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Efficacy and Controversies Surrounding Electroconvulsive Therapy for Treatment-Resistant Depression: A Literature Review

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ABSTRACT

Electroconvulsive therapy (ECT) remains a vital treatment option for individuals with treatment-resistant depression (TRD). Despite its historical stigma, controversy, and limited accessibility, ECT has been demonstrated to be beneficial and effective in severe cases of depressive disorders, where medication fails to produce results. It has been utilized since 1938 as a therapeutic technique for various psychiatric disorders, often used as an alternative to chemically induced seizures. The public's perspectives on ECT hold significance as they can shape attitudes toward patients undergoing this therapy and the discrimination associated with receiving ECT. Additionally, the perspectives of patients who may benefit from ECT and those who are already undergoing treatment are crucial as they can influence treatment decisions and consent processes. This literature review examines the efficacy and controversies surrounding ECT in the management of TRD. Studies assessing the effectiveness of ECT in TRD, along with associated adverse effects and ethical considerations, are reviewed. Additionally, the role of ECT in contemporary psychiatric practice and its comparison with alternative treatments for TRD are discussed. The review highlights the complex interplay between clinical efficacy, safety, patient preferences, and societal perceptions in shaping the utilization of ECT in the treatment of TRD.

KEYWORDS: Electroconvulsive Therapy; Depressive Disorder, Treatment-Resistant; Mental Health; Mental Disorders

DEFINITIONS OF ABBREVIATIONS

ECT - Electroconvulsive Therapy

TRD - Treatment-Resistant Depression

MDD - Major Depressive Disorder

HDRS - The Hamilton Depression Rating Scale

MADRS - Montgomery-Asberg Depression Rating Scale

CGI - Clinical Global Impressions Scale

BT - Bitemporal

BF - Bifrontal

RUL - Right Unilateral

tDCS - Transcranial Direct Current Stimulation

DLPFC - Dorsolateral Prefrontal Cortex

rTMS - Repetitive Transcranial Magnetic Stimulation

DBS - Deep Brain Stimulation

C-ECT - Continuation Electroconvulsive Therapy

INTRODUCTION

Depressive disorders often manifest as chronic, recurrent, and debilitating conditions, significantly impairing the functioning and quality of life of affected individuals.¹ While antidepressant treatment is highly effective for many patients, a significant portion either do not respond adequately to antidepressants or cannot tolerate the side effects of the medications.² Individuals experiencing depressive disorders who do not improve with initial treatment trials are often labeled as having treatment-resistant depression (TRD). While the criteria for treatment resistance have varied over time, recent research often defines it as the lack of remission after undergoing two or more adequate antidepressant treatment trials.^{3,4}

Electroconvulsive therapy (ECT) stands as an efficacious treatment for depression⁵ and is recommended for patients with treatment-resistant depression (TRD) according to guidelines from several countries.^{6,7} ECT as compared to other treatments is found to be the most efficacious for symptom remission of major depressive disorder (MDD).⁸

Electroconvulsive therapy (ECT) is a medical procedure conducted under general anesthesia, using electrical currents to induce brief seizures in the brain. Since its inception in 1938, ECT has primarily been utilized for treating schizophrenia, with its development pioneered by Cerletti and Bini.⁹ Numerous studies have explored the comparison between ECT and alternative treatments concerning response efficacy, typically defined as a minimum 50% reduction in scores from baseline. This evaluation was conducted using assessment tools such as the Hamilton Depression Rating Scale (HDRS), Montgomery-Asberg Depression Scale

(MADRS), or Clinical Global Impression (CGI) Scale, alongside an examination of total dropout rates at the conclusion of the included studies.¹⁰

ECT involves the application of small electric currents through the brain (up to 800 mA), intentionally triggering a short seizure. This process appears to induce changes in brain chemistry, swiftly alleviating symptoms of certain mental health conditions, particularly TRD and bipolar disorder.¹¹ Due to its proven effectiveness, often as the last possible effective therapy for severely ill individuals, the medical community should make every effort to rid electroconvulsive therapy of its negative reputation among the public and make it more accessible.

