# Efficiency and Safety Considerations of the Modified Electroconvulsive Therapy (MECT) in the Treatment of Depression Disorder

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**Keywords:** Modified electroconvulsive therapy; Electroconvulsive stimulation; Depression disorder; Memory loss; Cognition

**Abstract:** Modified electroconvulsive therapy (MECT), a controversial treatment of depression disorder, is the improved electroconvulsive therapy (ECT) that applies anesthetic to avoid harm to patients during the process. Electroconvulsive stimulation (ECS), the animal version of ECT, is analyzed to show the reasons that ECS can help treat depression might be the triggering of neurogenesis, or the reduction of microglial neurotoxicity. In the scope of microbiology, the antidepressant mechanism of ECS is possible due to its effect on mGluR1/5 and α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptors. Hamilton Depression Scale (HAMD) and Hamilton Anxiety Scale (HAMA) of participants is studied to prove the efficiency of MECT. The outcome of certain studies indicates that the remission rates of patients who underwent ECT (79%) overshadows that of patients with pharmacotherapy (25-35%). Furthermore, the anesthetic in MECT can still be improved from conventional barbiturates to ketamine for patients with severe depression. The memory loss might be caused by the inflammatory cytokines derived from peripheral blood or the rearrangement of connection from the hippocampus to frontotemporal connections and the amygdala. Several studies went through a number of cases, and their result proved that the MECT not only seldomly causes serious medical events, but also becomes an ideal method for the treatment of geriatric depression. Scientists should try to unravel the whole mechanism of MECT in the human brain so that the safety of MECT can be further improved, and the number of people accepting MECT will increase as well.

## 1. Introduction

Depression disorder is a well-known psychological disorder. Among the various kinds of depression disorder, major depression disorder is studied widely by the behavioral scientist. The DSM Diagnostic Criteria listed nine symptoms of major depression. The first one is whether one has depression mood every day. Second, the loss of interest toward almost all activity. Third, a significant weight change in one month, in which the word significant means “more than 5% of body weight”. Fourth, whether one has insomnia and hypersomnia. Fifth, whether one has psychomotor agitation or retardation. Sixth, whether one always feels fatigued. Seventh, the feeling of guilt even though one actually did nothing. Eighth, whether it is hard to think and concentrate on work. Ninth, whether one frequently has an extreme suicide attempt. If an individual has at least 5 of these symptoms, he or she will be considered to have a major depression disorder [1].

The invention of electroconvulsive therapy (ECT) can be traced back to the birth of its concept in 1934, inspired by malarial therapy for neurosyphilis. In 1938, this technique was first used on a human. Since then, ECT underwent a series of modifications such as the shortening of the stimulus duration in 1944 and the introduction of anesthesia in 1952. The Anesthetized ECT is also known as the modified electroconvulsive therapy (MECT) [2]. Compared to the traditional ECT, it avoids muscle convulsion and fractured bones by the intravenous injection of muscle relaxants and anesthetics to the patient before the treatment [3].

The purposes of this paper are to assess the effects and security of the MECT according to recent findings of its mechanism and the data of its positive and negative effects on patients. Through the investigation of these aspects, the advice of the future research interest will be given.

## 2. The Mechanism of Electroconvulsive Therapy (ECT) Can Be Explained with Its Animal Model Electroconvulsive Stimulation

### 2.1. Effect of Electroconvulsive Stimulation (ECS) on Depression in the Preclinical Studies

The scientists strived for decades to introduce and improve the mechanism of ECT. The Theories and techniques of ECT used today were based on the outcomes of electroconvulsive stimulation (ECS), the animal version of ECT [4]. The main reason that ECS can fight against depression disorder is that it can trigger neurogenesis, which might affect the pre-existing synaptic connections and therefore cause a negative impact on memory [5-6]. There is also a hypothesis that the reduction of microglial neurotoxicity by ECS might be the key for ECS to treat major depression [7]. A study with a rat model investigates the ECS effect on mice exposed to chronic social stress. Before undergoing the ECS treatment, the mice in the experimental group were placed with CD-1 rats characterized by highly aggressive features. This study shows that ECS can lead to behavioral and hippocampal alteration that relate to the side-effect of ECT but do not reverse the influence of the social stress [8].

### 2.2. The Possible Antidepressant Mechanisms of Electroconvulsive Stimulation on Depression

The antidepressant mechanism ECS can possibly be explained by its influence upon mGluR1/5 and α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptors (Fig.1). ECS can activate the presynaptic glutamatergic neurons and inhibit GABAergic neurons. Next, the glutamate is released to the synaptic cleft to activate the AMPAR and inhibited the N-methyl-D-aspartate receptor (NMDAR). Then, the BDNF released by AMPAR interacts with TrkB. Then, the signal is transmitted from activated Akt to mTORC1, and neurogenesis is induced. At the same time, Homer1 disturbs Homer1b/c and mGluR1/5 complexes. Then, the BK channel is incompletely opened by IP3R-released $Ca^{2+}$. This promotes hyperpolarization of the postsynaptic neuron so that the antidepressant effect presents [5].

