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The history of electroconvulsive therapy: From a controversial past to a merited present and towards an essential future

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Summary

Electroconvulsive therapy (ECT) is one of the oldest biological treatments in psychiatry.
ECT appeared in Europe in the 1930s. During the past century, it underwent several advances, setbacks, and successive adaptations. Despite its stigmatizing media coverage, it maintains its usefulness in current psychiatric clinical practice.
This paper aims to provide a summary of the history of ECT, its present state, and its future. It covers the long history of ECT, the requirements for informed consent, most accepted techniques, clinical indications, and required staff training. Additionally, we discuss the uncertain future of ECT in the face of new therapeutic options in modern psychiatry.

Keywords: *electroconvulsive therapy, history, informed consent, training, ketamine*

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INTRODUCTION

Electroconvulsive therapy (ECT) is one of the oldest and most controversial biological treatments in psychiatry (Mihaljević-Peleš et al., 2018). Despite its public and professional stigmatization, it survives in the present day (Kropotov, 2016).

ECT has been validated to be a highly effective safe, and even lifesaving for severe and resistant psychiatric conditions such as depression, catatonia, psychosis, and mania (Fink, 2009). ECT must not be considered only as a last resort treatment and it should be offered as viable option to patients at all stages of their illness process (American Psychiatric Association, 2001; Coentre et al., 2009; Taylor, 2007).

There are no absolute contraindications and it is usually safe for patients with comorbid medical conditions and pregnancy, thanks to modern anesthesia techniques and medications (Fink, 2011).

This paper summarizes the history of ECT, from its revolutionary appearance in Europe in the 1930s when electric current was discovered as a possible treatment for many medical conditions. We also review its diffusion throughout the world, with successive modifications of the technique and indications over time.

SUBJECT AND METHODS

A literature search was conducted *on the website* PubMed using appropriate keywords on the topic (history of electroconvulsive therapy). The cross-references from the obtained articles were also reviewed to get more relevant articles. Inputs were also taken from relevant books: Kaplan & Sadock's Comprehensive Textbook of Psychiatry (10th edition, 2017) and American Psychiatric Association (APA) Task Force on Electroconvulsive Therapy (2nd edition, 2001).

THE PAST

Electric current as treatment

The Romans were the first people to report the effects of the electric current on the nervous system. In the year 47 AD a Roman physician, Claudius Scribonius Largus, treated headaches using electrical discharges produced by torpedo electric ray (*Torpedo nobiliana*) for headache and paralysis (Bolwig & Fink, 2009). The same method was expanded to the treatment of hemorrhoids, gout, depression, and epilepsy, among other conditions (Sharifi, 2013).

For centuries, electricity was considered a mysterious force that defied understanding. Finally, in 1746 van Musschenbroek developed an experimental tool that could store an electrical charge and release it on demand. By 1800, around half a century later, the bimetallic piles of Alessandro Volta in Italy inspired a wider interest in the medical use of electricity (Bolwig & Fink, 2009).

Benjamin Franklin (1706-1790), one of the leaders of the American Revolution of 1776, contributed to the development of neurosciences by promoting experiments on the use of electricity as a possible cure for paralysis, hysteria, and melancholy (Finger, 2006).

Throughout the 19th century, electrotherapy (medical use of electricity regardless of its convulsive property) was the treatment of choice for various mental illnesses, however, with very limited effectiveness (Gilman, 2008).

The Beginnings of electroconvulsive therapy

By the beginning of the 20th century, several modalities of biological treatment for mental illnesses appeared, such as malariotherapy, narcotherapy, and insulin coma (Wright, 1990).

At the same time, the potential therapeutic effect of seizure activity on mental illness was verified. The first reports date back to the 16th century, when Paracelsus (1493-1541), considered by some to be the founder of modern pharmacology and the forerunner of ECT, administered camphor oil into the oral cavity to induce seizures and treat psychiatric illnesses, paving the way for chemical convulsive therapy (Boland et al., 2021).

