PHARMACOLOGICAL, CONVULSIVE AND OTHER SOMATIC TREATMENTS IN PSYCHIATRY

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ting up of units of symptoms. In paranoid reactions, for instance, the consolidation of a paranoid system can be prevented by interrupting the dangerous production of the system by means of repeated convulsive treatments. The fragments of the psychosis then lose actuality for the patient by means of such mechanisms as repression, amalgamation and objectivation. In case of relapse, the symptoms are often more colorless and have less psychotic content, and less affective charge than previously.

Another interesting problem is the patient's insight after the treatment, whereby distinction should be made between insight into the fact of having been sick at all, and insight into individual symptoms of the sickness. The concept of schizophrenic defect states which cannot be influenced any more is, according to Weitbrecht, not tenable since the introduction of active therapy; they cannot be compared with a scar because a process may be still going on. Cyclothymic depressions have many parallels to the schizophrenics as far as the response to shock treatment is concerned. Here, too, we can see a disappearance of the symptoms in toto, a dissolution of symptom-units and a change of symptoms. An essential difference is that relapses of manic-depressive cases are stable, uniform and not as different as the colorless symptoms of a schizophrenic relapse. A study by Gerstaker on the disturbances of thought in schizophrenics under convulsive therapy shows how the treatment isolates from an entirely disorganized thinking a rather resistive nucleus of thinking disorder which may be hardly noticeable but remains untouched. Such psychopathological studies on patients whose symptomatology can be changed at will by the treatment are a promising new approach.

Psychopathological aspects of the "post-electroshock" state were studied extensively and described in a monograph by Ebtinger. Most of the previous studies had been limited to the return of consciousness after one single treatment. This author follows the post-shock manifestations of an entire series of treatments and studies the parallel course of events in level and content of consciousness. Among other things he shows that memory is restored not simply from past to recent, but that lapses remain, particularly regarding the pathological period. When the treatment leads to a radical change of the clinical syndrome this always starts at the time of the return of consciousness. If there are no changes in this period the treatment has little chance of succeeding. Symptoms of acute psychosis usually show a complete change in the post-shock state, while symptoms of chronic psychosis remain unchanged. Ebtinger distinguishes three phases in the reconstruction: an excitation phase, a depressive phase, and the third phase in which consciousness is sufficiently restored to recognize and correct its own disturbances. It is certainly correct that the electric shock offers experimental conditions to study psychopathological changes, and we agree with the author that it is an important means to come to a better understanding of relations between organic pathological and psychopathological mechanisms.

Organic-Psychotic Reactions; Activation of the Psychosis

Different from the manifestations following each individual treatment are those organic mental symptoms which are caused by repeated convulsions.

They can be observed in practically every patient, although in widely varying degrees. They have been described as "organic-psychotic reactions occurring during ECT" (Kalinowsky). Korsakoff-like pictures are frequent. Some patients become bewildered, others show severe psychomotor excitement aggravated by delusional fears and hallucinations. Signs which differentiate these organic reactions from the patient's original psychosis are organic "blurring" of consciousness, greater emotional lability, more flighty delusions, more vivid hallucinations, and so on. These syndromes occur in neurotics as well as in psychotics. The pretreatment personality plays an important part in the determination of symptoms, as has been demonstrated in organic-psychotic reactions of varying etiology.

The correct recognition of these organic syndromes is of great practical importance. Therapy is often continued unnecessarily when an organic reaction is mistaken for residual symptoms of the original psychosis. Patients who have already improved from a depression may later show uncertainty and bewilderment of an organic type; if this is taken as a sign of depression, the patient may be subjected to further treatment, which only delays his recovery. Psychotic symptoms following a period of improvement, but still occurring during treatment, are usually an organic manifestation. Actual relapses seldom occur earlier than several days after discontinuation of treatment. Another frequent mistake is premature discontinuation of treatment because of an organic reaction which is taken for an aggravation of the patient's original psychosis. Interruption of therapy because of acute organic syndromes is unwarranted, particularly as further treatment usually leads to a less dramatic condition which may be characterized as temporary organic dementia. Whatever the degree of this organic reaction, it will disappear approximately a week or ten days after the last treatment. There are patients in whom, a few days after the course of treatment is terminated, a quiet confusional state is still followed by an acute delirium with vivid hallucinations and delusions, these being quite different in type from those of the original psychosis. If mistaken for relapse, these syndromes may lead to unnecessary reinstitution of treatment; if left untreated they subside spontaneously in a few days. In many instances they require great diagnostic scrutiny and are a difficult problem for the therapist.

