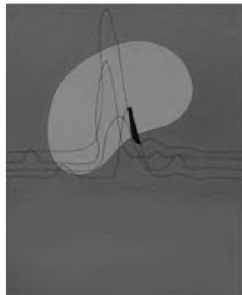




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Electroconvulsive Therapy

National Institutes of Health
Consensus Development Conference Statement
June 10-12, 1985



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Introduction

Electroconvulsive therapy (ECT) is a treatment for severe mental illness in which a brief application of electric stimulus is used to produce a generalized seizure. In the United States in the 1940s and 1950s, the treatment was often administered to the most severely disturbed patients residing in large mental institutions. As often occurs with new therapies, ECT was used for a variety of disorders, frequently in high doses and for long periods. Many of these efforts proved ineffective, and some even harmful. Moreover, its use as a means of managing unruly patients, for whom other treatments were not then available, contributed to the perception of ECT as an abusive instrument of behavioral control for patients in mental institutions for the chronically ill. With the introduction of effective psychopharmacologic medications and the development of judicial and regulatory restrictions, the use of ECT has waned.

The treatment is now used primarily in general hospital psychiatric units and in psychiatric hospitals. A National Institute of Mental Health hospital survey estimated that 33,384 patients admitted to hospital psychiatric services during 1980 were treated with ECT, representing approximately 2.4 percent of all psychiatric admissions.

Although ECT has been in use for more than 45 years, there is continuing controversy concerning the mental disorders for which ECT is indicated, its efficacy in their treatment, the optimal methods of administration, possible complications, and the extent of its usage in various settings. These issues have contributed to concerns about the potential for misuse and abuse of ECT and to desires to ensure the protection of patient's rights. At the same time, there is concern that the curtailment of ECT use in response to public opinion and

regulation may deprive certain patients of a potentially effective treatment.

In recent decades, researchers intensified efforts to establish the effectiveness of ECT and its indications, understand its mechanism of action, clarify the extent of adverse effects, and determine optimum treatment technique. Despite recent research efforts yielding substantial information, permitting professional and public evaluation of the safety and efficacy of ECT, the investigation of ECT has not generally been in the mainstream of mental health research.

To help resolve questions surrounding these issues, the National Institutes of Health in conjunction with the National Institute of Mental Health convened a Consensus Development Conference on Electroconvulsive Therapy on June 10-12, 1985. For 1 1/2 days, experts in the field presented their findings, and an audience, including health professionals, former patients, and other interested persons, discussed the issues. A consensus panel representing psychiatry, psychology, neurology, psychopharmacology, epidemiology, law, and the general public considered the scientific evidence and agreed on answers to the following questions:

- What is the evidence that ECT is effective for patients with specific mental disorders?
- What are the risks and adverse effects of ECT?
- What factors should be considered by the physician and patient in determining if and when ECT would be an appropriate treatment?
- How should ECT be administered to maximize benefits and minimize risks?
- What are the directions for future research?

What Is the Evidence That ECT Is Effective for Patients With Specific Mental Disorders?

Published controlled studies of ECT permit evaluation of its short-term efficacy in severe major depressions (delusional and endogenous), in acute mania, and in certain schizophrenic syndromes. The available controlled clinical trials do not extend beyond the treatment of the acute episode (i.e., about 4 weeks). These studies are difficult to compare because they have used differing diagnostic systems and research designs. Further, they have measured outcome only in terms of symptom reduction, not the quality of life and social functioning.

Depression

Studies of ECT in depression have used various control conditions for comparison, including "sham" ECT (e.g., all of the elements of the ECT procedure except the electric stimulus), tricyclic antidepressants (TCA), monoamine oxidase inhibitors (MAOI), combinations of antidepressants and neuroleptics, and placebos. The efficacy of ECT has been established most convincingly in the treatment of delusional and severe endogenous depressions, which make up a clinically important minority of depressive disorders. Some studies find ECT to be of at least equal efficacy to medication treatments, and others find ECT to be superior to medication. Not a single controlled study has shown another form of treatment to be superior to ECT in the short-term management of severe depressions. It must be noted, however, that those studies that found ECT to be superior to medication were not designed to study the persistence of this advantage of ECT beyond the short term. Moreover, the available evidence suggests that relapse rates in the year following ECT are likely to be high unless maintenance antidepressant medications are subsequently prescribed. Several studies suggest that ECT reduces symptoms in severely depressed patients who previously have not responded to adequate trials of antidepressant medication. The literature also indicates that ECT, when compared with antidepressants, has a more rapid onset of action.

