In Review

What We Have Learned About Electroconvulsive Therapy and Its Relevance for the Practising Psychiatrist

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In this narrative review, the current knowledge base on the efficacy and the practice of electroconvulsive therapy (ECT) is reviewed, and its relevance for the practising psychiatrist is appreciated. In the past decade, several large-scale studies have confirmed the significant superiority of ECT in the treatment of severe and refractory psychiatric conditions, such as major depressive disorder and bipolar disorder. However, the efficacy of ECT is not reflected in current treatment algorithms, where ECT is often reserved as a last resort. However, clinical characteristics, such as the presence of psychotic symptoms, suicidality, or catatonic signs, should prompt the clinician to consider ECT earlier in the treatment course. ECT is a safe procedure, without absolute contraindications for its use. Nevertheless, patients' fears and complaints should be acknowledged, and patients should be adequately informed about expected benefits and possible risks, such as memory problems, that are generally transient. Research focusing on further minimizing memory problems, while maintaining a superior efficacy, is ongoing. Adequate continuation treatment, either pharmacotherapy or continuation ECT, after a successful ECT course is of vital importance to maintain the benefits achieved and should be the focus of future research.

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Clinical Implications

- ECT is highly efficacious for the treatment of major depressive disorder, bipolar disorder, and catatonia.
- The presence of psychotic symptoms, suicidal thoughts, or catatonic signs should prompt the clinician to consider ECT earlier in the treatment course.
- Current standards of ECT practice have been able to reduce side effects.

Limitations

- Our review is narrative and limited to literature with a clear relevance for the referring psychiatrist.
- More studies are needed on continuation pharmacotherapy and continuation ECT after a successful ECT course.

Key Words: electroconvulsive therapy, mood disorders, depressive disorder, bipolar disorder, schizophrenia, continuation electroconvulsive therapy, catatonia

There is a reasonable evidence base for the use of ECT: it does not rest simply on anecdote, habit, and tradition.^{1, p 807}

E CT is the oldest somatic treatment in psychiatry still available. Between roughly 1960 and 1980, ECT disappeared from the awareness of most clinicians, except insofar as they read negative and stereotyped references to it in the popular press.² From the 1990s on, ECT has gained a renewed scientific interest, with the number of RCTs almost tripled, from 49 between 1980 and 1989 to 135 between 2000 and 2009. The question remains whether the increasing scientific interest has been able to provide clinically relevant insight in when and how ECT should be administered, to provide an effective and safe treatment for people who are the most severely ill. Focusing on the most recent evidence, published in the past decade, this narrative review aims to summarize the current knowledge base on the efficacy and the practice of ECT, and its relevance for the practising psychiatrist.

For Whom Is ECT Indicated?

Mood Disorders

Unipolar Depression. In most countries, more than 80% of all ECT treatments are performed for the treatment of MDEs.^{3,4} In the past decade, the significant superiority of ECT above ADs in the treatment of unipolar depression has been confirmed in several studies and meta-analyses,

Abbreviations used in this article

AD	antidepressant
BD	bipolar disorder
BPD	borderline PD
CANMAT	Canadian Network for Mood and Anxiety Treatments
C-ECT	continuation ECT
CORE	Consortium for Research in ECT
CUC	Columbia University Consortium
DSM	Diagnostic and Statistical Manual of Mental Disorders
ECT	electroconvulsive therapy
HDRS	Hamilton Depression Rating Scale
MDD	major depressive disorder
MDE	major depressive episode
PD	personality disorder
NMS	neuroleptic malignant syndrome
RCT	randomized controlled trial
YMRS	Young Mania Rating Scale

translating to a mean difference of 5.2 points on the HDRS.¹ Remission rates of 75%⁵ or higher⁶, after a mean number of 8 treatment sessions⁵ are reported repeatedly in large RCTs. Two multisite collaborations, the CORE study⁷ and the CUC study,⁸ are illustrative.9 In the first phase of these relapse prevention studies, a total of 684 patients (70% female, aged between 55 and 59 years), with a unipolar depression that had failed medication trials, were treated with ECT. Remission rates were 86% (341/394 completers) and 55% (159/290 completers), respectively. Mean HDRS scores dropped from about 34, pretreatment, to about 6, posttreatment. A recent multicentre trial from the same CORE group, comparing the 3 commonly used electrode placements in 230 patients with unipolar and bipolar depression,¹⁰ confirmed remission rates of 55% to 64% after a mean of 6 treatment sessions, that is, within 2 to 3 weeks.