It is not always easy to differentiate these organic-psychotic reactions from activation of the patient's psychosis, the latter apparently a much rarer occurrence. Activation of the psychosis can be best recognized when a quiet, blocked schizophrenic after the first treatment becomes acutely disturbed, actively delusional and hallucinating. We agree with Osgood that such change of symptoms, although impressive, should not be considered an aggravation of the patient's condition. More frequently an apparent depression clears up during the first few treatments, but is then replaced by the appearance of acute schizophrenic symptoms. In these instances, the superficial layer of "depression" has been removed by the treatment, and the underlying schizophrenic symptoms become overt. Halpern reports such instances under the title of "electroshock as a diagnostic aid in schizophrenia." The same is seen, when the depressive overlay of a schizophrenic psychosis is removed with antidepressive drugs.

memory loss spans several weeks often — not minutes as their experts say — p967

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CHAPTER 27

Psychopharmacology and Electroconvulsive Therapy

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■ SOMATIC TREATMENTS: AN INTRODUCTION

Somatic treatments of psychiatric illnesses include the use of medication, ECT, light therapy, sleep modification techniques, and psychosurgery. Although there is convincing evidence that the proper application of each of these categories of somatic treatment is beneficial in selected clinical situations, this chapter focuses predominantly on psychopharmacology and ECT, which constitute the most commonly utilized somatic interventions. The use of a somatic treatment for a psychiatric illness is a decision that should be made only after careful consideration of many factors for that individual patient. A medication, per se, is never the treatment of a patient; rather, medications may be important components of a larger treatment plan ranging from comprehensive medical evaluation to continuous assessment of the treatment plan and outcome. The clinician must be guided by sound therapeutic principles to ensure adequate diagnosis, correct choice of a drug or other somatic treatment, proper communication with the patient and the family related to risks and benefits of the approach, and clear instructions related to administration, side effects, evaluation of response, and discontinuation of treatment.

□ Decision to Use a Somatic Treatment

All psychiatric patients require a skilled and thorough psychiatric, neurological, and physical evaluation (MacKinnon and Yudofsky 1991). Organic etiologies of psychological symptoms must be considered for all patients. Frequent organic causes of psychiatric symptoms include the effects of 1) concomitant medications, 2) abused substances, 3) central nervous system (CNS) dysfunction, and 4) endocrine disorders.

For example, if a patient's mood disorder is related to alcohol abuse, response to antidepressant medication will only occur upon discontinuation of the alcohol. On the other hand, not all patients with symptoms related to organic causes require medi-

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Throughout this chapter we provide specific guidelines for the safe and effective use of psychopharmacological agents and electroconvulsive therapy (ECT). Some of these recommendations have been supported by an official American Psychiatric Association (APA) task force. Other guidelines are ones that the authors have developed after careful review of the literature and in consultation with recognized experts in psychopharmacology. The authors expect that future research will necessitate the revision of some of these guidelines. Additionally, although the authors endeavored to provide therapeutic guidelines that are safe and rational, the reader must consider the unique clinical states of each patient and utilize or modify judiciously the recommendations included in this chapter according to the special needs of the individual patient.

only after thorough evaluation and carefully documented approval by the relevant nonpsychiatric medical specialists.

