Convulsive Therapy in Schizophrenia?

by Max Fink and Harold A. Sackeim

Abstract

Schizophrenia is a clinical syndrome of extraordinary importance and complexity. Its early identification is difficult, and our concepts of its main characteristics have undergone many changes in the past century. Electroconvulsive therapy (ECT) was introduced as a treatment for dementia praecox. The initial reports were salutary, and the treatment was widely applied until it was replaced by psychoactive drugs. ECT was reintroduced in the 1970s in the treatment of therapy-resistant disorders. The initial reviews argued that ECT was not applicable in patients with schizophrenia, a conclusion based mainly on experience with chronic forms of the disorder. This article assesses the role of ECT in schizophrenia today. We find it to be an effective treatment for psychosis. ECT is particularly applicable in patients with first-break episodes, especially those marked by excitement, overactivity, delusions, or delirium; in young patients, to avoid the debilitating effects of chronic illness; and in patients with syndromes characterized by catatonia, positive symptoms of psychosis, or schizoaffective features.

Schizophrenia Bulletin, **22(1): 27–39, 1996.**

Convulsive therapy was an accepted treatment for patients with dementia praecox from its introduction in 1934 until its replacement by psychoactive medications after their introduction in the 1950s. Electroconvulsive therapy (ECT) was resurrected a decade later for treating therapy-resistant affective disorders, for which it continues to be used successfully. As interest in ECT was renewed, its merit in treating patients with schizophrenia was generally denied. This view persists, as do questions about effective therapies for the condition. Currently, differing views of etiology, pathogenesis, and pathology encourage a wide range of pharmacological, social, psychological, and milieu therapies.

Christison et al. (1991) found eight treatments to be superior to placebo in treating persistent disabling symptoms of schizophrenia: clozapine, lithium, benzodiazepines, ECT, reserpine, carbamazepine, propranolol, and L-dopa. They noted that much of the large literature for ECT was limited by serious methodological flaws. Nevertheless, they concluded that the positive symptoms of psychosis and the motor symptoms of catatonia are likely to respond. They qualified their assessment, however, stating that legal and political issues limiting the general use of ECT cannot be ignored.

In another article, Wyatt (1991) assessed the impact of neuroleptic drugs on the natural course of schizophrenia. Noting that the more chronic and debilitating forms of schizophrenia—those defined as simple, hebephrenic or nuclear—became rarer as effective treatments were introduced, he concluded that early intervention increased the likelihood of an improved lifelong course. Wyatt ob-

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served that "some patients are left with a damaging residual if a psychosis is allowed to proceed unmitigated. While psychosis is undoubtedly demoralizing [Miller 1989] and stigmatizing, it may also be biologically toxic" (p. 347). Citing data from pneumoencephalographic, computed tomography, and magnetic resonance imaging studies, he also suggested that "prolonged or repeated psychoses might leave . . . biochemical alterations, gross pathological or microscopic scars, and changes in neuronal connections . . ." (p. 347).

A study by Haas et al. (1994) supports the hypothesis that rapid resolution of an acute psychosis may be essential to preventing long-term deterioration. They studied the timing of the first neuroleptic medication after onset of illness in 150 patients with schizophrenia. Patients who received their first treatment 2 or more years after onset of psychotic symptoms showed a less adequate treatment response at hospital discharge, more severe negative symptoms, and worse global functioning than patients who received treatment sooner. These findings were not accounted for by duration of illness or premorbid psychosocial adjustment. The investigators concluded that failure to treat may be associated with worse treatment response and a more severe course of illness.

Theories that prolonged illness may result in persistent brain damage and debilitation are speculative. Not so speculative, however, are the conclusions of studies seeking evidence of persistent brain damage because of ECT. These studies find no basis for fears that repeated induced seizures, as presently practiced, result in persistent changes in brain structure (Devanand et al. 1994).

