



Disponible en ligne sur

ScienceDirect
www.sciencedirect.com

Elsevier Masson France

EM|consulte
www.em-consulte.com



Commentary

ECT: An essential therapy in psychiatry

ECT : une thérapie essentielle en psychiatrie

Anne Sauvaget^{a,b,*}, Samuel Bulteau^{a,c,d}, Filipe Galvao^{a,e}, David Szekely^{a,f},
Philippe Fossati^{a,g,h}, Emmanuel Poulet^{a,e,i,j,k}

^a Association Française de Psychiatrie Biologique et de Neuropsychopharmacologie (AFPBN), STEP Section (Stimulation transcrânienne en psychiatrie), Saint-Germain-en-Laye, France

^b Nantes Université, CHU Nantes, Movement, Interactions, Performance, MIP, UR 4334, 44000 Nantes, France

^c CHU Nantes, Department of Addictology and Liaison Psychiatry, Inserm-U1246 SPHERE University of Nantes and University of Tours, Nantes, France

^d UMR 1246 SPHERE, University of Nantes, University of Tours, INSERM, Nantes, France; CHU Nantes, Department of Addictology and Psychiatry, 44000 Nantes, France

^e Centre Hospitalier le Vinatier, 69500 Bron, France

^f Department of Psychiatry, Centre Hospitalier Princesse-Grace, 98000 Monaco

^g Paris Brain Institute - Institut du Cerveau (ICM), UMR 7225/UMRS 1127, CNRS/INSERM, Sorbonne university, Paris, France

^h Department of psychiatry, Pitié-Salpêtrière hospital, DMU Neuroscience, Sorbonne university, Assistance publique-Hôpitaux de Paris (AP-HP), Paris, France

ⁱ INSERM, U1028, CNRS, UMR5292, Lyon Neuroscience Research Center, PSYR2 Team, 69000 Lyon, France

^j Lyon University, Université Lyon 1, 69100 Villeurbanne, France

^k Department of Emergency Psychiatry, University Hospital Edouard Herriot, Hospices Civils de Lyon, 69000 Lyon, France

ARTICLE INFO

Article history:

Received 6 February 2022

Accepted 4 May 2022

Available online xxx

Keywords:

ECT

Electroconvulsive therapy

Medical device

Guidelines

Psychiatry

ABSTRACT

At a time when innovations in psychiatry are booming, particularly in the field of medical devices, we thought it necessary, as members of French Society for Biological Psychiatry and Neuropsychopharmacology (AFPBN), to reconsider one of the oldest medical devices in psychiatry: the ECT apparatus. First, we recall the regulatory aspects of ECT. National guidelines define means of implementation and conditions of administration of ECT. Second, we remind of the indications and levels of evidence of ECT in the main psychiatric disorders, including catatonia. Then, we synthesize the place of ECT alongside other brain stimulation therapies, especially repetitive Transcranial Magnetic Stimulation (rTMS). Furthermore, we explain the general effects of ECT: increased neuronal plasticity and neurogenesis, enhancement of the stress axis, resistance to oxidative stress, improved vascular endothelial function, activation of microglia and astrocytes, decrease in inflammatory events by upregulation of neuroinflammatory cytokines, and production of mitochondrial ATP. These effects appear from the first sessions and continue during the course of ECT treatment, suggesting activation of endogenous neuroprotection. Finally, we remember that most patients perform as well or better on neuropsychological assessments after ECT, relative to pre-ECT results, and this improvement continues over the following months. Memory disorders reported post-ECT are not all attributable to ECT. They may be subjective in nature or linked to residual depressive (and possibly comorbid neurodegenerative) symptoms later attributed to ECT, on the basis of preexisting negative representations. We urgently need to reemphasize the crucial role of ECT in psychiatric treatment strategies as well as the need to update ECT recommendations.

© 2022 L'Encéphale, Paris.