Side Effects

For each treatment, there is an initial confusional period that lasts for approximately 30 minutes. Memory impairment that occurs with ECT is highly variable. Whereas certain patients report no problems with their memory, others report that their memory "is not as good as it used to be" before receiving ECT (Squire and Slater 1983). When memory of patients receiving ECT is carefully studied, it has been found that patients who experience retrograde amnesia (i.e., diminished ability to recall information that was recently learned before ECT was administered) following bilateral ECT seem to have recovered complete memory functions by 6 months after treatment, with little evidence that new learning ability is still deficient at that time (Squire et al. 1975). In those patients who do have memory impairment following bilateral ECT, information acquired during the days and weeks prior to, during, and for several weeks following ECT may be permanently lost. The use of brief pulse stimulation, instead of sine wave stimulation, can reduce the memory impairment still further (Squire et al. 1975). Unilateral stimulation results in fewer cognitive problems, although its efficacy also may be less (Sackheim et al. 1993). Other cognitive deficits include memory deficits for nonverbal information and transient disorientation (Sackeim et al. 1986).

□ Conclusion

After more than 50 years of use, electroconvulsive therapy remains a safe, specific, and effective treatment regimen in psychiatry. The treatment is particularly effective in those patients with severe depressions that may include delusional, suicidal, or psychomotor components. New technologies involving varying electrode placement as well as reduced energy requirement to initiate seizures have led to fewer side effects while maintaining therapeutic advantage of this procedure. It is important, as with all somatic interventions in psychiatry, that ECT be recognized as a specific therapeutic tool that is only one component of a larger treatment plan and that includes psychosocial and other biologic interventions. Adequate time must be allocated to discuss with and answer questions of patients and their families about the risks, benefits, side effects, and overall experience of the procedure.

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Electroconvulsive Therapy in the Medically Ill

Electroconvulsive therapy (ECT) is the application of a series of electrically induced seizures in order to produce a clinical remission in severe episodes of susceptible disorders. At present in the United States, ECT is administered each year to 30,000–80,000 individuals (American Psychiatric Association, 1978; Thompson, 1986), nearly all of whom suffer from major depressive disorder, schizophrenia, or mania (American Psychiatric Association, 1980).

The fact that ECT still remains a clinically viable treatment modality, after nearly 50 years and the development of literally dozens of psychopharmacologic alternatives, is in itself a testimonial to its therapeutic potency and also to its capacity to evolve over the years into a safer, if not a more acceptable, treatment modality. At intervals during this time period, panels of scholars have carefully considered the question of whether a role for ECT still exists in contemporary psychiatric practice. One of the most recent of these evaluations was undertaken in June 1985 by a National Institute of Mental Health (NIMH)/National Institutes of Health (NIH) Consensus Development Panel (Consensus Conference, 1985). In agreement with virtually all previous such investigations, the panel concluded that ECT is, when properly administered, a safe and effective procedure for which there continues to be an established clinical need.

At present, ECT is typically not, at least in the United States, a "first-line" treatment. Its use is generally reserved for those who either have not responded to psychopharmacologic trials (see Chapter 4) or cannot tolerate such an attempt, whether for reasons of adverse effects or because of an urgent need for immediate relief (Fink, 1979; Weiner, 1979). In practice one frequently finds that such individuals are more severely ill not only from a psychiatric perspective, but from a medical standpoint as well. More and more often it is the elderly, frail, chronically physically ill patient who is considered for referral for ECT. In such a situation, the referring physician must be able to carefully evaluate the delicate balance of risks and benefits that represent the logical determinants of clinical choice. The presence of significant

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"absolute" contraindications to ECT, there exist a variety of situations characterized by the presence of significantly increased risk of death or serious morbidity. In such cases the clinical need for ECT must be particularly well established and documented. In addition, efforts must be made, where possible, to modify the ECT procedure to minimize the likelihood of adverse sequelae. Relative contraindications to ECT include the following conditions, all of which will be discussed later in this chapter: space-occupying intracerebral lesion, recent myocardial infarction, and leaky or otherwise unstable aneurysm.