Delusional Depression

ECT is highly effective in the treatment of delusional depression. It is superior to either antidepressants or neuroleptics used alone and is at least as effective as the combination of antidepressants and neuroleptics. ECT is often effective in patients who have previously failed to respond to medication. The duration of the therapeutic effect beyond the initial acute episode is not clear.

Endogenous/Melancholic Depression

The severe endogenous/melancholic depressions are characterized by early morning awakening, marked weight loss, psychomotor retardation and/or agitation, diurnal variation, and lack of reactivity. ECT is at least as effective as TCA and more effective than sham ECT

in the short-term treatment of these severe endogenous/melancholic depressions. ECT appears to be more effective than MAOI in the treatment of severe depressions, but available studies have generally used relatively low MAOI doses. There is evidence for the efficacy of ECT in those endogenous depressives who have not responded to an adequate trial of antidepressants. The long-term efficacy of ECT with endogenously depressed patients is not known.

Other Depression

The majority of depressed persons encountered in medical and psychiatric settings do not have the severe endogenous/melancholic or delusional depressions described above. ECT is not effective for patients with milder depressions, i.e., dysthymic disorder (neurotic depression) and adjustment disorder with depressed mood. Patients with major depression that is nonendogenous/nonmelancholic have not yet been extensively studied. Because of this, it is unclear whether their response to ECT would be more like those with dysthymic disorders or those with endogenous/melancholic features.

Acute Manic Episode

ECT and lithium appear to be equally effective for acute mania, and either is superior to hospitalization without somatic therapy. A treatment regimen in which ECT is used for the acute episode, followed by lithium maintenance, does not appear to be associated with an increased risk of early relapse compared with lithium treatment alone.

Schizophrenia

Neuroleptics are the first line of treatment for schizophrenia. The evidence for the efficacy of ECT in schizophrenia is not compelling but is strongest for those schizophrenic patients with a shorter duration of illness, a more acute onset, and more intense affective symptoms. ECT has not been useful in chronically ill schizophrenic patients. Although ECT is frequently advocated for treatment of patients with schizophreniform psychoses, schizoaffective disorders, and catatonia, there are no adequate controlled studies to document its usefulness for these disorders.

Other Disorders

There are no controlled studies supporting the efficacy of ECT for any conditions other than those designated above (i.e., delusional and severe endogenous depression, acute mania, and certain schizophrenic syndromes).

What Are the Risks and Adverse Effects of ECT?

To maximize the benefits of ECT and minimize the risks, it is essential that the patient's illness be correctly diagnosed, that ECT be administered only for appropriate indications, and that the risks and adverse effects be weighed against the risks of alternative treatments. Risks and adverse effects of ECT can be divided into two categories: (1) Those medical complications that can be substantially reduced by the use of appropriately trained staff, best equipment, and best methods of administration and (2) those side effects, such as spotty but persistent memory loss and transient posttreatment confusion, that can be expected even when an optimal treatment approach is used. In this report, we will focus on the risks still present with adequate treatment techniques.

In the early days of ECT, mortality was a significant problem. The commonly quoted overall mortality rate in the first few decades was 0.1 percent or 1 per 1,000. Over the years, safer methods of administration have been developed, including the use of short-acting anesthetics, muscle relaxants, and adequate oxygenation. Present mortality is very low. In the least favorable recent series reported, there were 2.9 deaths per 10,000 patients, another series, 4.5 deaths per 100,000 treatments were reported. Overall, the risk is not different from that associated with the use of short-acting barbiturate anesthetics. The risk of death from anesthesia, although very small, is present and should be considered when evaluating the setting for performing ECT.

In the past, up to 40 percent of patients suffered from various complications, the most common being vertebral compression fractures. With present techniques, these risks have been virtually eliminated. In one recent study of almost 25,000 treatments, a complication rate of 1 per 1,300 to 1,400 treatments was found. These included laryngospasm, circulatory insufficiency, tooth damage, vertebral compression fractures, status epilepticus,

peripheral nerve palsy, skin burns, and prolonged apnea.