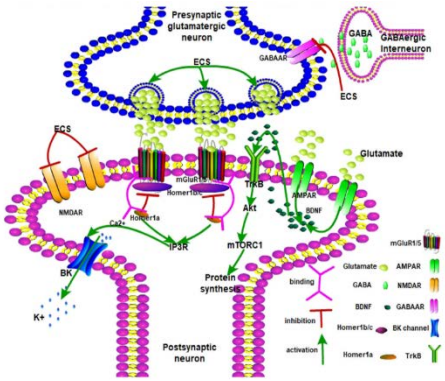


Fig. 1 The potential mechanism of ECS on nervous system.

## 3. Efficiency and New Breakthrough of Modified Electroconvulsive Therapy (MECT)

### 3.1. Evaluating the Efficacy of MECT by Hamilton Depression Scale (HAMD) and Hamilton Anxiety Scale (HAMA)

The Hamilton Depression Rating Scale (HAMD) is commonly used to rate the level of depression. Seventeen items of HAMD score the severity of depression in a range of 0 to 52, in which each item reflects an individual symptom [9]. Similarly, the Hamilton Anxiety Scale (HAMA) is a scale measuring the Severity of anxiety neurosis [10]. A study of MECT on 43 older patients (18 male and 25 female) shows that the HAMD scores and HAMA scores of participants were lower after the MECT

treatment than that before the treatment shows that the MECT help remit the depression. The rate of efficacy of MECT was calculated as 67.44% after 4 weeks of treatment in the study [3].

### 3.2. Recent Clinical and Research Breakthroughs of Modified Electroconvulsive Therapy (MECT)

According to the comparative trials, the effects of ECT against depression surpass any pharmacologic agent. A study with 217 participants shows that, among 86% of patients who completed ECT three times a week, 75% of them remitted and 79% get improvement [11]. In contrast, pharmacotherapy only shows 25-35% remission rates [12].

Another more recent study applied Montgomery-Asberg Depression Rating Scale (MADRS) and MoCA to evaluate the effectiveness of ECT on older people with bipolar depression. The MADRS rates the degree of depression disorder from 0 to 60 score, in which 0 to 6 are classified as normal and score less than 10 are considered remission [13]. The MoCA scored from 0 to 30, is used to rapidly analyze the cognitive ability of subjects across several domains [14]. In the study, 34 patients were included. The MADRS of 20 patients was collected and showed a dramatic decrease from more than 25 to less than 15, which was close to the level of remission. On the other hand, the mean MoCA scores of 34 participants increased from $23.7 \pm 4.6$ before treatment to $26.4 \pm 3.6$ afterward, embodying an improvement in patients' cognition [15].

Compared to conventional barbiturates, ketamine was found to be a better candidate of anesthetic in MECT. It can help patients rapidly recover from the feeling of depression. This property makes ketamine an appropriate choice for treating depressed patients who have an acute attempt at suicide: it not only works as an antidepressant but also helps them out of the suicidal attempt [16].

## 4. Side Effect and Potential Risk of Modified Electroconvulsive Therapy (MECT) to the Depression Patient

### 4.1. Cognitive Side-Effects of Electroconvulsive Therapy

In 2020, A group of experts in academic and clinical fields discussed ECT's side effects. They pointed out that the "independent variables" of ECT's cognitive side-effects are the domains of cognitive function, various parameters of ECT such as pulse width and some treatments, and individual situation of the patient [17].

The domain of cognitive function composes of several branches. The first is non-memory cognition. The executive function and processing speed are damaged in the subacute period (0-3 days) after ECT treatment. In this period, the attention is intact. During the short-term period (4-14 days), these abilities return to or even exceed the baseline, which is defined as the level before the ECT [18-21]. Considering patient with severe depression disorder often has cognitive damage, this overall improvement can be regarded as the result of effective treatment. The long-term observation (14 days to 2 years) shows no evidence of impairment of this non-memory cognition [18]. Second, the anterograde memory is impaired in the first 3 days after ECT treatment and recovered to baseline in a short-term period. No evidence shows that the anterograde memory is damaged in the long term [18, 22]. The third is retrograde memory. The autobiographical memory is mostly reported among categories of retrograde memory by patients exposed to ECT, but episodic, semantic memory is influenced by ECT as well [23-24]. In some reports, the memories don't come back to the patient spontaneously. It is noteworthy that females and people undergoing bilateral ECT have a higher risk of the loss of retrograde memory [17, 25].