The mortality associated with ECT is quite low, typically quoted at 1 in 10,000 patients (Fink, 1979). This figure is comparable to that corresponding to brief periods of anesthesia alone. At the same time, however, it must also be pointed out that advanced age, along with the presence of significant intercurrent medical disease, may substantially raise the risk of both death and serious morbidity. Major medical sequelae that can be produced by a course of ECT are uncommon (Frederiksen & d'Elia, 1979; Heshe & Roeder, 1976). The most frequent such events are severe delirium and prolonged cardiac arrhythmia. Less serious, and also more prevalent, adverse sequelae of ECT are transient cardiac arrhythmia, prolonged apnea, oral trauma, injury to dental structures, and mild to moderate levels of delirium. As will be described, modifications of ECT technique may prevent or at least ameliorate many of these events.

Adverse effects produced by ECT can be explained in terms of the medical physiology of induced seizures. Profound autonomic surges during and following the ictal discharge lead to systemic hypertension and abrupt transitions in cardiac rate and output (Perrin, 1961). The hypertension, in combination with an ictal loss in cerebrovascular autoregulation, results in a transient breakdown in the blood–brain barrier and an accompanying increase in intracerebral pressure (Bolwig, Hertz, & Westergaard, 1977). The sudden increase in cardiac output, particularly in the presence of a preexisting impairment of myocardial blood supply, may precipitate significant myocardial ischemia (Deliyiannis, Eliakim, & Bellet, 1962).

In addition to vascular effects, the ictal discharge transiently disrupts neuronal metabolism, eliciting nonspecific encephalopathic changes in the electroencephalogram (Weiner, 1983), which build up over the treatment course and which are correlated with behavioral aspects of delirium, such as disorientation. Along with these global cerebral effects, certain areas of the brain, such as the hippocampus, are particularly sensitive to metabolic dysfunction and other pathophysiologic changes, and may account for the more specific form of cerebral impairment (i.e., amnesia) that is often present during and immediately following a course of ECT (Squire, 1986).

Alterations of cerebral function raise the possibility of pathologic changes in cerebral anatomy, a consideration that is particularly of concern given the complaints of severe and permanently altered cognitive function elicited from a small minority of ECT recipients (Breggin, 1979). A careful evaluation of the literature does not allow the conclusion that ECT is associated with a significant risk of "brain damage" per se (Kolbeinsson, Arnaldsson, Petursson, & Skulason, 1986; Weiner, 1984), although a subtle, persistent retrograde amnesia, at least for recent weeks and months prior to the ECT, can be present in some circumstances. As with many other of the adverse effects already described, this amnesia can be considerably attenuated by modifications in ECT technique.

ECT TECHNIQUE

A thorough medical evaluation is a necessary prerequisite to a determination of potential risks with ECT (Abramczuk &

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32.28
ELECTROCONVULSIVE THERAPY

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INTRODUCTION

Electroconvulsive therapy (ECT) is a procedure in which generalized seizures lasting 25 to 150 seconds, induced by the passage of an electrical current through the brain under general anesthesia, and muscle relaxation are used for therapeutic purposes. One of the most effective and safest available treatments for depression, ECT has also been found beneficial in mania, schizophrenia, catatonia, and other neuropsychiatric conditions.

HISTORY

Seizures produced by camphor were used to treat psychosis and mania in the 16th century by Phillipus Paracelsus and in the late 19th century by Leopold von Auenbrugger, W. Oliver, and Carl Weickhardt. The first modern application of convulsive therapy occurred in January 1934, when Ladislas J. von Meduna, who was apparently unaware of the earlier work, introduced camphor-induced seizures as a treatment for schizophrenia. Von Meduna thought that schizophrenia and epilepsy antagonize each other because catatonic and schizophrenic patients appear to be less psychotic after spontaneous seizures than before the seizures. He also thought that schizophrenia and epilepsy accompany each other at a lower than expected rate, which did not turn out to be true. Of the first 26 schizophrenic patients treated by von Meduna, 10 recovered, 3 improved, and 13 were unchanged. He then began using intravenous pentylenetetrazol (Metrazol) to avoid the discomfort associated with the long onset of action of intramuscular camphor in oil. Von Meduna continued to use pentylenetetrazol as a primary treatment and as a means of augmenting ECT, but the substance is now available only experimentally.