In 1934, Ladislas Meduna (1896-1964), a Hungarian neuropsychiatrist, guided by his theory of biological antagonism between epilepsy and schizophrenia (Swartz, 2009; Fink, 2004), successfully treated one patient in a catatonic stupor and five patients with schizophrenia, through chemically induced seizures by intramuscular injections of camphor oil (Faedda et al., 2010). Later, he started using metrazol, which produced an immediate seizure, unlike camphor oil, whose effect took several minutes.

Discovery of electroconvulsive therapy

The beginning of ECT application in the treatment of mental illnesses is mainly attributed to the Italian doctor Ugo Cerletti (1877-1963) (Fink, 2001; Shorter & Healy, 2007). In 1935, he was appointed director of the Department of Neurological and Mental Diseases at Sapienza, in Rome, where he first used the pharmacological induction of seizures with metrazol for the treatment of his patients with schizophrenia.

Cerletti then postulated that electricity could replace metrazol in inducing seizures and started his experiments on animals. He began to place an electrode in the animal's mouth and another in the anus (Fink, 2004), however, it caused the death of many animals (Wright, 1990; Fink, 2004) due to cardiac arrhythmias. Lucio Bini, who collaborated with Cerletti, suggested bitemporal placement of electrodes (Wright, 1990; Endler, 1988), and, since the adoption of this method, animal deaths ceased to occur (Endler, 1988). In addition, Cerletti and Bini established the convulsive dose and the fatal dose of electric current by experimenting with animals (Endler, 1988).

In April 1938, a patient with schizophrenia, Enrico X, underwent the first session of ECT and after the 11th session he was discharged with no symptoms (Aruta, 2011). On May 28 of 1938, Cerletti and Bini made a scientific communication on the success of this discovery, at the Royal Medical Academy in Rome (Metastasio & Dodwell, 2013). In the next year, the prototype ECT device was patented and marketed all over the world (Endler, 1988).

Advances and retreats in the diffusion of electroconvulsive therapy

In 1940's there was an expansion in the use of ECT, mainly due to the increase of psychiatric hospital admissions. In this context, there was an expansion in the use of ECT. After its introduction in England and the USA (Endler, 1988), its use spread between 1940 and 1950 in several European countries, such as Germany, France, and Austria (Shorter & Healy, 2007).

In the 1950s, ECT had become a standard treatment for hospitalized patients with depression, and was widely accepted in European psychiatry, after the United States military used it extensively during World War II. However, by the 1960s, ECT suddenly disappeared from psychiatric training due to the growing power of the pharmaceutical industry, psychoanalysis, and antipsychiatry (Mihaljević-Peleš et al., 2018).

After the war, political and ideological factors played a significant role in psychiatry. In 1952, the Soviet Union issued a directive that restricted convulsive therapy due to its Western origin, which effectively banned the use of ECT for over a decade, influencing the use of ECT in some communist countries. In addition, from 1950 to 1989, Central-Eastern Europe faced significant obstacles in accessing scientific information from the Western world due to Cold War restrictions which shaped the use of ECT in these countries (Gazdac et al., 2013).

Due to the emergence of several antidepressant drugs developed by the pharmaceutical industry from the 1950s onwards and the stigma that was progressively associated with ECT, which was enhanced by the film *One Flew Over the Cuckoo's Nest* (1975) (Mihaljević-Peleš et al., 2018), there was an accentuated decline in the use of this technique, between 1960 and 1980 (Pandurangi et al., 2011).

From 1980 onwards, several efforts were made to ensure standardization of the ECT technique, with the publication of recommendations for its application and commitment to the training of physicians, by various academic associations in the United States, England, and Scandinavia, among other countries (Coentre et al., 2009). In 1978, the American Psychiatric Association (APA) published recommendations for applying ECT (American Psychiatric Association, 1978).

