has decided in the Mental Health Care Bill of 2010 that they will scrap direct ECT. The Health Ministry recommended a ban on the whole procedure. Written, informed consent of the patient is important before ECT is administered. The World Health Organization, in its 2005 publication "Human Rights and Legislation WHO Resource Book on Mental Health," specifically states, "ECT should be administered only after obtaining informed consent."

Summary

With the development of new techniques for application of ECT like placements of electrodes, waveforms and dosing, anaesthetic agent, radioimaging, new amendment and knowledge about mechanism of action, adverse effects has reduced and its public perception regarding its use has improved in a positive sense.

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