During the few minutes following the stimulus, profound and potentially dangerous systemic changes occur. First, there may be transient hypotension from bradycardia caused by central vagal stimulation. This may be followed by sinus tachycardia and also sympathetic hyperactivity that leads to a rise in blood pressure, a response that may be more severe in patients with essential hypertension. Intracranial pressure increases during the seizure. Additionally, cardiac arrhythmias during this time are not uncommon (but usually subside without sequelae). Thus, certain patient groups that would be adversely affected by these manifestations are at increased risk.

There are two categories of central nervous system effects: The immediate consequences of the ECT seizure and the more enduring effects, both of which are affected by the treatment course. Immediately after awakening from the treatment, the patient experiences confusion, transient memory loss, and headache. The time it takes to recover clear consciousness, which may be from minutes to several hours, varies depending on individual differences in response, the type of ECT administered, the spacing and number of treatments given, and the age of the patient.

The severity of this acute confusional state is greatest after bilateral sine wave treatment and least when nondominant unilateral pulsed ECT is administered. Severity also appears to be increased by longer seizure duration, close spacing of the treatments, increasing dosage of electrical stimulation, and each additional treatment.

Depressive disorders are characterized by cognitive deficits that may be difficult to differentiate from those due to ECT. It is, however, well established that ECT produces memory deficits. Deficits in memory function, which have been demonstrated objectively and repeatedly, persist after the termination of a normal course of ECT. Severity of the deficit is related to the number of treatments, type of electrode placement, and nature of the electric stimulus. **Greater deficit occurs from bilateral than from unilateral placement. Sine wave current has been found to impair memory more than pulsed current.**

The ability to learn and retain new information is adversely affected for a time following the administration of ECT; several weeks after its termination, however, this ability typically returns to normal. **There is also objective evidence, based on neuropsychological testing, of loss of memory for a few weeks surrounding the treatment; such objective tests have not firmly established persistent or permanent deficits for a more extensive period, particularly for unilateral ECT. However, research conducted as long as 3 years after treatment has found that many patients report that their memory was not as good as it was prior to the treatment. They report particular difficulties for events that occurred on average 6 months before ECT (retrograde amnesia) and on average 2 months after the treatment (anterograde amnesia). Because there is also a wide difference in individual perception of the memory deficit, the subjective loss can be extremely distressing to some and of little concern to others.**

There are other possible adverse effects from ECT. Some patients perceive ECT as a terrifying experience; some regard it as an abusive invasion of personal autonomy; some experience a sense of shame because of the social stigma they associate with ECT; and some report extreme distress from persistent memory deficits. The panel heard eloquent testimony of these attitudes from former patients who had been treated with ECT. It is clear, however, that these attitudes are not shared by all ECT patients. The panel also heard moving testimony from former patients who regarded ECT as a wholly beneficial and lifesaving experience. There are insufficient systematic studies to permit any definitive assessment of the prevalence of these various perceptions among ECT patients.

Numerous ECT studies have been conducted with animal models. Many of these suffer from methodological shortcomings. In studies that have been controlled for fixation artifacts, hypoxia, and other methodological problems, neuronal cell death has not been detected. Cerebral vasospasm and alterations in capillary permeability are of short duration and of insufficient magnitude to lead to neuronal cell death. The precise mechanism of the anterograde and retrograde memory deficit has not been established; it may represent alterations in neuronal function that are not detectable with present methods. Computerized axial tomography (CAT) studies of patients who have had ECT are very preliminary and open to alternative interpretations. Definitive studies of *in vivo* brain metabolism with positron emission tomography (PET) and studies of tissue changes detectable by magnetic resonance imaging (MRI) remain to be done.

What Factors Should Be Considered by the Physician and Patient in Determining If and When ECT Would Be an Appropriate Treatment?

The consideration of ECT is most appropriate in those conditions for which efficacy has been established: Delusional and severe endogenous depressions, acute mania, and certain schizophrenic syndromes. ECT should rarely be considered for other psychiatric conditions. The decision whether to offer ECT to an individual patient should be based on a complex consideration of advantages and disadvantages for ECT and for each treatment alternative. Whether to use ECT should be based on a thorough review of severity of the patient's illness, medical indications and contraindications, and nonresponsiveness to other treatments. It should be emphasized that for certain patients with very specific and narrow indications, ECT may be the only effective treatment available. In certain circumstances of acute risk to life or of medical status incompatible with the use of other effective treatments, ECT may be the first treatment.

