Review

Electroconvulsive therapy (ECT): a safe and effective treatment*

Electroconvulsive therapy (ECT) is a modern, effective and safe medical treatment for severe mental health conditions. There is a continuous need to inform mental health professionals regarding indications, benefits, risks, and side effects of ECT. For this purpose, the psychiatric associations of Germany, Switzerland, Austria, and Italy summarize the latest scientific knowledge.



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Summary

This position paper aims to describe the current state of knowledge about ECT and, therefore, to facilitate the decision-making process for the use of ECT even in complex clinical cases, based on a risk-benefit assessment.

Specifically, the following points are covered:

Indications. ECT can be used for different psychiatric disorders in both acute treatment and to prevent relapses in the form of maintenance ECT. It is important to highlight that indications based on syndromes rather than diagnoses are gradually proving their validity in clinical practice.

Safety. ECT is one of the safest treatments performed under general anaesthesia and has been documented to cause no direct or indirect structural brain damage. On the contrary, recent studies have even highlighted an increase in the grey matter volume following ECT administration.

Side Effects. transient effects on cognitive function are the most relevant side effect of ECT. These are generally mild to moderate, and they usually resolve completely within a few days to a few weeks.

Mechanism of action. the proven effects of ECT are particularly evident in the areas of neuroplasticity, inflammation and functional connectivity.

Key word: electroconvulsive therapy (ECT), indications, safety, side effects; mechanism of action, risk-benefit assessment

Almost two decades respectively one decade have passed since the publication of the official recommendations for electroconvulsive treatment (ECT) by the German Medical Association (BÄK) in 2003 ¹ and by the German (DGPPN), Swiss (SGPP) and Austrian Associations (ÖGPP) for Psychiatry and the regional Trentino-South Tyrol Italian Society of Psychiatry (SIP) ² in 2012. Since then, important studies have been published regarding the indications for ECT. Evidence-based recommendations for the use of ECT have been included in the S3 guidelines for "Unipolar depression", "Schizophrenia" and "Diagnosis and therapy of bipolar disorders" ³⁻⁵. Furthermore, ECT has been integrated into

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* From: "Indikationen zur Elektrokonvulsionstherapie" *Translation by:*

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training curricula for psychiatrists in Germany and Austria. Moreover, additional reimbursement rates for ECT were integrated into the German reimbursement system for Psychiatry and Psychosomatic Medicine.

During the last 20 years, the number of ECT sessions in Germany nearly doubled ⁶, but this has only partially led to an improvement in the care of people with severe mental disorders, since the number of centres offering ECT has remained almost unchanged, although with an upward trend. An international survey has shown that German-speaking countries lag behind most industrialized countries in the use of ECT and that only about half of psychiatric clinics in Germany provide this therapeutic option.

Specific groups of patients, such as children and adolescents, people with intellectual disabilities, as well as forensic patients, have more difficulty accessing ECT, which has been repeatedly described as an ethically unacceptable limitation of the right of every individual to receive the best possible treatment ^{1,7}.

This position paper aims to describe the current state of knowledge on indications for ECT and facilitate clinical decision-making even in difficult cases, based on risk-benefit analyses. It is crucial to highlight that indications based on syndromes rather than diagnoses are proving increasingly useful in clinical practice. For example, affective, psychotic and catatonic syndromes respond to ECT relatively independent of the etiology.

Indications for ECT

General indications for ECT described by the German Medical Association in 2003 remain substantially unchanged. ECT is basically indicated when:

- there is a need for rapid improvement due to the severity of the psychiatric disorder;
- · risks of ECT are lower than alternative treatments.
- there is a known history of poor response to psychotropic medications (treatment resistance);
- there is a known history of good response to ECT;
- there have been episodes of intolerance and significant side effects to pharmacotherapy ^{1,8}.

ECT is used as part of a broader treatment approach that includes a combination of appropriate pharmacotherapy and psychotherapy. In some urgent cases, ECT alone as a life-saving treatment may create the basis on which patients can subsequently be integrated into a more complex therapeutic concept.

Whether ECT is offered as first-line treatment or only after other treatments have failed depends less on the diagnosis than on the level of acuteness and severity of the disorder and the risks associated with the individual course of the disease. ECT is not the last resort (no "ultima ratio") ². On the contrary, its early use during the course of treatment reduces suffering, disease duration, risk of chronicity and increases the likelihood of response to ECT ⁹.

For certain diagnoses, such as unipolar depression

or schizophrenia, randomized controlled studies and meta-analyses, constituting the highest level of scientific evidence, have led to corresponding recommendations in national and international guidelines.

However, exclusively considering the level of meta-analytic evidence is too limited ¹⁰, since randomized controlled trials are not feasible for medical or ethical reasons in some seriously ill populations. In these cases, clinical experience (i.e. empirical evidence, for example based on case series, case-control studies, etc.) has to and can fill these evidence gaps in order not to deprive patients of a potentially highly effective and sometimes life-saving treatment.