### 4.2. Loss of Autobiographical Memory and Short-term Reduction in New Learning

Wechsler Memory Scale (WMS) uses several subtests to evaluate the different aspects of intelligence [26]. Mini mental state (MMS) is a short questionnaire that contains 7 questions. It specifically evaluates the cognitive sides of mental functions regardless of mood, abnormal mental experiences and the form of thinking [27]. A study gives out that there are significant differences in memory scores after 2 weeks of MECT. After 4 weeks of treatment, the scores of MMSE underwent

a significant increase [3]. The report of another group of scientists that the learning ability of patients damaged by ECT will recover to the baseline by 14 days endorsed the finding of Jiang's group [17].

The rearrangement of connection from the hippocampus to frontotemporal connections and the amygdala is a possible reason for the memory loss caused by ECT [8]. More specifically, ECT can cause an augment of hippocampal volumes and the repair of abnormal hippocampal connectivity in patients with depression disorder [28]. Furthermore, a recent study shows that the risk of cognitive impairment is related to the inflammatory cytokines derived from peripheral blood [29].

### 4.3. Mortality Rate of Electroconvulsive Therapy

The death caused by ECT is rare. An article collects data of 766180 ECT treatments in 15 studies from 32 countries, in which 16 cases of ECT-related death were reported. These data show a 2.1 per 100000 mortality rate. Among these treatments, only one death was reported among 414747 treatments in studies after 2001, which shows the improvement of the ECT procedure [30]. Another more recent study analyzed 10016 records with a mean age of 56.6 years presented that the serious medical events happened 0.25 person per year in the group that receive ECT, while the 0.33 person per year rate for the control group. Furthermore, the suicide rate in the ECT group (less than 5 of 5008 people) was much lower than that of the control group (11 of 5008 people). This study concludes is that there is no evidence to show the ECT increased the risk of serious medical events, and ECT significantly decreased the suicide risk [31].

### 4.4. Electroconvulsive Therapy for Depression Did not Lead to a Clinically Significant Increased Risk for Serious Medical Events and Is Considered as the Best Way of Treatment in Some Situations

As mentioned in the last section, the mortality rate of ECT is extremely low. Moreover, in some specific situations, ECT is a better choice than other treatments. Old patients normally have a weaker tolerance to the medication. In this case, the ECT will be a good candidate for treating geriatric depression since the risk of complications is decreased. Interestingly, the study found that elderly patients often have a better response to ECT compared with young adults [32]. Another study learning the ECT on patients that lose their ability for consent. The result shows that the remission and response rates of these patients lacking the ability of consent are similar to those who have the ability of consent. The research group also states that ECT is the best choice for people with extremely severe depression disorder [33].

## 5. Perspectives for Its Improvement and Research Interest

Finding out the certain mechanism of ECT in the human brain is at the top of the to-do list. While the mechanism is understood, the comprehensive therapy that can reduce or even avoid the damage of ECT to the memory and cognitive ability will become a possible research interest that has a bright future.

What's more, the controversy of ECT is long-lasting. Even though some studies show that it is a reliable and safe method for treating depression disorder, the necessity of using ECT and its ethical problem is widely discussed in society. This dispute also reminds us that further improvement of the safety of ECT is needed so that ECT can be accepted by more people and help patients who need it.

Last but not least, the application of ECT should be considered given this COVID-19 Era. As a treatment that includes open airway management, ECT treatment is regarded as an aerosol generating process [34]. Given this information, doctors are confronted with an ethical problem that whether it is worthy to expose their patients to the risk of getting the pandemic during the clinical procedure of ECT. The possible solution is to build up a classification system that ranks patients according to their severity of depression [34]. This method regards ECT as a last resort. If doctors believe the ECT is not necessary, they should always consider other means of treatment.

## 6. Conclusion

This paper integrates recent findings to give out the assessment of the efficiency and security of MECT. The ECS in animals was applied to explain the mechanism of ECT. Studies show that ECT overshadows other treatments in treating geriatric depression because of its lower risk and higher efficiency. Furthermore, the effectiveness of ECT is proved by the measurement of several parameters such as HAMD, HAMA, MoCA, MADRS, WMS, and MMS. The studies focusing on the mortality rate of ECT reported only a few cases of death in meta-analysis. All these advantages indicate the reliability of ECT as a way against depression and the bright prospect of it. However, the memory loss and harm on human cognitive abilities of ECT cannot be ignored. The overcome of these side effects is the next step for researchers. And the technical improvement of ECT, while achieved by scientists, could lead to a higher acceptability of the whole society to ECT so that more patients will consider ECT treatment when it is indeed their best choice. Considering the COVID-19 pandemic nowadays, the trade-off between the risk of depression and the risk of pneumonia to patients becomes an ethical problem for doctors when they are considering ECT as a possible treatment.

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