The panel is concerned that ECT only be administered for the benefit of individual patients. Institutional factors (such as financial pressures created by prospective systems or staff convenience) should play no role in the decision to administer ECT.

Severity

Given a diagnosis for which the efficacy of ECT has been established, the immediate risk of suicide (when not manageable by other means) is a clear indication for the consideration of ECT. Acute manic episode—especially when characterized by clouded sensorium, dehydration, extreme psychomotor agitation, high risk for serious medical complications or death through exhaustion, and nonresponse to pharmacological interventions—are also clear indications for ECT. The severe and unremitting nature of the patient's emotional suffering, or extreme incapacitation, are also important considerations.

Medical Indications and Contraindications

The patient's medical status is often the determining consideration in the use of ECT. ECT may be necessary when the patient has medical conditions that preclude the use of TCA, MAOI, lithium, and neuroleptics. ECT should be considered in patients with severe depression or psychosis during the first trimester of pregnancy. Conversely, ECT is contraindicated for increased intracranial pressure, while space-occupying lesions in the brain, a recent history of myocardial infarction, and large aneurysms are relative contraindications for ECT. A personal history of nonresponsiveness to, or debilitating side effects (medical or psychological) from, ECT are also possible contraindications.

Nonresponsiveness to Other Treatments

ECT should be considered when alternative pharmacological and/or psychotherapeutic treatments have been given an adequate trial without efficacious response. When a patient is nonresponsive to other treatments, factors such as severity of the illness, its natural course, and the risk of other treatments worsening the course (as, for example, antidepressant medications precipitating a manic episode) need to be taken into account.

Informed Consent

When the physician has determined that clinical indications justify the administration of ECT, the law requires, and medical ethics demand, that the patient's freedom to accept or refuse the treatment be fully honored. An ongoing consultative process should take place. In this process, the physician must make clear to the patient the nature of the options available and the fact that the patient is entitled to choose among those options.

No uniform "shopping list" can be drawn up regarding the matters that should be discussed by patient and physician to assure a fully informed consent. **They should discuss the character of the procedure, its possible risks and benefits (including full acknowledgement of posttreatment confusion, memory dysfunction, and other attendant uncertainties), and the alternative treatment options (including the option of no treatment at all).** Special individual needs may also be relevant to some patients, for example, a personal situation that requires rapid remission to facilitate return to work and to reduce family disruption. In all matters, the patient should not be inundated with technical detail; the technical issues should be translated into terms meaningful and accessible to the patient.

It is not easy to achieve this ideal of "informed consent" in any aspect of medical practice; and there are special difficulties that arise regarding the administration of ECT. In particular, the patients for whom this procedure is medically appropriate may be suffering from a severe psychiatric illness that, although not impairing their legal competency to consent, may nonetheless cloud judgment in fully weighing all of the available options. Such judgmental distortion does not justify disregarding the patient's choices; rather it makes it all

the more important that the physician strive to identify and clarify the options that the patient alone is entitled to exercise.

The consent given by the patient at the outset of treatment should not be the final exchange on this issue but should be reexamined with the patient repeatedly throughout the course of the treatment. These periodic reviews should be initiated by the physician and not depend on patient initiative to "rescind" consent.

There are several reasons for this repeated consenting procedure: because of the relatively rapid therapeutic effect of the procedure itself, the patient after initial treatments is likely to have enhanced judgmental capacities; the risks of adverse effects increase with repeated treatments, so that the question of continued treatment presents a possibly changed risk/benefit assessment for the patient; and because of the short-term memory deficits that accompany each administration of ECT, the patient's recollection of the prior consenting transaction might itself be impaired, so that repeated consultations reiterating the patient's treatment options are important to protect the patient's sense of autonomy throughout the treatment process. Moreover, if the patient agrees, the family should be involved in each step of this consultative process.

In a small minority of cases, a patient will lack adequate legal capacity to consent to the proposed procedure. In such cases, timely court proceedings are necessary if treatment is to be provided. Legislation in a few states dictates that ECT may in no circumstance be provided to an involuntarily committed patient. The panel believes that such absolute bans are unduly restrictive and make treatment impossible for patients who might obtain more benefit, at acceptable levels of risk, from ECT than from alternative treatments.