Patients of an older age, that is, aged 65 years and older,¹¹ and who are more severly ill,¹² tend to respond better or faster. Melancholic features, such as an unchanging abnormal mood, vegetative signs, delusional thoughts, and psychomotor retardation or agitation, are predictors of good outcomes with ECT,¹³ although, in a large multicentre trial, DSM criteria of melancholic features failed to identify depressed patients more likely to respond to ECT.¹⁴ However, this merely illustrates the inadequacy of DSM criteria, poorly reflecting the classical criteria for melancholia.¹⁴ In these classical criteria, psychomotor disturbances are seen as the core symptoms^{13,15} that predict a good outcome after ECT.¹⁶

AD treatment failure should not discourage the clinician from prescribing ECT, because, although in some studies medication failure seemed to diminish response (for an example, see Dombrovski et al¹⁷), a large multicentre study proved otherwise. In this study, in 345 patients with unipolar depression, AD treatment failure was assessed using the Antidepressant Treatment History Form. No significant association was found between treatment failure with ADs and acute remission rates after ECT.¹⁸

The clinical situations in which ECT should be considered as a first-line treatment, according to the recent guidelines for the treatment of MDD by the CANMAT,¹⁹ are shown in Table 1.

Bipolar Depression. ECT is a consideration in a patient with a severe MDE not responding to ongoing therapy, regardless of the primary diagnosis. In a multicentre study comparing 3 electrode placements, remission and response rates in patients with unipolar depression (n = 170) and with bipolar depression (n = 50) were equivalent, achieving more than 60% within 3 weeks.²⁰ These results confirm the findings of 2 other recent studies, that bipolar depression responds as well to ECT unipolar depression.^{21,22} Moreover, in these studies it was found that bipolar depression responds even faster than unipolar depression.^{21,22} In one trial comparing the remission rates of patients with unipolar depression

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	ble 1 Indications for ECT as a first-line treatment: CANMAT guideline ¹⁹	
	Acute suicidal ideation ^a	Rapidly deteriorating physical status ^b
	MDE with psychotic features ^a	Catatonia ^b
	Treatment-resistant depression ^a	Prior favourable response ^b
		Repeated medication intolerance ^b
		During pregnancy, for any of the above indications ^b
		Patient choice°
 ^a Evidence from at least 2 RCTs with adequate sample sizes, preferably placebo-controlled, and (or) meta-analysis with narrow confidence intervals ^b Evidence from nonrandomized, controlled prospective studies or case series or high-quality retrospective studies ^c Expert opinion and (or) consensus 		

(n = 17), with bipolar I depression (n = 46), and with bipolar II depression (n = 67), not responding to pharmacological treatment, remission rates in the bipolar I and bipolar II group were 65.3% and 56.7%, respectively. However, the best results were achieved by unipolar depressed patients, with 70.5% remission rate.23 None of these studies found that mania was precipitated by ECT. Given the growing evidence to discourage the use of ADs in the treatment of bipolar depression, because of poor effectiveness and possible destabilizing effects, and the fact that patients with bipolar depression often fail to achieve full remission, ECT should be considered earlier in the treatment course.²² Interestingly, this line of thinking is acknowledged in a recently published psychopharmacology algorithm, stating that in bipolar depression, after initial evaluation and diagnosis, the psychiatrist should first assess whether there is an urgent indication for ECT before considering other treatment options.²⁴