There are various indications for ECT based on syndromes. Since response rates differ within the same syndrome (e.g. depressive syndrome) depending on the presence of certain clinical factors (e.g. age, chronicity, severity level, psychomotor symptoms, family history, etc.), no generalized hierarchical classification is made in terms of first or second choice treatment.

Table I shows existing indications with a selection of the relevant literature, with explicit reference to the recommendations of existing guidelines.

Table I. ECT indications.

| Indications | References |
|---|---|
| Unipolar depression/depressive syndromes | S3 guidelines for unipolar depression 4,8 |
| Schizophrenia and schizoaffective syndromes | S3 guidelines for schizophrenia ³ |
| Bipolar disorder (including depressive and manic syndromes, mixed states, rapid cycling, delusional mania and delusional depression) | S3 guidelines for the diagnosis and treatment of bipolar disorders 5,11,12 |
| Catatonic syndromes (including malignant catatonia and neuroleptic malignant syndrome) | S3 guidelines for schizophrenia 3,13,16 |
| Organic/neuropsychiatric syndromes as in the lines 1-4 | 17-21 |
| Treatment-resistant severe behavioural disorders (for example (auto) aggression) in neuropsychiatric disorders, dementia, autism spectrum disorders and other neurodevelopmental disorders | 22-27 |
| Autoimmune encephalitis (with severe and treatment resistant psychiatric symptoms) | 28 |
| Treatment resistant Parkinson's disease (with motor and psychiatric symptoms) | 17 |
| Treatment resistant status epilepticus | 29,30 |
| Treatment-resistant delirium (including treatment-resistant benzodiazepine or barbiturate withdrawal delirium) | 31-34 |

In addition to the well-established efficacy of ECT for acute treatment, there are now evidence-based strategies to prevent relapse using maintenance ECT ³⁵⁻³⁷. This should be offered as a therapeutic option to all patients who do not achieve symptom stability or who relapse even with optimized pharmacological and psychotherapeutic treatment. The frequency and duration of maintenance ECT should be adapted according to the individual course of the illness. Even very long-term ECT maintenance therapies do not carry a cumulative risk of cognitive impairment ³⁸, but instead have a positive effect on the long-term course of the disease.

Safety and impact on mortality and on suicidality

ECT is one of the safest treatment procedures performed under general anaesthesia. Until 2001, the mortality rate was approximately 1 per 50,000 treatment sessions; since then, this number has continued to decline, and it is lower than the mortality rate for comparable short-term surgical procedures ³⁹. The risk of treatment is therefore essentially the risk associated with anaesthesia.

It has been shown multiple times that there is no structural direct or indirect brain damage linked to ECT. On the contrary, over the last few years imaging studies have shown an increase in grey matter following ECT ⁴⁰.

ECT has an anti-suicidal effect with a large effect size, even 3-6 months following an ECT series 41,42. Even after one year, overall mortality of patients treated with ECT is approximately 50% lower compared to patients not treated with ECT 41.

Side effects

Transient effects on cognitive function are the most relevant side effect of ECT. Specifically, memory performance is mainly affected. Memory from before the ECT series and memory formation after the ECT series are only anecdotally affected. On the other hand, short-term cognitive side effects are common, usually mild to moderate, and they usually disappear completely within 15-30 days 43,44. Over time there is an improvement in cognitive function when assessing the group of patients treated with ECT as a whole, since the impairments associated with the psychiatric disorder are reduced when responding to ECT. Effect size and side effects do not differ in a clinically relevant way between right unilateral and bilateral stimulation when dose is adjusted accordingly. Dosing using the "age method" also requires adjusting the dose according to age and electrode placement. Serious side effects (such as hemodynamically relevant cardiac arrhythmias, severe increases in blood pressure, prolonged apnoea with muscle relaxation, aspiration and tardive seizures) are rare and, moreover, generally acutely treatable 36. Postictal agitation on awakening occasionally occurs (immediately after the treatment) and can usually be avoided by optimizing the anaesthetic regimen. About one-third of patients may

experience tension headaches following ECT, which can be treated effectively, even prophylactically, with analgesics. Nausea and vomiting after ECT/anaesthesia may occur and can also be prevented by prophylactic administration of antiemetics during anaesthesia. Performing an EEG prior to ECT is no longer considered mandatory. Following an ECT series, non-specific EEG changes often occur for several weeks and without any correlating clinical symptoms. Retrospectively patients rated ECT as "good to very good" ⁴⁵.

Mechanism of action

The induction of a generalized seizure, meaning the synchronised activation of a group of cerebral neurons, is a necessary condition for the effectiveness of the treatment ⁴⁶. This seizure, along with the brain's ability to end the seizure "on its own" using a large variety of mechanisms, in turn, leads to the changes that contribute to the recovery of patients suffering from different severe psychiatric disorders ⁴⁶. Replicated effects of ECT, some of which have been meta-analytically confirmed, concern neuroplasticity (increase in neuronal growth factors and regional grey matter increases) ^{40,47,48}, inflammation (reduction of inflammatory mediators) ⁴⁹, functional connectivity (normalization of pathologically altered brain functions) ^{50,51} and anticonvulsant effect (increase in GABA levels and change of GABA/glutamate ratio) ^{46,52}.