Convulsive therapy was developed following reports that dementia praecox was rare in patients with severe epilepsy and that posttraumatic seizures in patients with dementia praecox ameliorated the psychotic condition (Meduna 1985). The treatment was developed in 1934 using biochemical induction of seizures; and in 1938, electrical induction facilitated the treatment and encouraged its widespread use (Fink 1979*a*). In its more than 60 years of use, clinical application of ECT has become safer. Patients are treated under anesthesia and with muscle paralysis, oxygenation, and attention to new induction methods that ensure adequate seizures (Abrams 1987, 1992; American Psychiatric Association 1990; Sackeim et al. 1993).

At the same time, our methods of identifying and classifying patients with severe psychotic disorders have changed greatly. The most prominent changes are reflected in the many labels used for disorders: schizophrenia, dementia praecox, "the group of schizophrenias," schizophrenic reaction, schizoaffective disorder, and, in Europe, cycloid psychoses. Disorders are further defined as paranoid, catatonic, hebephrenic, positive- and negative-symptom, nuclear, and reactive. The schizophrenia described in *DSM–III–R* (American Psychiatric Association 1987) and *DSM–IV* (American Psychiatric Association 1994) classifications represents many disorders, and few argue for a single pathogenesis. Indeed, in discussing the diagnosis and classification of schizophrenia in *DSM–IV*, Andreasen and Carpenter (1993) note that "heterogeneity in the clinical presentation of schizophrenia is certain, and heterogeneity in pathophysiology and etiology is likely" (p. 199). A review of 100 years of outcome studies in schizophrenia treatment reveals great diversity in diagnostic and outcome criteria (Hegarty et al. 1994). For almost all of this century we have spoken of "the schizophrenias," and the fact that neurobiological studies have not defined a distinct genetic or neuropathological form of the disorder encourages such a view.

A conspicuous example of the imprecision of our nosological criteria is seen in our views of the catatonic syndrome. Catatonia is a motor disorder frequently seen in patients with affective disorders, especially mania (Abrams and Taylor 1976*a*; Abrams et al. 1979), with organic affective disorders (Gelenberg 1976), and with schizophrenia. But in *DSM–III* (American Psychiatric Association 1980), catatonia is recognized *only* as a type of schizophrenia.[1] For many clinicians, the presence of catatonia indicates a defined form of a specific disorder classified as schizophrenia, which warrants treatment with neuroleptic drugs. Unfortunately, such classification is often incorrect, since most patients with catatonic signs are probably suffering not from schizophrenia but from mood disorders. Historically, patients with catatonia were the first treated by Meduna when he introduced convulsive therapy, and

[1] *DSM–IV* recognizes a form of catatonia that is defined as a "catatonic disorder due to a general medical condition" (293.89) and accepts catatonia as a specifier for affective disorders, in addition to recognizing a catatonic form of schizophrenia (295.3x).

by Cerletti and Bini when they tested electrical inductions. Catatonia in each of its varieties—in affective illness and secondary to systemic disorders, and in the form seen as neuroleptic malignant syndrome—is remarkably responsive to ECT (Pataki et al. 1992; Fink 1994). In patients with the malignant variety of catatonia, ECT is described as lifesaving (Philbrick and Rummans 1994).

Diagnostic uncertainty is also evident in discussions of cycloid psychosis, a subtype of psychosis recognized in Europe but not included in *DSM* classifications. Cycloid psychosis as defined by Leonhard (1961), Perris (1974), and Cutting et al. (1978) is a psychotic episode that resolves completely and that is accompanied by mood swings and at least two of the following features: perplexity or confusion, paranoialike symptoms, motility disturbances, ecstasy, or pan-anxiety. The syndrome's closest approximation in *DSM–III* is schizoaffective disorder, but this association has been criticized (Maj 1984). Indeed, the cumulative risk in women is said to be 0.7 percent, about half that of schizophrenia (Lindvall et al. 1986). In ICD–10 (World Health Organization 1992), cycloid psychosis is recognized as an independent diagnostic category (F23.0, F23.1). Both cycloid psychosis (Perris 1974; Ottosson 1995) and schizoaffective psychosis (Ries et al. 1981; Lapensee 1992) respond rapidly to ECT.