It may be desirable for physicians with patients for whom the prospect of ECT is a foreseeable but not immediate possibility to discuss this in advance with the patient when his or her judgment appears least compromised by the underlying disease process. Such advance discussion would serve as a nonbinding guide both to the patient and physician and would be another means to enhance the patient's autonomous choice in weighing the risks and benefits of this procedure and its alternatives.

How Should ECT Be Administered To Maximize Benefits and Minimize Risks?

Once the patient and the physician have decided that ECT may be indicated, the patient should undergo a pretreatment medical examination that includes a history, physical, neurologic examination, EKG, and laboratory tests. Medications that affect the seizure threshold should be noted and decreased or discontinued when clinically feasible. MAOI should be discontinued 2 weeks before treatment, and patients should be essentially lithium-free. Severe hypertension should be controlled before beginning treatment. Because some patients with compromised cardiovascular status will be receiving ECT, cardiac conditions should be evaluated and monitored closely. Educating the patient and the family through discussion and written and/or audiovisual material describing the procedure is necessary prior to obtaining written informed consent.

An area should be designated for the administration of ECT and for supervised medical recovery from the treatment. This area should have appropriate health care professionals available and should include equipment and medications that could be used in the event of cardiopulmonary or other complications from the procedure.

A health professional specifically trained and certified in the use of brief anesthetic procedures should administer the anesthesia. The treatment team should include nursing personnel trained in ECT procedures and recovery.

Typically, ECT is administered as follows: the treatment is given in the early morning after an 8- to 12-hour period of fasting. Atropine or another anticholinergic agent is given prior to the treatment. An intravenous line is placed in a peripheral vein, and access to this vein is maintained until the patient is fully recovered. The anesthetic methohexital is given first, followed by succinylcholine for muscle relaxation. Ventilatory assistance is provided with a positive pressure bag using 100 percent oxygen. The EKG, blood pressure, and pulse rate should be monitored throughout the procedure. Stimulus electrodes are placed either bifrontotemporally (bilateral) or with one electrode placed frontotemporally and the second electrode placed on the ipsilateral side (unilateral). Bilateral ECT may be more effective in certain patients or conditions. It has been established, however, that unilateral ECT, particularly on the nondominant side, is associated with a shorter confusional period and fewer memory deficits. Also, a brief pulse stimulus is associated with fewer cognitive defects than the traditional sine wave stimulus. Seizure threshold varies greatly among patients and may be difficult to determine; nevertheless the lowest amount of electrical

energy to induce an adequate seizure should be used. Seizure monitoring is necessary and may be accomplished by an EEG or by the "cuff" technique. In this technique, a blood pressure cuff is placed on an arm or leg and is inflated above systolic pressure prior to the injection of a muscle relaxing agent. In unilateral ECT, the cuff should be on the same side as the electrodes to ensure that a bilateral seizure occurred.

The number of treatments in a course of therapy varies. Six to twelve treatments are usually effective. In the United States, the usual frequency is three times weekly; in the United Kingdom, the standard practice is two treatments weekly. Regressive ECT (a large number of treatments given within a short period for the purpose of achieving a persistent organic brain syndrome) is no longer an acceptable treatment form. Multiple-monitored ECT (several seizures during a single treatment session) has not been demonstrated to be sufficiently effective to be recommended. There are no controlled studies on the periodic use of ECT after remission of the acute episode or as a maintenance regimen to prevent recurrence of new episodes. Following ECT, most depressed patients should be continued on antidepressant medication or lithium to reduce relapse.

The panel is concerned that there are only limited data on the manner and extent of ECT administration in the United States and on the training of personnel involved in it. A national survey should be undertaken to assemble basic facts about the status of ECT treatment.

Medical school curricula should include education in the use of ECT. Psychiatric residency programs should include complete ECT training: indications, contraindications, risks, clinical management, informed consent, and evaluation of outcome. The American Board of Psychiatry and Neurology should include questions about ECT in its oral and written examinations.

The panel believes it is imperative that appropriate mechanisms be established to ensure proper standards and monitoring of ECT. Hospitals and centers using ECT should establish review committees modeled on other medical-surgical review committees and should formulate rules and regulations to govern the privileging of physicians giving the treatments. Stringent peer review consistent with Joint Commission for the Accreditation of Hospitals' standards should monitor ongoing utilization of ECT. Periodic inspection of the equipment is also essential. As experience accumulates, consideration should be given to the adequacy of existing monitoring and review mechanisms.

What Are the Directions for Future Research?