Depressive Mood Disorders With Psychosis. Although remission rates in MDD are high, in patients suffering from depressive disorder with psychotic features, even higher remission rates can be achieved, with improvement in symptomatology often more robust, compared with nonpsychotic patients. In 253 patients with nonpsychotic (n = 176) and psychotic (n = 77) unipolar major depression, the overall remission rate after an acute course of bilateral ECT was 87%.⁶ The remission rate for the psychotic patients was 95%, while for the nonpsychotic patients it was 83%, even though the psychotic patients were sicker at baseline, with a pretreatment mean HDRS score of 37.8, compared with 33.8 for the nonpsychotic patients with depression. The decrease in HDRS scores from baseline measures was significantly greater for the psychotic, compared with the nonpsychotic, patients with depression. Remission occurred within a 2-week period. In a Dutch retrospective study,²⁵ psychotic patients with depression (n = 26) showed both significantly higher response (92%, compared with 55%) and remission rates (57%, compared with 24%) than nonpsychotic patients with depression (n = 29). The mean number of treatments needed to achieve full remission (an HDRS score 7 or less), was lower in the deluded sample (10.4) than in the nondeluded sample (13.7). Remission rates with pharmacotherapy are significantly lower.²⁶ A recent multicentre RCT, with 122 patients with psychotic depression, revealed remission rates of 28.2% with 7 weeks of venlafaxine (375 mg/d) and 41.5% with venlafaxine–quetiapine (375 mg/d to 600 mg/d). Given this evidence, ECT should be considered as a first-line treatment when psychotic features are present during an MDE.^{19,27,28}

Suicide Risk. The presence of suicidal thoughts and acts is another major reason to consider ECT earlier in the treatment course, as a rapid reduction in expressed suicidal intent can be expected. In the CORE study, 131 of 444 patients with unipolar depression reported suicidal thoughts and acts (a score of 3 or 4 on item 3 on the HDRS). Expressed suicide intent was shown to be relieved (score 0) within 1 week or 3 ECT sessions in 38%, within 2 weeks in 61%, and in 81% by the end of the treatment.²⁹ It is of note that all patients in this large trial suffered from primary mood disorders. Suicidal tendencies are indications for ECT "in the context of an otherwise ECT-responsive mood or psychotic disorder,"^{30, p 111} as stressed by Rasmussen and Lineberry.

Mania

In mania, both pure mania and mixed mania, reported remission rates are comparable to those seen in depression.³¹ In 3 recent trials, which were designed to study different ECT techniques, ECT proved highly efficacious. Thirty-six manic inpatients, with a baseline YMRS score of about 42, were randomized to either bifrontal ECT or bitemporal ECT. By the end of the study, after 21 days, 87.5% of the bifrontal group and 72.2% of the bitemporal group had met the response criterion, that is, 50% reduction from baseline YMRS.³² In a similar trial, also comparing bifrontal and bitemporal ECT, all completers (18/28) showed a reduction greater than 50% on YMRS scores (mean baseline YMRS 37.1; YMRS at treatment end 8.3).³³ A third recent trial,³⁴ designed to compare different stimulus intensities, showed that 88% of 50 manic patients with a minimum baseline YMRS score of 26, who had not responded to medication, remitted (YMRS score of less than 10) after a mean number of 3.5 treatment sessions or 12 days. ECT is generally used in patients who are intolerant of, or refractory to, lithium and other antimanic agents. However, ECT need not be considered a last resort treatment in mania. In severe cases where the patient is at significant risk of harming self or others, requiring physical restraint or large doses of sedatives, or when the symptoms are life-threatening owing to exhaustion, ECT should be considered earlier.^{27,34} In delirious or excited mania, a clinical condition that remains ill-defined, where mania and delirium coincide, patients present with a rapid onset of excitement, restlessness, paranoia, fever, tachycardia, and hypertension, often accompanied by catatonic signs. In this lifethreatening condition, the efficacy of ECT is comparable to its efficacy in catatonia, and can thus offer prompt relief.^{35,36}

Schizophrenia

Although in some eastern European³⁷ and Asian countries³⁸ schizophrenia remains the first indication for ECT, in western Europe and America schizophrenia is not a common basis for referral. Nevertheless, high-quality evidence from 9 RCTs shows a short-term, small but significant, improvement in global symptom severity³⁹ in patients with or without concurrent antipsychotic medication.⁴⁰ Overall the evidence for the efficacy of ECT in psychotic disorders is less robust than in mood diorders, and the position of ECT in schizophrenia is still undefined. A treatment with ECT in patients with severe and clozapine-resistant psychosis should, however, not be withheld.