Convulsive therapy was initially associated with a 2 percent incidence of fractures of the extremities, a 17 percent incidence of dislocations, and a 50 percent incidence of compression fractures of the spine. Those risks were eliminated when psychiatrist A. E. Bennett introduced muscle relaxants to the procedure in 1940. Bennett used curare, which had been encountered by Sir Walter Raleigh in the 16th century and which was shown to block the neuromuscular junction by physiologist Claude Bernard in 1849. Curare was made available to Bennett by a pharmaceutical company that obtained it as a plant extract from an explorer returning from South America. After using curare to protect patients from pentylenetetrazol-induced convulsions, Bennett found that fractures only occurred when the curare wore off before the convulsion occurred. He predicted that when synthetic neuromuscular blocking agents became available, it would be "illegitimate to administer convulsive shock therapy without this safeguard."

The use of electricity to induce seizures was introduced in April 1938 by Ugo Cerletti and Lucio Bini and was imported to the United States by Lothar Kalinowsky and others in 1939. Bini originally thought that electrical induction may be dangerous when a number of dogs died in early experiments and when he heard that electricity is used in slaughterhouses to kill animals. However, he realized that it is passing the current through the heart that is fatal in the laboratory. Passing an electric current through the head is not harmful in itself and is used in slaughterhouses only to render animals unconscious, so that they can be killed painlessly. That history is sometimes misquoted by anti-ECT activists to show the dangerousness of ECT.

The first patient to receive ECT was found wandering around in a disorganized state, alternating between muteness and incoherent gibberish. After being given a subconvulsive stimulus to induce unconsciousness before the actual seizure, he awoke to speak his first coherent words: "Not another! It will kill me!" After some discussion, the investigators decided that the patient was wrong, and they administered a convulsive stimulus. The patient had a full recovery after 11 ECT treatments. When he was asked, "What's been happening to you?" he replied, "I don't know. Perhaps I've been asleep."

In 1957 the pharmacologist J. C. Krantz discovered that the inhalation of hexafluorinated diethylether (Indoklon) produces convulsions. Used first by itself and then with an anesthestic, the drug was found

TABLE 32.28-9
Medications Used to Treat Hypertension during ECT

Medication	Reported Dose and Route	Comments
Propranolol (Inderal)	1–2 mg IV	β-blockers useful for tachyarrhythmias and hypertension but can cause bradycardia and hypotension. Prophylactic propranolol has been associated with cardiac arrest after subconvulsive stimulation
Labetalol (Normodyne)	0.05–0.20 mg/kg IV	Intermediate half-life useful for postictal hypertension; has been combined with nifedipine
Esmolol (Brevibloc)	100 mg IV	Half-life of 9 minutes useful for intraictal hypertension
Nifedipine (Procardia)	10–20 mg sublingual	Few side effects; controls blood pressure but not pulse
Nitroglycerin (Nitrogard)	1 tab sublingual	Dilatation of cerebral vessels helpful in preventing increased intracranial pressure
Sodium nitroprusside (Nipride)	50 mg in 500 ml 5% dextrose in water (D5W) continuous infusion	Used only in ICU
Hydralazine (Apresoline)	20 mg IV	Long duration of action; high incidence of tachycardia
Trimethaphan (Arfonad)	3–4 mg/min IV infusion	Hypotension common

that raise the seizure threshold, hyperventilation, decreasing the dose of the anesthetic, and using an anesthetic that does not raise the seizure threshold. Pharmacological enhancement of seizures can be accomplished with 500 to 2,000 mg of intravenous caffeine sodium benzoate 5 to 10 minutes before seizure induction or 500 to 800 mg of intravenous pentylenetetrazol 60 to 90 seconds before induction. It has recently been demonstrated that caffeine prolongs seizures but does not lower the seizure threshold with right unilateral ECT, suggesting that it may not be helpful when it becomes difficult to exceed the seizure threshold in patients receiving that type of ECT.