R É S U M É

À l'heure où les innovations thérapeutiques en psychiatrie sont en plein essor, notamment dans le champ du dispositif médical, il nous a paru essentiel, en tant que société savante (Association Française de Psychiatrie Biologique et Neuropsychopharmacologie), de faire un point sur l'une des thérapies les plus anciennes en psychiatrie utilisant un dispositif médical : l'électroconvulsivothérapie (ECT). En France, la pratique de l'ECT est strictement encadrée et réglementée par des recommandations nationales, qui en

Mots clés :

ECT

Électroconvulsivothérapie

Dispositif médical

Recommandations

Psychiatrie

* Corresponding author at: CETIP, Psychiatrie Universitaire, Hôtel Dieu 3ème Nord - aile HNB, 1, place Alexis-Ricordeau, 44000 Nantes, France.

E-mail address: anne.sauvaget@chu-nantes.fr (A. Sauvaget).

définissent les modalités de mise en œuvre et les conditions de réalisation. Dans tous les cas, le recueil du consentement du patient est indispensable. Dans les situations où le patient n'est pas en mesure de consentir, il est obligatoire de s'appuyer sur la personne de confiance désignée par le patient, et, pour les patients majeurs protégés, de leur représentant légal. Un bilan pré-thérapeutique, clinique et paraclinique, est réalisé avant la mise en œuvre du traitement par ECT, pour éliminer les contre-indications éventuelles, à l'ECT ou à une anesthésie. Nous rappelons les principales indications psychiatriques, de l'ECT, avec ses niveaux de preuve, selon les recommandations internationales. La question du positionnement de l'ECT par rapport aux autres techniques de neuromodulation, notamment la rTMS est fréquemment évoquée. Ces deux techniques ont toute leur place car leurs indications ne se superposent que très partiellement. La rTMS a une efficacité bien démontrée et est indiquée dans les dépressions à niveau bas de résistance, après échec à un antidépresseur et lorsque le risque vital n'est pas engagé. Les taux de réponse à la rTMS dans la dépression sont inférieurs à ceux de l'ECT : ils varient entre 40 et 50 % et les taux de rémission entre 25 et 30 %. Les effets généraux de l'ECT sont : augmentation de la plasticité neuronale et de la neurogenèse, amélioration de l'axe du stress, de la résistance au stress oxydatif, et de la fonction endothéliale vasculaire, activation de la microglie et des astrocytes, diminution des phénomènes inflammatoires, par la régulation à la hausse des cytokines neuro-inflammatoires, production d'ATP mitochondrial. Au plan neuronal, les ECT entraînent un remodelage synaptique en lien avec la libération de neurotransmetteurs (GABA, monoamines), mais aussi de facteurs neurotrophiques indispensables à la plasticité cérébrale. En termes neuromorphologiques et de connectivité fonctionnelle, les ECT régénèrent et améliorent les régions suivantes : gyrus dentelé de l'hippocampe, gyri frontal supérieur et moyen, cortex cingulaire antérieur sous-génual. Ces effets apparaissent dès les premières séances et se poursuivent au cours du traitement ECT, suggérant qu'une neuroprotection endogène puisse être mobilisée. L'ECT améliore les fonctions exécutives corrélativement à l'amélioration de la dépression. La majorité des patients ont des bilans neuropsychologiques stables ou améliorés en post-ECT comparativement aux performances avant l'ECT, et l'amélioration se poursuit dans les mois qui suivent l'ECT. En outre, l'incidence des maladies neurodégénératives type maladie d'Alzheimer diminue significativement chez les sujets atteints de troubles de l'humeur, bénéficiant d'ECT versus ceux qui n'en bénéficient pas. Le principal effet indésirable mnésique de l'ECT concerne la mémoire antérograde (apprentissage à mesure récents). Ce phénomène, fréquent pendant la cure initiale (2 séances/semaines), est rapidement résolutif, le plus souvent dans les 15 jours suivant la dernière séance, et au maximum à 2 mois. Les troubles de la mémoire rétrograde (événements anciens) peuvent dans certains cas durer jusqu'à 6 mois voire au-delà, avec un retentissement fonctionnel moindre que ne l'aurait une atteinte des fonctions exécutives ou de la mémoire antérograde. Les troubles mnésiques rapportés en post-ECT ne sont pas tous imputables à l'ECT mais peuvent être de nature subjective, et/ou liés à la symptomatologie dépressive résiduelle (et éventuellement neurodégénérative comorbide), puis attribués à l'ECT à posteriori, en fonction de représentations négatives préexistantes. A ce titre la qualité de l'information prodiguée au patient avant l'ECT est primordiale. Les effets mnésiques de l'ECT sont à mettre en perspective avec les effets thérapeutiques de l'ECT, traitement le plus efficace des états dépressifs sévères avec : jusqu'à 80 % de réponses et 60 % de rémissions ; une amélioration de la qualité de vie ; une diminution de la mortalité et des réhospitalisations. En conclusion, l'ECT possède des effets à la fois structuraux et fonctionnels, sur le système nerveux central mais aussi systémiques, de nature neuro-protectrice, neurotrophique et améliore la plasticité cérébrale, permettant de contre-carrer et réparer au niveau biologique les mécanismes physiopathologiques à l'origine de nombreux troubles neuropsychiatriques (neuroprogression pathologique). Il est urgent de réaffirmer l'importance cruciale de ce dispositif médical dans les stratégies thérapeutiques en psychiatrie et sa place de l'ECT dans l'organisation des soins. L'actualisation des recommandations sur l'ECT est désormais plus que nécessaire.