Our views of the role of ECT in treating psychotic disorders are largely based on the studies of the prepsychotropic drug era, when the practice and administration of ECT was rather gross, diverse diagnostic schemes were used, and neither researchers nor clinicians appreciated the effects of duration of illness, positive and negative symptoms, or social factors on clinical outcomes. With these caveats regarding diagnostic imprecision and an uncertain assessment of ECT's adequacy, we seek to review the published studies and determine what contribution, if any, can be considered in the current treatment of patients with schizophrenia.

Pre-1980 Studies[2]

Our judgment of the role of ECT in treating patients with schizophrenia is based on clinical experience with diverse populations defined as suffering from schizophrenia. Some authors recognized that this population is heterogeneous and that many of the patients included in the studies may well have been suffering from affective or other mental disorders that mimic schizophrenia. The most relevant variable in assessing efficacy appeared to be the duration of illness. Meduna (1939), after inducing repeated seizures by injecting camphor or Metrazol (pentylenetetrazol) in more than 100 patients with dementia praecox, concluded that illnesses lasting less than 2 years had good prognosis, while those lasting longer than 2 years showed poor results.

Acute Schizophrenia. In the clinical studies done before the advent of psychotropic medications, psychotic symptoms were reduced and hospitalization periods shortened in approximately 75 percent of ECT and Metrazole treated cases (Guttman et al. 1939; Zeifert 1941; Danziger and Kendwall 1946; Kino and Thorpe 1946; Baker et al. 1960*a*; Goller 1960). Improvement rates of 84 percent with pentylenetetrazol and 80 percent with ECT were reported (Zeifert 1941). Patients receiving ECT showed better discharge rates, better symptom evaluations, and fewer relapses than patients treated with psychotherapy, milieu therapy, or sedatives (Goldfarb and Kiene 1945; McKinnon 1948; Palmer et al. 1951; Wolff 1955). They exhibited an improvement rate of 50 to 70 percent, compared with a rate of 10 to 30 percent for historical controls (Hamilton and Wall 1948; Ellison and Hamilton 1949; Gottlieb and Huston 1951; Currier et al. 1952; Bond 1954). Shorter hospitalization periods and better discharge rates were found in patients treated with ECT, compared with those treated by psychotherapy or insulin coma (Rachlin et al. 1956).

With the advent of psychotropic medications, interest shifted to comparisons between ECT and pharmacotherapy, either singly (Langsley et al. 1959; Baker et al. 1960*a*, 1960*b*; Childers 1964) or combined (King 1960; Ray 1962; Childers 1964; Smith et al. 1967). In first-admission or acute schizophrenia patients, phenothiazines and ECT reduced psychotic features equally (Langsley et al. 1959; Baker et al. 1960*a*, 1960*b*; King 1960; Childers 1964). Patients receiving from 12 to 20 ECT treatments or from 300 to 1,200 mg/day of chlorpromazine (CPZ) exhibited equivalent reductions in symptom ratings by blind raters on nurses' ward observations and

[2]For a detailed critical review of the evidence regarding ECT's efficacy in schizophrenia, see Krueger and Sackeim (1995).

improved discharge evaluations (Langsley et al. 1959).

Virtually all the studies comparing either a neuroleptic medication or ECT with a neuroleptic-ECT combination found the latter more effective. Patients treated with ECT with or without CPZ showed more improvement than those treated with either fluphenazine (20 mg/day) or CPZ (1 gm/day) alone (Childers 1964). Smith et al. (1967) examined consecutive patients with schizophrenia admitted to a community acute treatment facility. The identified patients were treated with CPZ alone (average 655 mg/day) or CPZ (400 mg/day) combined with bilateral ECT 3 times a week (ECT/CPZ). Ratings using the In-Patient Multidimensional Psychiatric Scale (Lorr and Klett 1966) found overall improvement in both groups within the first 6 weeks. Hostility, feelings of unreality, and ideas of persecution responded more rapidly to ECT/CPZ than CPZ alone, while memory deficit and confusion scores, when rated at 3 and 6 weeks of treatment, were found to have increased more with ECT/CPZ. The mean length of hospitalization after admission was 159 days for CPZ alone and 102 days for ECT/CPZ. Sixty days after admission, 84 percent of the CPZ group and 48 percent of the ECT/CPZ group remained hospitalized. The authors also noted that 8 of 24 patients (33%) in the CPZ and 2 of 20 (10%) in the ECT/CPZ groups were rehospitalized in the year after their original admission.