CONTROVERSIES AND WIDESPREAD MISINFORMATION

Despite its unmatched track record of safety and effectiveness, ECT remains a subject of controversy beyond psychiatric circles, primarily due to worries regarding cognitive decline and misconceptions about the informed consent procedure. Moreover, the media frequently misrepresents ECT, and certain individuals and organizations with specific social and political motives persist in disseminating distorted information about the treatment.¹²

From the early days of commercial cinema to the modern days, numerous movies have played a significant role in perpetuating the negative and outdated perception of ECT, portraying this treatment method as a tool for torture. Movies and television programs are an important source of public information. In the majority of scenes, ECT is used as a metaphor for repression, mind and behavior control, and is shown as a memory-erasing, painful and damaging method, adding to the stigma already associated with ECT. Only a few exceptions paint a truthful picture of this indispensable treatment in modern psychiatry.¹³

Interestingly and simultaneously troubling, the belief persists among medical students and sometimes even among medical practitioners that ECT is a painful, outdated, harmful, or useless method. An example of the issue is illuminated by a survey conducted among second-year medical students: the study uncovered significant adverse perceptions towards electroconvulsive therapy within a portion of the cohort. Notably, 40% of respondents believed that psychiatrists frequently misused ECT, while 31% perceived it as a tool to punish violent or uncooperative patients. Surprisingly, few students possessed knowledge of the

typical treatment frequency, duration, or the fact that it is administered under general anesthesia. Particularly striking was the observation that students who considered themselves as highly knowledgeable about psychiatric illness had a greater bias against ECT. Moreover, there was no variance in the sources of negative perceptions among students, with movies and college courses being the most common. These findings underscore the urgent need for comprehensive education on ECT within medical school curricula.¹⁴

ECT TECHNIQUES

Electrode placement, stimulus dose, and pulse width are parameters used to assess the effectiveness, safety, and tolerability of ECT treatment. Presently, three standard placements are commonly employed in practice: bitemporal (BT), bifrontal (BF), and right unilateral (RUL). In essence, it has been argued that all of these placements are associated with symptom improvement following the intervention. Modern ECT techniques relies on a square wave brief or ultra-brief pulse stimulus to initiate a seizure, starting from the seizure threshold induced at the beginning of the procedure. The standard (brief) pulse width typically ranges between 0.5 and 2 milliseconds, whereas the ultra-brief pulse width is reduced to less than 0.5 milliseconds. In BT ECT, the stimulus is administered in a standardized manner at a range between 1.5- and 2.5-fold the seizure threshold, while for RUL ECT, the stimulus should be equal to or greater than five times the threshold.¹⁵

In order for the seizure induced by ECT to produce an antidepressant effect, the energy dose must be administered in a way that surpasses the seizure threshold. The methodology for dose administration suggests that the dose can be established during the initial ECT treatment session either through empirical titration or by using formulas that estimate the dose based on the patient's full age (for RUL electrode placement) or half age (for BT electrode placement). Bjølseth et al. conducted a comparison between bifrontal (BF) and right unilateral (RUL) interventions shortly after ECT cessation, as well as three months later, in a sample of elderly patients aged between 60 and 85 years. The authors observed that a formula-based (age-based) dosage might not offer optimal stimulation for elderly patients, as it has been demonstrated that the seizure threshold tends to rise with age.¹⁶

When higher energy doses are administered, formula-based RUL ECT does not exhibit any variance from BT ECT in terms of its antidepressant efficacy. RUL ECT is considered safer, as it is associated with a lower incidence of elevated blood pressure and fewer instances of consciousness disturbances.¹⁷

EFFECTS AND SAFETY

Like any other medical procedure, ECT carries certain manageable risks and may result in adverse effects. Medical complications associated with ECT include those related to general anesthesia or cardiac function. Non-medical adverse effects encompass immediate post-procedure disorientation and confusion, which typically resolve shortly after, as well as long-term difficulties, such as memory impairment that may persist over an extended period.¹⁵ Medical consequences are infrequently documented, yet an examination of research conducted on individuals with pre-existing severe cardiovascular conditions who underwent a regimen of ECT revealed that any mild to severe complications that surfaced were transient and did not hinder the completion of treatment. Furthermore, ECT is deemed efficacious and relatively safe, albeit necessitating specialized monitoring.¹⁸