ECT use has decreased worldwide since the 1950s development of psychopharmacology. (Gazdag et al., 2013) but it is still widely used for specific indications, remaining one of the most effective treatments in psychiatry (Gazdag et al., 2009). ECT has come to be considered a therapeutic option for treatment-resistant conditions and pathologies that require life-saving interventions such as starvation, catatonia, and severe suicidal ideation (Fink, 2004).

The utilization rate, indications, and technical parameters of ECT practice throughout the world are heterogeneous and the exact patterns of use are difficult to determine due to lack of data (Gazdag et al., 2017). Over the past decades, the use of ECT across the world has varied. While some countries (such as Germany, Netherlands, Poland, and Lithuania) have reported an increase in the use of ECT, others have reported a significant decrease (United Kingdom, Hungary, Latvia, United States and Australia). On the other hand, some countries have reported a high and steady use (India, Slovakia, and Estonia), and others a low and steady use (Bulgaria, Serbia and Croatia) (Gazdag et al., 2013). The use of ECT was banned in Slovenia in 1994 (Gazdag et al., 2017).

Technical evolution of electroconvulsive therapy

Throughout its evolutionary process, ECT underwent several technical improvements, from aspects related to the anesthetic technique to aspects related to ECT itself (Fink, 2001; Fink, 2004).

Concerning the anesthetic technique, the advent of muscle relaxation stands out (first with curare and later with succinylcholine in 1951), but there were other improvements, such as the use of short-acting anesthesia and pre-oxygenation to lower the convulsive threshold (Boland et al,. 2021). In addition, the seizure and post-procedure complications became thoroughly monitored (American Psychiatric Association, 2001).

Despite the potential benefits of ECT, some side effects were observed, and cognitive effects were quite prominent which led to the exploration of the best stimulus and placement of electrodes. One of the most important advances in the technique has been the modification of the electrical stimulus from sinusoidal current (8ms) to brief (0.5-1.5 ms), maintaining clinical effect and resulting in less cognitive impairment (Sackeim et al., 2008). Goldman introduced unilateral ECT in 1949 (Mihaljević-Peleš et al., 2018). A rigorous original study conducted by Sackeim and colleagues demonstrated a valuable advantage for ultra-brief pulse right unilateral (RUL) ECT in cognitive outcomes and no significant difference in efficacy compared with brief pulse RUL ECT. Nowadays the application of the stimulus on the non-dominant hemisphere is considered consensual since it proved best regarding the lesser impact on post-procedure retrograde memory (Sackeim et al,. 2008; Loo et al., 2012).

THE PRESENT

Clinical indications for electroconvulsive therapy

The indications for ECT have been established through randomized, controlled trials that compared ECT with placebo interventions or alternate treatments, as well as through reports of uncontrolled clinical series, case studies, and surveys of expert opinion.

The decision to recommend the use of ECT for a specific patient involves a risk/benefit analysis. This includes the patient's diagnosis and severity of illness, treatment history, speed of action and efficacy of ECT, medical risks, and any anticipated adverse effects (American Psychiatric Association, 2001).

Although primarily used to treat severe and treatment-resistant depression, ECT may benefit patients with schizophrenia (Ravanić et al., 2009; Sagud, 2022), schizoaffective disorder, catatonia, neuroleptic malignant syndrome, and bipolar disorder (Salik & Marwaha, 2022).

The main major diagnostic indications for ECT are:

- major depression: unipolar major depression (single and recurrent episode) and bipolar major depression;
- mania: manic episode in bipolar disorder and mixed episode in bipolar disorder;

- schizophrenia: psychotic exacerbations, catatonic type of schizophrenia, and when there is a history of a favorable response to ECT;
- related psychotic disorders: schizophreniform disorder and schizoaffective disorder. ECT may also be useful in patients with psychotic disorders not otherwise specified when the clinical features are similar to those of other major diagnostic indications.

While electroconvulsive therapy (ECT) has shown to be effective in treating certain mental health conditions, its efficacy for other diagnostic indications remains unclear. In cases where there is only partial consensus supporting its use, ECT should only be performed after standard treatment alternatives have been considered as a primary intervention. However, the presence of these disorders should not prevent its use in patients with a clear concurrent major diagnostic indication for ECT.