Catatonia

The most dramatic improvement with ECT is encountered in patients presenting with catatonia, regardless of the underlying condition.⁴¹ Catatonia is a consideration in every patient with dysregulation of motor behaviour, particularly those in whom changes in consciousness and mood are also present.⁴² These patients present with stupor, mutism, refusal to eat or drink, automatic obedience (responding to tactile stimuli despite instruction to the contrary), excitement or hypokinesis, or repetitive movements. They hold abnormal rigid body positions, and show motor and other behavioural resistance to following simple requests or commands.42 Catatonia is common among chronically ill psychotic patients, but is more frequent in patients with mood disorders.⁴³⁻⁴⁵ In pediatric populations, catatonia is reported among those with mental retardation and autistic spectrum disorder.^{46,47} Recently, it was shown that most, if not all, patients with anti-N-methyl-D-aspartate-receptor encephalitis present with catatonic symptoms.48 Malignant catatonia is a syndrome of acute onset, fever, and autonomic instability of life-threatening dimensions. Both the NMS and the toxic serotonin syndrome are viewed as malignant catatonia.41 Benzodiazepines are the treatment of first choice in catatonia, with reported remission rates of 80% or higher within days.^{42,43} Should initial treatment with benzodiazepines fail, ECT is to be used without delay. RCT evidence is, apart from a small trial in 18 patients with nonaffective catatonia, not responsive to lorazepam, showing superiority of ECT over risperidone,49 lacking. However, there is an extensive case literature, confirming the clinical experience of extremely high rates of response of catatonia (including NMS) after the first few ECT treatments. When catatonia is relieved, continuing ECT can also treat the underlying psychiatric

disorder.⁴¹ The recent CANMAT guideline for the treatment of MDDs considers ECT as a first-line treatment in case of catatonic signs (Table 1).¹⁹

Personality Disorders

ECT is not helpful in patients with a lifelong history of emotional dysfunction, situational maladjustment, or PD.²⁷ However, the presence of a comorbid PD should not exclude patients from ECT treatment for a severe, medication-resistant depression or suicidality. Although the presence of a comorbid BPDS will lower the chance of achieving a favourable response to ECT, patients with a depression and a PD other than BPD will respond to ECT as well as depressed patients without a PD.⁵⁰ This was shown in the acute phase of the CUC continuation study.⁸ Patients with a primary diagnosis of unipolar major depression and a comorbid BPD (n = 20) achieved lower remission rates (20%), compared with the group with other PD (n = 42; remission rate 52.4%) and the group with no PD (n = 77; remission rate 65.3%).

Impediments and Risks

Pre-ECT Evaluation

ECT is a safe procedure. There are no absolute contraindications for its use. Apart from a clinical history, a physical examination, and a review of laboratory data, in healthy patients no other examinations are mandatory. Laboratory testing can be tailored to the patient's medical history and medications, and electrocardiograms are advisable in patients aged 50 years and older.⁵¹

Consent

A written informed consent is a necessary part of ECT in the United States and Canada. For the consent to be deemed valid, it must include information about benefits and risks of the treatment, information about alternatives to ECT, and an assessment of the patient's decision-making capacity.³ Several educational aids can help the practitioner in providing adequate information, such as *Shock*, the book⁵² and DVD⁵³ by Dukakis, or the recent *Electroconvulsive Therapy: A Guide for Professionals and Their Patients*, by Fink.²⁷

Monotherapy or Combination?

While most guidelines advise against the combination of ADs and ECT because of a lack of advantage and a possible increase in side effects, evidence emerges from a large RCT that the addition of nortryptiline, more than venlafaxine, might enhance the efficacy of ECT in MDD.⁵⁴ However, these data have to be replicated before altering clinical practice.