Other frequently reported adverse effects include headache and feelings of nausea or vomiting, temporary blood pressure elevation and cardiac arrhythmias.^{17,19} Among geriatric patients documented side effects were dizziness and muscle pain, as well as thirst or dry mouth, constipation, drowsiness, insomnia and dysuria.²⁰ Before recommending an ECT treatment course for this patient group, careful consideration may be necessary. Elderly patients (aged over 65 years) may exhibit a decreased responsiveness to ECT, an increased likelihood of experiencing prolonged cognitive side effects (including delirium), and may also be susceptible to acute cardiovascular complications, as well as other medical issues, including heightened intolerance to antidepressants.²¹ Conversely, research indicates that advanced age is associated with favorable outcomes, including higher rates of remission, quicker responses, and improvements in clinical manifestations such as suicidal thoughts, suicide risk, and psychotic symptoms. To achieve optimal outcomes in this demographic, certain ECT approaches may involve electrode placement in the non-dominant right unilateral (RUL) or bifrontal (BF) positions, while the use of ultra-brief ECT warrants careful consideration due to the requirement for more treatment sessions.^{21,22}

THE INFLUENCE OF ECT ON BRAIN FUNCTION AND STRUCTURE

Numerous studies have demonstrated that ECT modifies cerebral blood flow and glucose metabolism, employing neuroimaging methods such as positron emission tomography (PET), single-photon emission computed tomography (SPECT), and functional magnetic resonance imaging (fMRI).²³ ECT additionally regulates neurotransmission processes and impacts the expression and release of various neurotransmitters in the brain. This includes transcription factors, neurotrophic factors, and hormones.²⁴ Electroconvulsive therapy affects the transmission of nearly all major neurotransmitters in the brain, including serotonin, dopamine, acetylcholine, endogenous opioids, epinephrine, and norepinephrine.²⁵ ECT has been found to change the levels of different biochemical mediators, such as neurotrophic factors, leading to alterations in brain neuroplasticity. This trophic effect involves both the protection of neurons and an increase in neuronal proliferation. Interestingly, even a single electroconvulsive stimulus prompts the proliferation of neurons in the dentate gyrus of the hippocampus, with these newly formed neurons capable of surviving for several months.²⁶

Research has also indicated that ECT induces alterations in the volume of the entire brain, including its constituents such as gray matter, white matter, and other brain structures.²⁷

COMPARISON WITH OTHER TREATMENT METHODS

The efficacy of ECT in depression treatment is widely recognized. Comparative studies have demonstrated that ECT exhibits a stronger antidepressant effect compared to other pharmacological agents, including monoamine oxidase inhibitors, tricyclic antidepressants, and selective serotonin reuptake inhibitors (SSRIs).²⁸ Patients begin to observe improvement in their well-being after about six sessions of ECT. Electroconvulsive therapy is considered to be the gold standard for the treatment of severe depression and especially those with TRD when immediate relief from symptoms is expected.²⁹ However, many people refuse ECT due to the stigma associated with it, besides ECT is not advisable to a small percentage of people due to medical reasons. Therefore, the quest for alternative treatment methods is crucial. Repetitive transcranial magnetic stimulation, ketamine, and transcranial direct current

stimulation (tDCS) are among the alternative treatment modalities under investigation for their effectiveness in treating TRD.³⁰

Transcranial Direct Current Stimulation

tDCS is a noninvasive therapeutic method for various neurological and psychiatric disorders.³¹ Its mechanism is based on addressing the neuropsychological traits observed in major depressive disorder, specifically hypoactivity in the left dorsolateral prefrontal cortex (DLPFC) and hyperactivity in the right DLPFC.³² This neuro-modulation technique involves delivering low-intensity current directly to cortical regions, thereby influencing neuronal networks.³³ Meta-analyses of tDCS therapy have demonstrated its efficacy in treating major depressive disorder.³⁴

There is limited research on tDCS in TRD, with only a small number of studies available. People with TRD often exhibit poor compliance with conventional medications due to perceived lack of benefit, and while ECT is regarded as the gold standard for treatment, many are reluctant to pursue it due to stigma, instead preferring noninvasive and safer treatment options. Therefore, alternative options such as tDCS need to be evaluated for their effectiveness compared to ECT. The study conducted by Ramasubramanian et al. demonstrated that tDCS led to significant improvement in depressive symptoms among patients with TRD. However, ECT was found to be more effective than tDCS in terms of its antidepressant effects. Therefore, tDCS could be considered as a viable alternative for patients who are not suitable candidates for ECT and are seeking alternative treatments.³⁰