© 2022 L'Encéphale, Paris.

At a time when therapeutic innovations in psychiatry are booming, particularly in the field of medical devices, the authors, as representatives of a learned society, thought it necessary to reconsider one of the oldest medical devices in psychiatry: electroconvulsive therapy (ECT) machines.

Regulatory aspects

It should firstly be recalled that, in France, ECT is subject to strict national guidelines that define means of implementation and conditions of administration [1]. Institutions offering ECT are certified by the French National Authority for Health (Haute Autorité de santé, HAS) and must have obtained the approval of their Regional Health Agency (Agence Régionale de Santé).

In all cases, patient consent is prerequisite. When patients are unable to express their will, consent must be obtained from the personal representative chosen by the patient or, in the case of

adults under guardianship, the designated guardian. Consent is later sought directly from patients, when improvement of their clinical condition allows it, so that they may make therapeutic decisions. For consolidation and maintenance ECT to prevent relapse or recurrence of their illness, patients must provide consent biannually.

Clinical, psychiatric, and preanesthesia evaluations are performed before commencing an ECT program, to rule out contraindications to either ECT or anesthesia. Intracranial hypertension is currently the only absolute contraindication to ECT because of the risk of cerebral involvement, due to increased intracranial pressure during a seizure. The other contraindications, which are relative, are based on an assessment of the benefit/risk ratio for each patient. They take into account the risks inherent to anesthesia and curarization, of a cardiovascular, respiratory and allergic nature, or to ECT, of a neurological or cardiovascular nature [1].

Evidence and guidelines

ECT can be offered as a curative procedure for indications supported by high levels of evidence, depending on disease progression and degrees of resistance to other pharmacological and psychotherapeutic treatments, and for prevention of relapses or recurrences.

Extensive clinical research has been conducted over the years to determine the indications for this treatment and define the conditions for its prescription. According to the main recommendations published by learned societies to date, (ANAES [1], World Federation of Societies of Biological Psychiatry (WFSBP) [2], Royal Australian and New Zealand college of psychiatry [3], Canadian Network for Mood and Anxiety Treatments [4], National Institute Clinical Excellence (NICE) [5], ECT should no longer be considered a “last chance” treatment. It can or should be offered as first-line therapy for severe forms of depression, when the prognosis is life-threatening and a rapid response may be expected. This is the case in depression with psychotic or catatonic characteristics, when there is major risk of suicide, when refusal to eat or drink exposes the individual to risk of death, or in the absence of any other therapeutic solution. Apart from these emergency situations, ECT is recommended as a third-line therapy for treatment-resistant depression.