The other diagnostic indications include mental disorders resulting from medical conditions (such as severe secondary affective and psychotic conditions, and catatonic states that display symptoms similar to those of primary psychiatric diagnoses), delirium due to various causes (including toxic and metabolic), and other medical disorders (such as Parkinson's disease, neuroleptic malignant syndrome, and intractable seizure disorder). There is also evidence that neuroleptic-induced extrapyramidal symptoms and parkinsonism may improve with ECT.

The primary use of ECT includes situations in which ECT may be used before a trial of psychotropic medication, such as:

- need for a rapid, definitive response because of the severity of a psychiatric or medical condition;
- when the risks of pharmacotherapy outweigh the risks of ECT (for example, in pregnancy and patients with Parkison's disease, in which some medications are contraindicated);
- history of poor medication response or good ECT response in one or more previous episodes of illness;
- the patient's preference.

The secondary use of ECT includes:

- treatment resistance;
- intolerance to or adverse effects with pharmacotherapy (in Parkinson's disease;
- rapid need for definitive response due to deterioration of psychiatric or medical condition (American Psychiatric Association, 2001).

Informed consent

When considering electroconvulsive therapy (ECT) as a treatment option, patients must be fully informed about several crucial aspects. This is formalized by signing an informed consent document which, according to guidelines, must include information regarding the reason for ECT recommendation, alternative treatments, the procedure itself, risks, benefits, number of sessions, behavioral restrictions, clinical staff availability, and the right the patient has to withdraw from the treatment.

When dealing with patients with no capacity to consent, healthcare providers should adhere to local laws. Whenever a delay in treatment could result in severe impairment or death, ECT may be administered without signing an informed consent document. Previously expressed positions by the patient when in a state of presumed capacity, as well as the opinions of significant others (such as family) must also be considered (American Psychiatric Association, 2001).

The technique

ECT generally is considered a low-risk procedure, but many patients referred for therapy present with significant medical comorbidities with the potential to complicate anesthetic management. As with any patient who is to receive an anesthetic, a complete and thorough pre-anesthetic evaluation is mandated (Bryson et al., 2017).

ECT often is administered in off-site locations, outside of the traditional operating room setting. This may be a dedicated suite for ECT, an area used for multiple different procedures, or even the postanesthesia care unit. Heart rate, blood pressure, electrocardiogram, capnography, and temperature monitoring should be readily available. In addition, equipment to emergently secure the airway must be immediately available. Patients with severe debilitation, including substantial medical or psychiatric illness, may begin in an inpatient setting and move to an outpatient setting as needed (American Psychiatric Association, 2001).

Several well-designed trials, reviews, and meta-analyses have been published comparing different electrode placements – right unilateral (RUL), bitemporal (BT), and bifrontal (BF) (Sienart et al., 2018). Each standard electrode placement in contemporary ECT practice, when given with appropriate electrical stimulus dosing, is a highly effective antidepressant technique. Right unilateral at six times the seizure threshold and bifrontal and bitemporal at one and a half times the seizure threshold are all highly efficacious electrode placements for use in ECT

for the treatment of major depression. Because bitemporal placement results in more rapid depressive symptom reduction, it is the preferred electrode placement when the clinical situation requires urgent improvement (APA Task Force on ECT. 2nd edition. 2001). Right unilateral ECT is preferential since it minimizes retrograde amnesia (Kellner et al., 2010).

The ECT stimulus is either a brief pulse (0.5 to 2.0 milliseconds) or an ultra-brief pulse (less than 0.5 milliseconds) waveform, which is more tolerable (Sienart et al., 2018).

Following initial dose calculation during the primary ECT session, the dose at subsequent ECT sessions for bilateral ECT is 1.5 to 2 times the seizure threshold, and for right unilateral is six times the seizure threshold. During ECT treatment, the seizure threshold commonly increases as the patient develops tolerance (Salik & Marwaha, 2022).