In patients with schizophrenic psychosis, it is suggested that the combination of ECT and antipsychotics results in faster and more pronounced symptomatic improvement than monotherapy with either of these treatments,^{55,56} and some authors have given preference to clozapine in combination with ECT.^{57,58} However, to date, the superiority of the ECT

antipsychotics combination has not been proven,³⁹ even though most recent guidelines advise to combine ECT and antipsychotics for the treatment of clozapine-resistant schizophrenic psychosis.

Some authors have cautioned strongly against the combination of lithium and ECT, because of a higher risk of neurological complications and cognitive side effects. However, hundreds of patients are described as without increase in complications, memory impairment, or recovery times.⁵⁹ If ongoing lithium has provided clear benefit, it is probably safe to continue it during index ECT at a low blood level.⁵⁹ Apart from lithium, anticonvulsants are used increasingly in BD. Although the combination of anticonvulsants and ECT is not paradoxical,⁶⁰ data regarding the efficacy of the combination are lacking. Anticonvulsants do not necessarily have to be tapered off before starting ECT, but can have a negative influence on the length of ECT-induced seizures.⁶⁰ Recent data suggest that this is not the case with therapeutic doses of lamotrigine.⁶¹

Side Effects

Since its introduction in 1938, the technique of ECT has changed considerably. The routine use of hypnotics and muscle relaxants has eradicated serious complications such as muscle tears or bone fractures. The use of a stimulus with a brief pulse instead of a sine wave, continuous oxygenation, and a better control of blood pressure have lowered the risks of prolonged memory loss.

Today, headache and nausea are the most common immediate side effects, which can be treated (prophylactically) with analgesic and antiemetic drugs. General disorientation in the immediate postictal phase is a common but self-limiting occurrence.⁶² After ECT, patients can experience difficulties in their ability to acquire and retain new information. This anterograde memory impairment will, for the most part, recover to baseline levels by 1 month follow-up.62 Retrograde amnesia, the inability to recall past events and information learned before the treatment, has been reported especially after bilateral ECT,62 and objective measures found it to be relatively short lived (less than 6 months posttreatment).⁶³ The nature and extent of retrograde memory impairment, of which patients are complaining most often,⁶⁴ remain, however, to be systematically examined.⁶² Efforts are made to further minimize cognitive side effects, by using different electrodepositions and waveforms. However, the 3 commonly used electrode placements are highly effective, and their cognitive profile does not seem to differ dramatically.¹⁰ Recent studies have shown convincingly that the use of a stimulus with an ultrabrief pulse width (0.3 ms) produced no deterioration in a wide range of cognitive measures.^{65,66} However, there remains a concern of lower AD efficacy of ultrabrief ECT, with patients needing additional treatment sessions to achieve results comparable to those achieved with standard pulse ECT.67-69 Nevertheless, patients who were treated with this technique exhibited a high degree of satisfaction.⁷⁰ The recent evidence is a step forward toward further tailoring the treatment to the patient. In patients

with severe cases, where the definite and fast improvement of a life-threatening condition outweighs the possible emergence of cognitive side effects, standard pulse ECT is, without any doubt, the treatment of first choice, with any of the 3 electrode positions. In patients for whom avoiding cognitive side effects is of greater importance, an ultrabrief stimulus can be used, with a unilateral or bifrontal placement.⁶¹

What To Do After Successful ECT?