In non-treatment-resistant depression, ECT is more effective than sham ECT and pharmacotherapy, with response rates between 60% and 80% and remission rates between 50% and 60% [6].

Psychotic and catatonic features are strongly predictive of a response. Recent CANMAT recommendations summarize the levels of evidence for ECT in depression, ranging from Level 1 (backed by scientific evidence) to Level 4 (expert opinion, but no scientific demonstration) [4]. There is Level 1 evidence for ECT in cases of intense suicidal ideation, psychotic features, or resistant depression; and Level 3 evidence in cases of intolerance to medication, catatonic characteristics, a history of good response to ECT, rapid deterioration in physical condition, or during pregnancy [7].

In schizophrenia, ECT is recommended as a third-line therapy, after failure of a proper antipsychotic treatment. Recent work has demonstrated the value of ECT in treatment-resistant schizophrenia, potentiating clozapine (commonly administered for resistant schizophrenia) and having a response rate of 50% [8]. This indication is supported by Level 2 evidence according to the RANZCP [3,8] and a grade 4 WFSBP recommendation [2].

In catatonia, associated with high morbidity and mortality, and for which there are few specific therapeutic solutions, numerous case studies have documented the effectiveness of ECT. The FDA recently recognized catatonia as one of two ECT indications [9]; and other guidelines recommend ECT as a first-line treatment for catatonia [1,5].

In manic episodes of bipolar disorder, the effectiveness of ECT is recognized for forms refractory to drug treatment—but these are rare, and ECT is not frequently indicated for this condition.

Other indications have been evaluated, including Parkinson's disease, neuroleptic malignant syndrome, and refractory epilepsy, but they are corroborated by lower levels of evidence due to the paucity of randomized controlled studies. Due to a favorable efficacy-to-tolerance ratio, ECT for severe forms of depression may be administered during any trimester of pregnancy.

Role of ECT in relation to other neurostimulation therapies

The question of the place of ECT alongside other brain stimulation therapies, especially repetitive Transcranial Magnetic Stimulation (rTMS), is frequently raised. ECT and rTMS are not equivalent: their indications only slightly overlap. The efficacy of rTMS has been well established in depression with a low level of

resistance, after failure of an antidepressant and when the patient's condition is not life-threatening [10]. Response rates vary from 40% to 50%, which is lower than for ECT, and remission rates range from 25% to 30% [10]. There is less consensus on the validity of including transcranial Direct Current Stimulation, Vagus Nerve Stimulation, and Deep Brain Stimulation in the therapeutic arsenal, due to lower levels of evidence and fewer studies evaluating them [4].

Mechanisms

The general effects of ECT are: increased neuronal plasticity and neurogenesis, enhancement of the stress axis, resistance to oxidative stress, improved vascular endothelial function, activation of microglia and astrocytes, decrease in inflammatory events by upregulation of neuroinflammatory cytokines, and production of mitochondrial ATP. At the neuronal level, ECT cause synaptic remodeling in connection with the release of neurotransmitters (GABA and monoamines) as well as neurotrophic factors essential for cerebral plasticity. In terms of neuromorphology and functional connectivity, ECT regenerates and functionally enhances the hippocampal dentate gyrus, superior and middle frontal gyri, and subgenual anterior cingulate cortex. These effects appear from the first sessions and continue during the course of ECT treatment, suggesting activation of endogenous neuroprotection [11].