The presence of an anesthesiologist during ECT enables a safe and pain-free experience for the patient with continuous monitoring of vital signs, including blood oxygen saturation and ECG (Bryson et al., 2017).

The patient is often hyperventilated via a bag valve mask with 100% oxygen before the procedure to induce cerebral vasoconstriction via hypocarbia, increasing seizure intensity (Salik & Marwaha, 2022). This technique is most important in patients with a greater seizure threshold or a history of inadequate seizure length (Bryson et al., 2017).

Methohexital is the preferred choice for anesthesia induction due to its favorable pharmacokinetics, moderate anticonvulsant properties and safety. Propofol, a potent anticonvulsant, is chosen for patients at risk of prolonged seizures but may not be ideal for those with a high seizure threshold or a history of short seizures (APA, 2001; Vaidya et al., 2012). Etomidate is a reasonable alternative for patients prone to a significant hypotensive response to propofol or methohexital, though it may lead to adrenal suppression (Archambault et al., 2012; Bryson et al., 2017). Ketamine is a suitable alternative for anesthetic induction in ECT, particularly when seeking seizure enhancement and rapid therapeutic response (Bryson et al., 2017).

Skeletal muscle relaxation during ECT minimizes the motor seizure component, avoiding musculoskeletal injury. The depolarizing neuromuscular relaxant succinylcholine is the most commonly used agent. However, nondepolarizing neuromuscular relaxants are preferred in cases of neuromuscular disease or injury, burn injury, pseudocholinesterase deficiency, severe osteoporosis, severe muscular rigidity, or personal or family history of malignant hyperthermia (Salik & Marwaha, 2022).

The ECT stimulus results in direct stimulation of the pterygoid, masseter, and temporalis muscles, and muscle relaxants do not prevent the contraction of these muscles, requiring the placement of a bite block for lingual and tooth protection.

An electromyography (EMG) sensor is placed on the right foot to measure the motor component of seizure activity. As an alternative to EMG, a blood pressure cuff is inflated 20% above systolic blood pressure on the patient's ankle before administering the paralytic to prevent it from entering the foot, allowing a visual monitor of seizure activity with measurement of tonic-clonic contractions (Bryson et al., 2017).

Although most therapeutic ECT seizures last from 15 to 70 seconds, electrical brain activity recording via electroencephalogram lasts about 25 percent longer than motor seizures and is thoroughly analyzed after the procedure (Mayur et al., 1999).

Seizures lasting less than 15 seconds may not be clinically effective, requiring a follow-up with a short period of hyperventilation and restimulation with a higher electrical current. On the other hand, if a seizure lasts more than two minutes, to suppress seizure activity and avoid neurologic injury, propofol or methohexital (at half dose) or benzodiazepines may be administered (Salik & Marwaha, 2022).

Training in electroconvulsive therapy

Some characteristics such as gender, training, and clinical orientation seem to affect psychiatrists' use of ECT, making its use highly variable. Improving the quality and consistency of ECT training in medical school, residency, postdoctoral fellowships, and psychiatry board examinations would lead to the development of a broader clinical consensus regarding ECT and could narrow variability in its use (Hermann et al., 1998).

Throughout the years major technical advances directed toward maximizing ECT efficacy and minimizing its risks and discomfort have occurred in instrumentation, stimulus dosing, and electrode placement as well as anaesthetic recommendations. With the growing complexity of ECT practice, however, in the late 80's it was time for the APA to examine training practices in medical schools, psychiatric residency, and continuing medical education programs and the criteria for certification in psychiatry (Fink, 1998).

Nowadays board certification in psychiatry requires no evidence of experience or practical knowledge of convulsive therapy making it unwise to automatically give certified psychiatrists privileges in ECT (Fink & Sackeim, 1986).