May (1968) randomly assigned 228 "middle prognosis" patients with schizophrenia (probably intermediate between acutely and chronically ill) at Camarillo State Hospital to five treatment groups: psychotherapy alone, trifluoperazine or CPZ alone, individual psychotherapy plus these neuroleptic medications, ECT, or milieu therapy. ECT was more effective than psychotherapy alone or milieu therapy, resulting in a level of short-term improvement almost as high as neuroleptic therapy alone (May and Tuma 1976; May et al. 1976, 1981). In followup reports, May et al. (1981) concluded:

> Patients who had been treated with ECT fared, in the long run, at least as well as those given drug therapy, and in some respects even better, but not to a statistically significant extent. It seems that the status and role of ECT in the treatment of schizophrenia merit serious objective study. The empirical results support both its efficacy and the need for further studies and are contrary to the emotional and at times inflammatory attacks on this treatment. [p. 783]

Chronic Schizophrenia. The contrast between these positive reports for patients with acute forms of the illness and those for patients with chronic forms is striking. Following ECT, only 10 to 20 percent of the long-term mentally ill were discharged (Kalinowsky 1943; Shoor and Adams 1950; Brussel and Schneider 1951). Symptom reduction, particularly decreases in excitement, hyperactive motor behavior, and the need for restraints, is generally described shortly after ECT. In open comparisons of ECT with milieu, psychoactive medication, and insulin coma therapies, little difference among the treatments was reported (Cheney and Drewry 1938; Chafetz 1943; Gottlieb and Huston 1951; Funk et al. 1955; Rouleau et al. 1955; Stinson et al. 1972). There was no difference in short-term evaluations of improvement among patients treated with ECT, insulin coma, and psychotherapy (Gottlieb and Huston 1951).

Controlled trials also found little difference among various treatments of patients with chronic conditions (Riddell 1963; Heath et al. 1964). Miller et al. (1953) compared the effects of ECT, anesthesia alone, ECT and anesthesia, and subconvulsive currents in the chronic mentally ill and reported each to be ineffective. In clinical results in randomly assigned chronic, psychotic, hospitalized veterans, Brill et al. (1959) found no differences in unmodified ECT, ECT with succinylcholine, ECT with thiopental, thiopental alone, and nitrous oxide treatments. They concluded that ECT was ineffective in chronic schizophrenia.

This experience in patients with sustained chronic illness leaves unanswered questions. In most early studies, the patients were institutionalized on a long-term basis, with unremitting illness. This group did not benefit from ECT. However, many patients with a long history of schizophrenia have an intermittent course, with periodic exacerbations of psychotic symptoms. It is not known whether ECT is of value in such patients, independent of their duration of illness.

Technical Aspects. The efficacy of ECT in schizophrenia may depend mainly on the duration of the illness, as Meduna (1939) already noted. Successful treatment also requires special consideration of the number, frequency, and adequacy of induced seizures. Improvement in psychosis and return to the community was estimated at 50 to 70 percent in patients

who have been ill for less than 1 year, but was reduced to less than 20 percent in patients who have been continuously ill for more than 3 years (Ross and Malzberg 1939; Kalinowsky 1943; Kalinowsky and Worthing 1943; Danziger and Kendwall 1946; Miller et al. 1953; Naidoo 1956; Brill et al. 1959).

Courses of treatment with fewer than 20 seizures may be less effective than longer courses (Kennedy and Anchel 1948; Glueck et al. 1957; Baker et al. 1960*a*, 1960*b*; Jacoby and van Houten 1960; Murillo and Exner 1973; Exner and Murillo 1977). An example is seen in the study by Baker et al. (1960*b*), who reported greater efficacy after 20 treatments than after 12.