Beneficial and adverse cognitive effects

ECT has positive cognitive effects that have been described in detail. It improves executive functions while relieving depression, which has a very negative cognitive impact [12]. Most patients perform as well or better on neuropsychological assessments after ECT, relative to pre-ECT results, and this improvement continues over the following months. In addition, the incidence of neurodegenerative diseases such as Alzheimer's disease decreases significantly in subjects with mood disorders who undergo ECT, in comparison with those who do not.

The main adverse effect of ECT on memory is anterograde amnesia (i.e., loss of memory of later events). It frequent occurs during the initial course of treatment (2 sessions/week) and rapidly resolves (usually in the 15 days following the last session, and in 2 months at most). Retrograde amnesia usually does not exceed 6 months, with less functional impact than impairment of executive functions or anterograde amnesia would have [13]. Patients receiving maintenance ECT (e.g., once a month) exhibit good cognitive tolerance.

Memory disorders reported post-ECT are not all attributable to ECT. They may be subjective in nature or linked to a residual depressive (and possibly comorbid neurodegenerative) symptoms later attributed to ECT, on the basis of preexisting negative representations [14]. This underscores the importance of patient education. ECT can be an alternative to further medication and limits the risk of iatrogenesis, particularly in the elderly. Stimulation parameters (e.g., duration of stimulus, strength of stimulus, and positions of electrodes) can be adapted on a case-by-case basis to optimize tolerance.

The effects of ECT on memory should be put into perspective by recognizing its therapeutic effects: ECT is the most effective treatment for severe depressive states, offering high rates of response (80%) and remission (60%), enhanced quality of life, lower mortality, and less rehospitalization [15–18].

Conclusion

In addition to systemic effects, ECT has structural and functional effects, of a neuroprotective and neurotrophic nature, on the central nervous system. It improves cerebral plasticity and makes it

possible to counteract and repair, on the biological level, the physiopathological mechanisms at the origin of many neuropsychiatric disorders (neuroprogression). We urgently need to reemphasize the crucial role of ECT in psychiatric treatment strategies [19] and update ECT recommendations [20].

Disclosure of interest

The authors declare that they have no competing interests.

Funding source

No funding was received to write this article.

Author contributions

All the authors (AS, SB, FG, DS, PF, EP) wrote the manuscript together and approved the final version.

Acknowledgments

We kindly thank Jason Miller for his editing assistance.