ECT has been underinvestigated in the past. Among the most important immediate research tasks are:

- Initiation of a national survey to assemble the basic facts about the manner and extent of ECT use, as well as studies of patient attitudes and responses to ECT. Better understanding of negative, positive, and indifferent responses should result in improved treatment practices.
- Identification of the biological mechanisms underlying the therapeutic effects of ECT and the memory deficits resulting from the treatment.
- Better delineation of the long-term effects of ECT on the course of affective illnesses and cognitive functions, including clarification of the duration of ECT's therapeutic effectiveness.
- Precise determination of the mode of electrode placement (unilateral versus bilateral) and the stimulus parameters (form and intensity) that maximize efficacy and minimize cognitive impairment.
- Identification of patient subgroups or types for whom ECT is particularly beneficial or toxic.

Conclusion

Electroconvulsive therapy is the most controversial treatment in psychiatry. The nature of the treatment itself, its history of abuse, unfavorable media presentations, compelling testimony of former patients, special attention by the legal system, uneven distribution of ECT use among practitioners and facilities, and uneven access by patients all contribute to the controversial context in which the consensus panel has approached its task.

The panel has found that ECT is demonstrably effective for a narrow range of severe psychiatric disorders in a limited number of diagnostic categories: delusional and severe

endogenous depression and manic and certain schizophrenic syndromes. There are, however, significant side effects, especially acute confusional states and persistent memory deficits for events during the months surrounding the ECT treatment. Proper administration of ECT can reduce potential side effects while still providing for adequate therapeutic effects.

The physician's decision to offer ECT to a patient and the patient's decision to accept it should be based on a complex consideration of advantages and disadvantages of ECT compared with alternative treatments. An ongoing consultative process, requiring time and energy on the part of both patient and physician, should occur.

Much additional research is needed into the basic mechanisms by which ECT exerts its therapeutic effects. Studies are also needed to better identify subgroups for whom the treatment is particularly beneficial or toxic and to refine techniques to maximize efficacy and minimize side effects. A national survey should be conducted on the manner and extent of ECT use in the United States.

These recommendations reflect the consensus of the panel. We have been careful to narrowly delineate when and how, in our judgment, ECT should be administered. To prevent misapplication and abuse, it is essential that appropriate mechanisms be established to ensure proper standards and monitoring of ECT.

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Supplemental Information for NIH Consensus Statement on Electroconvulsive Therapy

Since the NIH Consensus Statement on Electroconvulsive Therapy was issued, additional information has become available that supplements the original statement. The following articles also provide additional information to the original consensus statement.

- **Abrams R.** (1992), *Electroconvulsive Therapy*, 2nd edition, New York, Oxford University Press
- A task force report (hardcover book) from the American Psychiatric Association (1990): *The Practice of ECT: Recommendations for Treatment, Training, and Privileging*
- the quarterly journal, *Convulsive Therapy*
- a special issue of the *Psychopharmacology Bulletin* with the complete proceedings of a 1993 NIMH ECT workshop entitled "New Directions for ECT Research", Volume 30, No. 3 (1994)
- A valuable companion to the above is a book published by the American Psychiatric Press as #38 in the *Progress in Psychiatric Series: The Clinical Science of Electroconvulsive Therapy*, edited by CE Coffey (1993), with an introduction from NIMH by MV Rudorfer and FK Goodwin

For health care professionals, the following journal references may be useful:

- Potter WZ, Rudorfer MV, Manji H. The pharmacologic treatment of depression. *New England Journal of Medicine* 1991; 325:633-642.
- Sackeim HA, Prudic J, Devanand DP, et al. Effects of stimulus intensity and electrode placement on the efficacy and cognitive effects of electroconvulsive therapy. *New England Journal of Medicine* 1993; 328:839-846
- Potter WZ, Rudorfer MV, Electroconvulsive therapy -- A modern medical procedure (editorial). *New England Journal of Medicine* 1993; 328:882-883
- Finally, a forthcoming comprehensive chapter on ECT potentially can serve as a useful addendum to the above as an attachment to the consensus conference statement upon publication. Because it was written by a Government employee, it is not subject to copyright: Rudorfer MV, Henry ME, Sackeim HA. *electroconvulsive therapy*, in *Psychiatry*. Edited by Tasman A, Kay J, Lieberman JA. Philadelphia: WB Saunders Co, 1997. ISSN/ISBN: 0721652557.

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