Some physicians increased the frequency of seizures, inducing them daily or a few times a day (defined as "regressive therapy") (Kennedy and Anchel 1948; Glueck et al. 1957; Jacoby and van Houten 1960; Abrams and Fink 1972). In severely ill patients, the efficacy rates were greater after multiple treatments than after conventional courses of 3 times a week. Murillo and Exner (1973) and Exner and Murillo (1977) examined the efficacy of intensive ECT in patients who had failed extensive neuroleptic drug therapy. They reported the treatment to be superior to neuroleptic treatment or standard courses of ECT in the long-term indices of work record and number and duration of rehospitalizations. Indeed, quantitative electroencephalograms in 1-year followup found fewer abnormalities in those treated with regressive ECT than in those treated with pharmacotherapy alone. Despite these positive reports, regressive ECT was abandoned before its efficacy and safety were more rigorously evaluated.

Post-1980 Studies

Recent studies of the effects of ECT on patients with schizophrenia have been confounded by the continued use of neuroleptic drugs during the ECT trial or have specifically focused on combined use. Scientists seeking to learn the merits of ECT alone must consider studies of combined treatment to be contaminated. Clinicians seeking a more effective therapy, may consider the combination a strength.

In comparisons of ECT and sham-ECT combined with neuroleptic drugs, real ECT is more effective, with a more rapid onset than sham-ECT (Taylor and Fleminger 1980; Janakiramaiah et al. 1982; Brandon et al. 1985; Abraham and Kulhara 1987). Over the years, 10 studies have compared the efficacy of combined ECT and neuroleptic with neuroleptic alone in schizophrenia patients. Nine reported the combination to show a significant advantage in speed or quality of response (Ray 1962; Childers 1964; Smith et al. 1967; Taylor and Fleminger 1980; Janakiramaiah et al. 1982; Ungvári and Pethö 1982; Brandon et al. 1985; Abraham and Kulhara 1987; Das et al. 1991). Given the established efficacy of neuroleptic treatment alone and the statistical problems in establishing enhanced efficacy with an augmentation agent, the consistency of these findings is surprising. Indeed, we know of no pharmacological augmentation strategy with a comparable body of evidence.

Clearly, the most common occasion for considering the use of ECT is in medication-resistant schizophrenia patients. In recent years, a handful of open studies have suggested that psychotic patients who fail to improve with a neuroleptic (thiothixene, fluphenazine, or molindone) often respond when ECT is added (Friedel 1986; Gujavarty et al. 1987; Konig and Glatter-Gotz 1990; Milstein et al. 1990; Sajatovic and Meltzer 1993). Adding ECT to clozapine in therapy-resistant patients who failed the clinical trial with clozapine alone has been found to be safe and effective in a number of cases (Klapheke 1991; Landy 1991; Safferman and Munne 1992; Kales et al. 1995). Acceptance of these clinical observations is limited by the possibility that improvement resulted not from the addition of ECT but from the extension of neuroleptic drug treatment. The role of ECT in treating medication-resistant schizophrenia patients particularly needs controlled investigation.

Dodwell and Goldberg (1989) examined predictors of outcome in 17 patients with schizophrenic symptoms who were treated with ECT and concurrent neuroleptic medication. Five patients fulfilled criteria for schizophrenia and 12 for schizoaffective disorder. Short duration of illness and a paucity of premorbid schizoid personality traits, perplexity, and mood-congruent delusions or hallucinations were associated with good outcome. The patients believed they had benefited from ECT and agreed that they would willingly undergo treatment again. The authors concluded that prospective studies are warranted.