Risk-benefit assessment

Depending on the severity and acuteness of the psychiatric disorder, there are no absolute contraindications to ECT. A more detailed risk-benefit assessment is needed for patients with severe pre-existing somatic comorbidities. Hence, an individual and interdisciplinary risk-benefit assessment should be carried out. This includes factors that make anaesthesia more risky, such as a recent heart attack or severe untreated coronary artery disease, other severe functional cardiopulmonary limitations, treatment-resistant severe arterial hypertension, increased intracranial pressure, an extended and recent cerebral stroke, an intracerebral tumor with associated oedema, an acute glaucoma attack or vascular malformations with a known high risk of rupture. Advanced age 53, pregnancy 54, young age (children and adolescents) 55, inability to give consent 56,57 or cardiac pacemakers ^{58,59} do not constitute an increased risk.

Informed consent

As with all medical procedures, the patient or – if they are unable to consent – the patient's legal representative provide informed consent before undergoing the treatment. Under the strict limitations provided by article §1906a of the German Civil Code (BGB), ECT can also be performed against the will of the patient; existing case-control studies have shown similar good efficacy and positive retrospective evaluation of patients undergoing involuntary ECT ^{56,57,60}.

Participating Scientific Associations

- German Society for Psychiatry and Psychotherapy, Psychosomatics and Neurology (DPPPN)
- Swiss Society for Psychiatry and Psychotherapy (SGPP)
- Swiss Society for Interventional Psychiatry (SGIP)
- Swiss Society for Anxiety and Depression (SGAD)
- Austrian Society for Psychiatry, Psychotherapy and Psychosomatics (ÖGPP)
- Italian Society of Psychiatry (SIP), regional Trentino-South Tyrol section
- (German) Working Group for Neuropsychopharmacology and Pharmacopsychiatry (AGNP)
- German Society of Biological Psychiatry (DGBP)
- German Society of Brain Stimulation in Psychiatry (DGHP)

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Commentary

During the last decades and through continuous clinical and scientific progress Electroconvulsive therapy (ECT) has developed into a modern medical intervention. Although psychotherapy and pharmacotherapy have strongly improved the treatment of mental illness, they sometimes have a limited effect in patients with very severe psychotic, depressive or catatonic symptoms. Quite often these can dramatically improve with ECT. Bearing in mind the persistence of the illness, the side effects of the treatment are rather benign. Thereby, the therapy increasingly has gained worldwide acceptance, especially with patients and their caregivers.

Considering these insights, various academic conferences have been held in recent years in Italy, the birthplace of ECT. Symposia regarding the therapy were regularly organized within the annual meeting of scientific communities (e.g. SIP, SINPF, SOPSI) and projects were implemented to translate ECT literature into Italian language (e.g., the book "La terapia elettroconvulsivante. Un manuale per medici invianti e operatori con 22 illustrazioni", or the brochure "ECT by 24 questions", translated by the Italian Psychiatric Society) as to promote and disseminate scientific knowledge about brain stimulation therapies, especially with ECT.

Disregarding these efforts, the clinical supply with ECT has significantly decreased in Italy. In 2020, we published the paper "Electroconvulsive Therapy in Italy-Current Dissemination of Treatment and Determining Factors of the Past" demonstrating that the current number of ECT centers in Italy is very low in comparison to European and worldwide practice and that it has dramatically declined during the last 10 years. Furthermore, a north-south division in terms of

geographical distribution was observed: ECT centers are located almost exclusively in the north. Finally, in contrast to other countries worldwide, ECT is still on the decline in Italy. Here, the care of patients with severe mental illness requires a reconsideration of ECT as an evidence-based and modern treatment option in present and for the future.

It is important to assess the history of ECT with today's standards and not to assess modern ECT in view of its history 1. Not historical attributions, but modern standards of ECT should be considered in order to identify existing treatment potentials: "... it is to understand better the assumptions - and treatments - that we have inherited. and to gain a meaningful perspective on practice today" 2. This sets a stage for the translation and publication of the new position paper on indications for ECT, an effort lead by the German psychiatric association (DGPPN), in collaboration with German-speaking psychiatric associations from Germany, Switzerland, Austria and Trentino Alto Adige. It complements a prior publication of the consortium of professional associations on the timely and appropriate use of ECT 3. The recommendations of the present statement are based on the current state of knowledge about ECT and cover indications, safety and side effects, the mechanisms of action and the risk benefit aspects 4.

Translating and publishing the recent position paper on ECT from scientific psychiatric associations in Germany, Austria, Switzerland and Italy in *Evidence Based Psychiatric Care*, the open-access Journal of the Italian Psychiatric Association (SIP), is a further important step toward integrated, personalized evidenced-based medicine.

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