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EDITORIAL

- 1 Electroconvulsive therapy: 80 years old and still going strong
Gazdag G, Ungvari GS

REVIEW

- 7 Comorbidity of bipolar and anxiety disorders: An overview of trends in research
Spoorthy MS, Chakrabarti S, Grover S

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Electroconvulsive therapy: 80 years old and still going strong

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Abstract

Electroconvulsive therapy (ECT), which is among the oldest and most controversial treatments in the field of psychiatry, has its 80th birthday this year. In this brief historical overview, the discovery of the therapeutic effects of convulsive therapy by Laszló Meduna, and the circumstances that motivated Ugo Cerletti and Lucio Bini to use electricity as a means of seizure induction are described. Meduna's original theory about the antagonism between epilepsy and schizophrenia has been replaced by hypotheses on the mechanism of action of ECT. The position of ECT in modern psychiatry is also discussed with special attention to its most important clinical indications, including catatonia, and pre- and postpartum affective and psychotic states that are responsive to ECT and in which ECT may even be lifesaving. Adverse effects and comparison of ECT with recently developed brain stimulation methods are also reviewed. The negative media portrayal of ECT and its earlier misuse may have contributed to its negative professional and public perceptions indicated repeatedly in attitude surveys. This negative attitude has played an important role in the decreasing use of ECT in the developed world and a reduction in access to ECT, which constitutes a violation of psychiatric patients' right to an effective treatment.

Key words: Electroconvulsive therapy; History; Indications; Utilization; Attitudes

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Core tip: Electroconvulsive therapy (ECT), which is among the most controversial psychiatric treatments, has its 80th birthday this year. The introduction of convulsive therapy to psychiatry and changes in seizure induction from chemical to electrical are

outlined. The place of ECT in contemporary psychiatry, particularly its most important clinical indications, is briefly discussed. Negative media representation and historical misuse are likely to have contributed to negative professional and public attitudes towards ECT and, consequently, it decreased use. Recent limitations of access to effective treatment in many parts of the world constitute a violation of patients' rights.

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INTRODUCTION

Brief historical overview

Electroconvulsive therapy (ECT), one of the oldest treatment methods in the field of psychiatry, was first introduced 80 years ago in Rome when Ugo Cerletti and Lucio Bini used an electric current to elicit an epileptic seizure for therapeutic purposes^[1]. However, this was not the first use of an epileptic fit to treat mental illness. The idea of inducing epileptic seizures to treat patients was first proposed by Meduna^[2], a Hungarian neuropathologist and psychiatrist.

History of chemical convulsive therapy

The idea that a disease could be cured by inducing another disease was proposed by Wagner-Jauregg, who observed that high fever caused symptomatic improvement in general paresis of the insane and infected syphilitic patients with malaria to induce repeated bouts of high fever. In 1927, Wagner-Jauregg was awarded the Nobel Prize for developing the first effective biological treatment in the field of psychiatry^[3]. In the late 1920s, Meduna^[4], a researcher at the beginning of his professional career in the psychiatric department of the University in Budapest, was interested in the histopathology of epilepsy. Meduna^[4] observed that in the brains of epileptic patients, glial cells occupied the spaces left by lost neurons. In 1931, Hechst *et al*^[5], his departmental colleague who studied the histopathology of schizophrenia, described a reduction in the number of glial cells in the brains of schizophrenia patients. This finding strongly contrasted Meduna^[4]'s observations in the brains of patients with epilepsy.

Besides these neuropathological findings, clinical observations also appeared to indicate antagonism between epilepsy and schizophrenia. Nyírö *et al*^[6] reported that the rate of schizophrenia was significantly lower among patients with epilepsy than in the general population. Meduna^[4] was also intrigued by a report about two schizophrenia patients whose conditions remitted following episodic epileptic seizures^[7]. A report in which only 8 of 6000 schizophrenia patients suffered from epilepsy also appeared to support the antagonism theory^[8]. By then, Meduna^[4] had become convinced of an antagonism between schizophrenia and epilepsy, as he concluded in his autobiography: "...if I can stimulate epileptic seizures in schizophrenics then these... will alter the chemical and humoral processes in the body in a way... that the abatement of the disease will be made physiologically possible"^[9].

Meduna^[10] planned to induce a seizure using a chemical agent and proceeded to test the safety and effectiveness of several epileptogenic compounds for this purpose. Finally, Meduna^[10] identified camphor as the compound that satisfied his requirements. On January 2, 1934, he conducted the first human experiment involving intramuscular camphor injections^[11]. In the 2 subsequent years, Meduna^[12] treated more than 100 patients, of whom half recovered or significantly improved.

Introduction of electrically induced seizures

Although camphor was later replaced with intravenous cardiazol, chemical seizure induction remained somewhat unpredictable, with considerable interpersonal variance. Furthermore, the time interval between the injection and seizure was extremely stressful for the patients. These difficulties led Ugo Cerletti and his colleagues at the university psychiatric clinic in Rome to search for an alternative means of seizure induction.

Prior to his arrival in Rome, Cerletti already had some experience with electricity, as he had used an electric current in animal studies of epilepsy in Genoa^[13]. In Rome,

Cerletti continued these studies with the involvement of his assistant, Lucio Bini. The idea of using electricity to induce seizure first occurred to Cerletti and Bini when they witnessed cardiazol therapy in Vienna^[14]. After defining the parameters of a safe electric stimulus through animal studies, they performed the first electric seizure induction in a psychotic patient named Enrico X on April 11, 1938. Although the initial stimulation did not result in an epileptic seizure, stimulation at a higher voltage induced an eighty seconds tonic-clonic seizure on April 20. After 11 further treatments, Enrico recovered and was released from the university psychiatry clinic^[14]. Although the technical details of electric seizure induction were published shortly after the first treatment^[1], their results with electroshock therapy were not summarized until 2 years later, which attests to the careful attitudes of the inventors^[15].