Repetitive transcranial magnetic stimulation

Another known alternative for treating TRD is repetitive transcranial magnetic stimulation (rTMS). It is a non-invasive technique for which accumulated evidence has demonstrated efficacy for treating this condition. rTMS involves the use of rapidly changing electrical currents to generate a dynamic magnetic field. This field penetrates through the hair, scalp, and skull, reaching the cortex. Once in the cortex, it prompts changes in neuronal activity, both at the stimulated site and within connected neural networks. Numerous randomized controlled studies, spanning 3 to 6 weeks, have investigated the antidepressant effects of rTMS targeting the left dorsolateral prefrontal cortex.^{35,36} Unlike ECT, rTMS does not require anesthesia or induction of seizures. ECT seems especially preferable to rTMS for treatment of MDD with psychotic symptoms while for non-delusional MDD rTMS may have similar effect.³⁷

Deep brain stimulation

Deep brain stimulation (DBS) entails surgically implanting stimulation electrodes directly into specific brain regions to regulate both local and interconnected abnormal neural activity. This approach has been increasingly recognized as a promising alternative treatment for individuals with the most severe cases of treatment-resistant depression.³⁸ Because DBS is an invasive method, further research is needed before a clear determination can be made regarding its effectiveness compared to ECT in individuals with TRD. Nonetheless, DBS targeting different brain regions has demonstrated efficacy in patients who have not experienced relief from previous ECT.^{39,40} The stigma surrounding ECT leads a significant portion of patients to prefer undergoing invasive surgery over receiving even a single course of ECT. The exact mechanism of DBS remains unclear which causes side effects.⁴¹ Deep brain stimulation is one of the most invasive focal neuromodulation techniques available, with data supporting its safety and efficacy in addressing numerous movement disorders.⁴² However, it's important to note that in the realm of psychiatric disorders, DBS remains a relatively underexplored technique.

ENHANCING EFFECTIVENESS

The likelihood of relapse after successful antidepressant treatment, including electroconvulsive therapy, is significant. Therefore, researchers have been striving for years to develop methods that can assist in consolidating the therapeutic effects of ECT. Continuation treatment options include pharmacotherapy, psychotherapy, continuation ECT (C-ECT), or a combination of these interventions.

Considering pharmacotherapy, lithium has been proposed as an effective means to prevent relapse. Patients receiving lithium were less prone to experiencing depressive relapse following a successful acute course of ECT, in contrast to those receiving post-ECT prophylaxis without lithium. Some limited evidence has shown that older patients may derive greater benefit from continuation treatment with lithium compared to younger patients.⁴³ Following a successful acute course of ECT, sustaining remission from depressive symptoms poses a significant challenge for both clinicians and patients, given that the reported relapse rate can be as high as 84% within the initial 6 months post-ECT.⁴⁴ While earlier controlled

trials of continuation medication alone yielded promising results, it is not universally effective for all patients, as indicated by some studies demonstrating high relapse rates.^{45,46} Combining psychotropic medications may offer better relapse prevention compared to monotherapy. When utilizing a combination of two or more drugs, lithium augmentation appears to yield superior outcomes compared to antidepressants alone.⁴⁴

C-ECT refers to any treatment session administered after the initial course with the intention of preventing relapse or recurrence of depressive symptoms, rather than inducing a response or remission of an episode.⁴⁷ Relapse rates with placebo continuation therapy after index ECT are high.⁴⁴ Numerous studies confirm the advantages of continuation electroconvulsive therapy in maintaining remission. This could be particularly beneficial in situations where patients have not responded to multiple pharmacological agents, experience sensitivity to medication side effects, or express a preference for ECT over medication.^{46,48} Following an acute response to ECT, the prevailing clinical practice often involves discontinuing ECT and transitioning solely to medications for continuation therapy, despite the fact that some patients who undergo electroconvulsive therapy have not previously responded to medications or psychotherapy.⁴⁹

CONCLUSION

Electroconvulsive therapy (ECT) is a crucial option for treating treatment-resistant depression (TRD), despite historical stigma and limited accessibility. It has demonstrated efficacy where medication fails and is recommended in various guidelines. However, misconceptions persist, fueled by media portrayal and insufficient education among medical professionals. Efforts to address these issues and optimize treatment protocols are essential to ensure access to this vital therapy for individuals with TRD, ultimately improving clinical outcomes and quality of life.

DISCLOSURE

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