References

- [1] ANAES. Indications et modalités de l'électroconvulsivothérapie. Fédération Française de Psychiatrie 1997.
- [2] Schläpfer TE, George MS, Mayberg H. WFSBP Guidelines on brain stimulation treatments in psychiatry [Internet]. World J Biol Psychiatry 2010;11:2–18 [cited 2022 Feb 6] Available from: <https://pubmed.ncbi.nlm.nih.gov/20146648>.
- [3] Weiss A, Hussain S, Ng B, et al. Royal Australian and New Zealand College of Psychiatrists professional practice guidelines for the administration of electroconvulsive therapy. Aust N Z J Psychiatry [Internet] 2019;53(7):609–23 [cited 2022 Feb 6] Available from: <https://pubmed.ncbi.nlm.nih.gov/30966782>.
- [4] Milev RV, Giacobbe P, Kennedy SH, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) 2016 clinical guidelines for the management of adults with major depressive disorder: Section 4. Neurostimulation treatments [Internet]. Can J Psychiatry 2016;61:561–75 [cited 2022 Feb 6] Available from: <https://pubmed.ncbi.nlm.nih.gov/27486154>.
- [5] National Institute for Clinical Excellence. Guidance on the use of electroconvulsive therapy. NICE 2010.
- [6] Geddes J, Carney S, Cowen P, et al. Efficacy and safety of electroconvulsive therapy in depressive disorders: a systematic review and meta-analysis. Lancet (London, England) [Internet] 2003;361(9360):799–808 [cited 2022 Feb 6] Available from: <https://pubmed.ncbi.nlm.nih.gov/12642045>.
- [7] Tørring N, Sanghani SN, Petrides G, et al. The mortality rate of electroconvulsive therapy: a systematic review and pooled analysis [Internet]. Acta Psychiatr Scand 2017;135:388–97 [cited 2022 Feb 6] Available from: <https://pubmed.ncbi.nlm.nih.gov/28332236>.
- [8] Petrides G, Malur C, Braga RJ, et al. Electroconvulsive therapy augmentation in clozapine-resistant schizophrenia: A prospective, randomized study. Am J Psychiatry [Internet]. 2015 2015;172(1):52–8 [cited 2022 Feb 6] Available from: <https://pubmed.ncbi.nlm.nih.gov/25157964>.
- [9] Food and Drug Administration. Neurological devices; reclassification of electroconvulsive therapy devices; effective date of requirement for premarket approval for electroconvulsive therapy devices for certain specified intended uses. Final order. Fed Regist [Internet] 2018;83(246):66103–24 [cited 2022 Feb 6] Available from: <https://pubmed.ncbi.nlm.nih.gov/30596410>.
- [10] Bulteau S, Guirrette C, Brunelin J, et al. Mood disorders: When should we use repetitive transcranial magnetic stimulation? Press Médicale [Internet] 2019;48(6):625–46 [cited 2022 Feb 6] Available from: <https://pubmed.ncbi.nlm.nih.gov/31155435>.
- [11] Yrondi A, Sporer M, Péran P, et al. Electroconvulsive therapy, depression, the immune system and inflammation: A systematic review [Internet]. Brain Stimul 2018;11(6):29–51 [cited 2022 Feb 6] Available from: <https://pubmed.ncbi.nlm.nih.gov/29111078>.
- [12] Porter RJ, Baune BT, Morris G, et al. Cognitive side-effects of electroconvulsive therapy: what are they, how to monitor them and what to tell patients. BJPsych Open [Internet] 2020;6(3) [cited 2022 Feb 6] Available from: <https://pubmed.ncbi.nlm.nih.gov/32301408>.
- [13] Osler M, Røzang MP, Christensen GT, et al. Electroconvulsive therapy and risk of dementia in patients with affective disorders: a cohort study. Lancet Psychiatry [Internet] 2018;5(4):348–56 [cited 2022 Feb 6] Available from: <https://pubmed.ncbi.nlm.nih.gov/29523431>.
- [14] Sigström R, Nordenskjöld A, Jureus A, et al. Long-term subjective memory after electroconvulsive therapy. BJPsych Open [Internet] 2020;6(2):348–56 [cited 2022 Feb 6] Available from: <https://pubmed.ncbi.nlm.nih.gov/32148217>.
- [15] Giacobbe P, Rakita U, Penner-Goeke K, et al. Improvements in health-related quality of life with electroconvulsive therapy: a meta-analysis. J ECT 2018;34(2):87–94.
- [16] Liang CS, Chung CH, Ho PS, et al. Superior anti-suicidal effects of electroconvulsive therapy in unipolar disorder and bipolar depression. Bipolar Disord 2018;20(6):539–46.
- [17] McCall WV, Lisanby SH, Rosenquist PB, et al. CORE/PRIDE Work Group Effects of continuation electroconvulsive therapy on quality of life in elderly depressed patients: A randomized clinical trial. J Psychiatr Res 2018;97:65–9.
- [18] Slade EP, Jahn DR, Regenold WT, et al. Association of electroconvulsive therapy with psychiatric readmissions in US hospitals. JAMA Psychiatry 2011;74(8):798–804.
- [19] Sauvaget A, Poulet E, Mantovani A, et al. The psychiatric neuromodulation unit: Implementation and management [Internet]. J ECT 2018;34:211–9 [cited 2022 Feb 6] Available from: <https://pubmed.ncbi.nlm.nih.gov/29944606>.
- [20] Bulteau S, Baeken C, Poulet E. ECT—for a European scientific concern. Encéphale. Elsevier Masson SAS 2020;46:233–4.