MECHANISM OF ACTION

Subsequent research could not confirm Meduna^[12]'s hypothesis on antagonism between epilepsy and schizophrenia, and the mechanism of action of ECT remains to be elucidated. In response to frequent criticism regarding the latter point, significant efforts have been made to clarify the mechanism underlying ECT. One theory explains the therapeutic effects of ECT by referring to its effects on neurotransmitters, particularly the serotonin and dopamine systems^[16]. Another theory conceptualizes depression as a pro-inflammatory state wherein ECT acts on cytokines, thereby treating the inflammation and normalizing mood^[17]. Furthermore, clinical evidence indicates a hypertensive surge during ECT that causes transient blood-brain barrier permeability which may also play a role in its therapeutic effect^[18]. Animal studies suggest that electrically induced seizures have epigenetic effects that may also add to the clinical effectiveness of ECT^[19]. Finally, the most promising new findings appear to involve ECT-induced changes in structural brain plasticity. Recent studies also identified ECT as a strong stimulator of neurogenesis by promoting the proliferation of stem cells^[20].

PLACE OF ELECTROCONVULSIVE THERAPY IN MODERN PSYCHIATRY

Notwithstanding major advances in psychopharmacology and several recently introduced brain stimulation methods, ECT is not a closed chapter in the history of psychiatry but is rather a treatment modality used widely throughout the world^[21]. ECT has well-defined indications^[22,23] and remains one of the most effective treatment methods in psychiatry^[24].

ECT in the treatment of affective disorders

Meduna^[12] considered convulsive therapy as a treatment for schizophrenia. However, it was soon found to be even more effective for the treatment of affective disorders^[25]. Currently, major depression is the first indication for ECT^[22,23,26]. Between the 1960s and 1980s, several studies investigated the efficacy of ECT. The majority of randomized controlled studies confirmed the superiority of ECT relative to sham ECT or antidepressants for the treatment of affective disorders, and these findings were supported by meta-analyses^[24,27-29].

Independent of its antidepressant effects, ECT also has a clear anti-suicidal effect^[30]. Therefore, ECT is recommended as the first choice of treatment for patients at a high risk of suicide^[31].

In pharmacotherapy-resistant patients, maintenance ECT proved to be an effective alternative in relapse prevention^[32].

ECT in psychosis and schizophrenia

In several developing countries, including India^[33] and China^[34], the two most populous nations, schizophrenia remains the first indication for ECT. Although antipsychotics are equally effective for schizophrenia^[35], financial reasons may explain the common use of ECT in this patient population^[36]. Unmodified ECT is still practiced in the developing world due to limited financial resources^[34].

Resistance to pharmacotherapy remains a serious problem in the treatment of schizophrenia^[37]. ECT could be an augmentation strategy to enhance the effects of antipsychotic drugs^[38]. ECT could also augment clozapine in clozapine-resistant patients^[39]. Psychotic conditions that respond well to ECT include catatonia and pre- and postpartum psychotic states^[40]. Combining maintenance ECT with antipsychotic

medications is an effective strategy for relapse prevention in schizophrenia^[41].

Adverse effects of ECT

From the beginning, psychiatrists' intentions was to make ECT as safe as possible by decreasing its side effects to the minimum. As a result of these efforts, muscle relaxation^[42] and anaesthesia^[43] were introduced by the early 1950s. The importance of minimizing cognitive side-effects was recognized early and unilateral stimulation technique was introduced as early as 1954^[44]. Recent efforts to further reduce cognitive side effects focus on changing from brief to ultra brief pulse stimulation^[45]. While a few individual testimonies reported longlasting and severe memory disturbances after ECT^[46], extensive psychological tests could not detect significant memory deficits beyond six months following a course of ECT^[47].

ATTITUDES TOWARDS ECT

ECT is probably the most controversial form of treatment in medicine. It has been banned in certain parts of the world^[48] while remaining widely practiced in other countries^[49]. Besides economic and socio-cultural factors, historical contexts, such as the misuse of ECT during the Nazi era^[50], might have contributed to the negative perceptions of this form of therapy. Misleading media representations of ECT have contributed further to this negative image. For example, the portrayal of ECT in the film "One Flew over the Cuckoo's Nest" by Milos Forman, has had a huge and long-lasting effect on perceptions, although other movies and social media have also presented a grossly distorted image^[51]. Recently, however, a slow tendency towards a more objective depiction of ECT has been observed^[52]. In contrast to its negative image in the media and the public misperception^[53,54], attitudes towards ECT in patients, relatives and the mental health professionals are mainly positive^[55,56].

COMPARISON OF ECT WITH RECENTLY DEVELOPED BRAIN STIMULATION METHODS

In the last two decades several new neurostimulation methods have been introduced in psychiatry mainly from the field of neurology. These include transcranial magnetic stimulation (TMS), vagus nerve stimulation, deep brain stimulation, transcranial direct current stimulation. Most of these new techniques were introduced to treat major depression. To date, only TMS has been compared with ECT in randomized controlled trials, which consistently proved the superior efficacy of ECT in the treatment of major depression^[57]. No other neurostimulation technique has a firm place in the treatment algorithm for major depression^[58].

CONCLUSION

After 80 years, electroconvulsive therapy remains one of the most effective treatment modalities in psychiatry. However, the popular image of ECT is controversial and mainly negative. This perception can sometimes hinder its use, thereby violating the rights of patients to access to an effective and sometimes lifesaving treatment.

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