Inadequate seizures When seizures last fewer than 20 seconds, the physician usually waits 60 to 90 seconds, because of the relative refractory period after a partial seizure, and then applies a higher stimulus intensity than before. If that approach is not effective, techniques for missed seizures are used to produce seizures of adequate duration, since the cumulative time of several inadequate seizures does not equal one therapeutic seizure.

Prolonged seizures Seizures lasting more than 180 seconds lead to excessive postictal confusion and amnesia. Those seizures can be terminated by another dose of barbiturate anesthetic or an intravenous benzodiazepine, such as 5 to 10 mg of diazepam or 1 to 2 mg of midazolam (Versed). Oxygenation is maintained, and more muscle relaxant is administered if necessary. Medications that lower the seizure threshold, such as theophylline (Quibron) and some antipsychotics, are discontinued, and multiple monitored ECT is avoided.

Tardive seizures Spontaneous seizures after ECT treatments have been reported in 1 in 500 to 1 in 1,000 patients. Many of those patients may have had preexisting seizure disorders, but some apparantly had idiopathic seizures. Those seizures are not likely to have been kindled by brief exposure to a suprathreshold stimulus, but some electrical aftermath of the therapeutic seizure can conceivably serve as a kindling focus.

Treatment-emergent confusion In 5 to 10 percent of patients, a confusional state lasting 15 to 30 minutes develops as the patient emerges from the postictal state. It is usually treated with another dose of methohexital or 5 to 10 mg of intravenous diazepam. Treatment-emergent agitation is sometimes treated with 0.5 to 2.5 mg of intravenous midazolam.

Treatment-emergent mania On emergence from a seizure, some patients go into a manic state manifested primarily as giddiness, which is differentiated from organic euphoria by the absence of confusion and amnesia. If treatment-emergent mania does not remit spontaneously, it responds to additional ECT treatment. Some clinicians believe that the syndrome indicates an affective overshoot of adequate limbic stimulation and is a sign that no further ECT is required for depression.

Sore muscles Muscle pain because of fasciculations caused by succinylcholine can be averted by administering 3 to 4.5 mg of curare or atracurium intravenously before succinylcholine. However, it may be necessary to increase the dose of succinylcholine by 10 to 25 percent.

Fear of ECT Patients are more than usually likely to become fearful in anticipation of each treatment if they experience confusion or do not understand the procedure. The problem is managed by open discussion, education, reassurance, and relaxation training.

Postictal and interictal delirium Disorientation, confusion, and EEG slowing in the postictal and interictal periods led to interruption of ECT 50 percent of the time in a recent retrospective study. Some reports suggest that postictal disorientation is greatest after the first treatment; other reports indicate that both postictal and interictal delirium increase in duration as ECT progresses. Delirium clears within days to weeks of the completion of ECT in the order of orientation to person, place, and time.

Delirium is more severe than with other approaches with bilateral ECT, use of the sinusoidal waveform, high-intensity stimulation, closely spaced treatments, multiple monitored ECT, anesthesia with ketamine or high doses of barbiturates, basal ganglia or subcortical white matter lesions visualized on brain imaging, and preexisting cognitive dysfunction or neurological disease. Although the mechanisms of delirium may be somewhat different from those of amnesia, treatment strategies are similar for delirium and amnesia.

Memory loss Evaluation of memory problems associated with ECT is confounded by the frequent finding of memory deficits in depression. One differentiating feature is that depression appears to be associated with impairment of the *acquisition* of new information, whereas ECT causes transient disruption of the *retention* of new information, with no change in acquisition or with increased acquisition.

ECT-induced amnesia tends to improve after each treatment, but the recovery of memory between ECT treatments is incom-