To administer ECT safely and effectively the treatment team must receive adequate training. This team is

composed of a properly qualified ECT psychiatrist, anaesthesiologist, and nurses or assistants. The responsibilities of such staff must be consistent with their training and clinical competence. For each position, the pool of available staff members should be kept as small as possible to maximize continuity of care and ensure that all elements have sufficient ongoing experience to maintain proficiency in ECT. Psychiatric, anaesthesiology, and nursing trainees with the proper training may assist in the performance of ECT-related duties but only under the supervision of credentialed staff (American Psychiatric Association, 2001).

No country in Europe has centrally organized ECT training. Theoretical ECT principles are taught in every residency program, but practical experience is not provided. Continuing Medical Education (CME) courses are a way of distributing ECT knowledge in some countries, such as Hungary and Serbia (Gazdag, 2017).

THE FUTURE

Psychiatry has made significant progress over time. Despite being one of the oldest biological treatments, ECT is still used, often in combination with medication, to treat refractory psychiatric conditions such as depression (Bow, 2018) and schizophrenia. However, the mechanism behind ECT's efficacy in general and in treatment-resistant conditions remains unclear.

Identifying markers of treatment-resistant conditions and predictors of ECT response is a priority to distinguish patients who will benefit from it the most and early on (Sagud, 2022). Predictive clinical factors include suicidal ideation (when using bilateral electrode placement), psychotic depression, and treatment resistance. However, depression severity and melancholia have conflicting data. Although biomarkers such as genetic, epigenetic, and proteomic factors, as well as laboratory and physiological markers, provide exciting possibilities for ECT precision, larger-scale validation studies are needed to ensure their clinical utility. Neuroimaging with machine learning shows promise for the future of precision psychiatry (Yao, 2019). Further randomized studies with larger sample sizes and double-blind designs are necessary to evaluate ECT techniques and drug administration (Ravanić, 2009).

New biological treatments such as Deep Brain Stimulation and Transcranial Magnetic Stimulation, as well as the potential benefits of hallucinogens like ketamine, offer possible alternatives to ECT in treating resistant psychiatric conditions.

Ketamine, an NMDA receptor antagonist, may be a promising antidepressant, especially for patients with suicidal thoughts/behaviors. Esketamine was approved for treating resistant depression in 2019, with well-defined indications, contraindications, and treatment regimens (Mihaljević et al., 2020). Ketamine has been used to enhance ECT-induced seizures and minimize cognitive side effects (Ostroff et al., 2005). It targets glutamate neurotransmission, which is impaired in treatment-resistant depression, leading to increased glutamic acid concentration, AMPA (alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid) receptor binding, and activation of the BDNF (brain-derived neurotrophic factor) signaling pathway. This promotes neurogenesis and neuroplasticity, normalizes emotion-regulating brain centers (such as the amygdala and parahippocampal gyrus) in depressed patients and also reverses prefrontal cortex neural atrophy (Kasmarek et al., 2021).

Taking this into account some studies have explored ketamine augmentation of ECT in treatment-resistant depression. The literature is inconclusive due to inconsistent findings across studies with varying methods and domains (Anderson, 2017)..

CONCLUSIONS

ECT evolved significantly since its creation and has survived to this day. It is a rapidly and highly effective treatment option that can be lifesaving. However, there is still some resistance to its use, due to a lack of knowledge from the public and some uninformed health professionals, boosted by the stigmatizing perceptions and the lack of a broad consensus among psychiatrists. ECT should be available and offered to all patients with clinical indications for its use.

A comprehensive educational and training experience in ECT should be provided to all psychiatry and anesthesiology residents, and medical and nursing schools students. Moreover, elective opportunities for advanced training in ECT should be available to convey the knowledge and skills for providing ECT safely and effectively.

More studies are needed to explore the mechanisms of action, efficacy, and safety of ECT. In addition, comparison studies between ECT and other treatment options (such as TMS and esketamine) in resistant depression are required. Further research is also required to identify markers of treatment-resistant conditions and predictors of response to currently available treatments to design more robust treatment plans, tailored for individual patients.

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