As with other psychiatric treatments, stopping ECT as soon as remission is achieved, caries a high risk of relapse. Relapse rates as high as 64% to 84% are reported, and relapse predominantly occurs within the first 6 months after a successful treatment course.8,71 Adequate post-ECT treatment, either pharmacotherapy or C-ECT, is indispensable. In a seminal paper, Sackeim et al⁸ randomly assigned 84 patients with MDD, remitted with ECT, to receive continuation treatment with placebo, nortriptyline, or a combination of nortriptyline and lithium. During a 24week follow-up period, 84% of placebo-treated patients and 60% of patients treated with nortrityline relapsed. The combination of nortriptyline and lithium was able to reduce the relapse rate to 39%.8 Using a similar design, the CORE group compared the lithium-nortrityline combination and C-ECT in 184 patients with unipolar depression who had remitted with a course of bilateral ECT. Relapse rates were 37%, during a period of 6 months, in both the C-ECT and the maintenance pharmacotherapy groups. It is noteworthy that the treatment schedule for C-ECT was fixed, that is, a total of 10 treatments during 5 months, starting weekly treatments (4), then biweekly (4), and then monthly (2). Most clinicians are convinced that relapse rates can be further reduced by adapting treatment schedules to symptom emergence in each patient,⁷² as was shown in a Swedish naturalistic cohort study.73 Treatment should be individualized, administering the minimum number of treatments necessary to achieve sustained remission. In patients with BD, it is often difficult to prolong the intertreatment intervals beyond 2 weeks.^{74,75} Controlled studies on C-ECT in mood disorders are scarce; in schizophrenia, they are virtually lacking. However, the few available data support the continuation of ECT in combination with antipsychotics in patients who have responded to an acute treatment with this combination.⁷⁶

There is no consensus on the length of C-ECT. As maintenance pharmacotherapy is advised to be lifelong in patients who are severely ill and medication-refractory, C-ECT should also be open-ended,⁷⁴ with reevaluations of the treatment plan at least every 6 months.²⁸ There is neither reason to set a lifetime maximum number of treatments²⁸ nor evidence that tolerance develops to ECT. Relapses during C-ECT usually respond rapidly to further ECT and to increases in treatment frequency.^{75,77}

Conclusions

In the past decade, several large multicentre studies have confirmed the AD efficacy of ECT in MDEs and BD.

However, the superior efficacy of ECT is not reflected in most of the current treatment algorithms that recommend ECT as a last resort. The presence of psychotic symptoms, suicidal thoughts and acts, or catatonic signs should prompt the clinician to consider ECT earlier in the treatment course. Fear of side effects, perhaps "as a result of professional and public preoccupation with the effects of ECT on memory and the failure to fairly consider the treatment's benefits compared with alternative treatments,"9, p 332 may be a factor explaining the reluctance of clinicians and patients alike to accept this highly effective treatment. However, recent research has shown that patients show high degrees of satisfaction, that cognitive side effects are generally transient, and that effective ECT can be achieved with minimal cognitive side effects. Research to further minimize cognitive side effects, without sacrificing efficacy, is ongoing. Whether concurrent pharmacotherapy use enhances the efficacy of ECT remains unclear. All the more, the need for adequate continuation treatment, either pharmacotherapy or C-ECT, after a successful ECT course is of vital importance to maintain the benefits achieved, and should be the focus of future research.

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Résumé : Ce que nous savons sur l'électroconvulsothérapie et son utilité pour le psychiatre clinicien

Dans cette revue narrative, les connaissances actuelles sur l'efficacité et la pratique de l'électroconvulsothérapie (ECT) sont examinée, et son utilité pour le psychiatre clinicien est évaluée. Dans les dix dernières années, plusieurs études à grande échelle ont confirmé la supériorité significative de l'ECT dans le traitement d'états psychiatriques graves et réfractaires, comme le trouble dépressif majeur et le trouble bipolaire. Cependant, l'efficacité de l'ECT n'est pas reflétée dans les algorithmes de traitement actuels, où l'ECT est souvent réservée en dernier recours. Toutefois, les caractéristiques cliniques comme la présence de symptômes psychotiques, de risque suicidaire, ou de signes catatoniques devraient pousser les cliniciens à envisager l'ECT plus tôt dans le cours du traitement. L'ECT est une intervention sécuritaire, dont l'utilisation ne comporte pas de contrindications absolues. Néanmoins, les craintes et les plaintes des patients doivent être accueillies, et les patients doivent être adéquatement informés des avantages escomptés et des risques possibles, comme les problèmes de mémoire, qui sont généralement transitoires. La recherche se penche à l'heure actuelle sur la manière de minimiser encore plus les problèmes de mémoire, tout en maintenant une efficacité supérieure. Un traitement continu adéquat, soit de pharmacothérapie, soit de continuation de l'ECT, après un cours réussi d'ECT est d'une importance capitale pour maintenir les avantages réalisés et devrait faire l'objet des futures recherches.