Finally, in an extended meta-analysis of the treatment of schizo-

phrenia over 100 years, Hegarty et al. (1994) found outcome assessments to depend on diagnostic style. Outcome was better when patients were diagnosed according to broad (non-Kraepelinian) or undefined criteria rather than narrow (Kraepelinian) criteria. Outcome evaluations for neuroleptic drugs and for convulsive therapies, in terms of percentages of patients improved, differ for these diagnostic styles. For neuroleptic drugs, percentages improved were 31.2 ± 17.3, 48.0 ± 17.6, and 51.9 ± 16.6 for cohorts diagnosed by Kraepelinian, non-Kraepelinian, and unspecified criteria. For the convulsive therapies, the percentages were 26.9 ± 13.8, 42.2 ± 19.8, and 44.0 ± 18.1, respectively. This study found convulsive therapies to be as effective as neuroleptic drugs—a particularly encouraging observation, since most therapists advise using neuroleptic drugs in almost all cases of schizophrenia, leaving convulsive therapy for neuroleptic-resistant cases.

Opinions of These Data

Reviewers typically note that these studies do not meet present standards of clinical evidence, then conclude that ECT has a limited role in treating schizophrenia (American Psychiatric Association 1978, 1990; Erwin and Thompson 1978; Fink 1978, 1979*a*, 1979*b*; Salzman 1980; Taylor and Fleminger 1980; Consensus Conference 1985; Small 1985; Abrams 1992).

A role assigned to ECT in treating schizophrenia was codified in the 1990 American Psychiatric Association Task Force report, which notes that "ECT is an effective treatment for psychotic schizophrenic exacerbations in the following situations: (1) catatonia (295.2x); or (2) when affective symptomatology is prominent; or (3) when there is a history of a favorable response to ECT" (p. 8). The report adds the caveat that ECT "is effective in related psychotic disorders, notably schizophreniform disorder (295.40) and schizoaffective disorder (295.70)," and "may also be useful in patients with atypical psychosis (298.90) when the clinical features are similar to those of other major diagnostic indications" (p. 8).

Abrams argues,

> There is little doubt that many patients diagnosed as having acute or schizoaffective schizophrenia respond remarkably well to ECT; there is also little doubt that most of these patients are misdiagnosed manics (Abrams and Taylor 1974, 1976*b*, 1981; Taylor and Abrams 1975). When the diagnosis of schizophrenia is made by first excluding patients with prominent affective symptoms (Taylor and Abrams 1978), most of the ECT-responsive clinical variance is thereby excluded. [1988, pp. 27–28]

But he later adds,

> This should not be taken to mean that patients with an early, insidious onset of emotional blunting, avolition, first-rank symptoms, and formal thought disorder should never be offered ECT. On the contrary, every such patient deserves one full trial of ECT (preferably earlier rather than later in the treatment course) to insure that no treatment will be overlooked that has a chance, however slim, of halting the otherwise relentless progression of this devastating illness (Abrams 1987). [1992, p. 30]

In partial response to Abrams, Kalinowsky (1988) noted,

> Schizophrenia as an indication for ECT should no longer be considered controversial. . . . In patients with acute schizophrenic symptomatology, even if they have no affective symptoms, ECT gives good results. This is particularly true for those patients who can be classified as having "cycloid" psychoses with schizophrenic symptomatology. [p. 99]

By contrast, Krueger and Sackeim (1995), the most recent reviewers of these same data note,

> There is little doubt that ECT is efficacious in the treatment of schizophrenia, at least in patients with acute exacerbations and/or relatively short duration of illness. In contrast, the available evidence suggests that the combination treatment of ECT and neuroleptic is superior in short-term outcome to that of ECT alone or neuroleptic alone. [p. 536]

These authors also report that ECT may exert long-term benefits; when schizophrenia patients are treated early, they may be less likely to exhibit delayed manifestations of neuroleptic-induced parkinsonism and tardive dyskinesia.

Clinical Considerations

More than five decades' worth of data suggest that many patients whose prognosis might otherwise be considered hopeless—especially those with catatonia, affective components, or positive symptoms of psychosis or who experience short periods of illness that do not respond to the usual medications—warrant any treatment that offers hope of improvement. The question is, For whom should ECT be considered? Psychiatrists should consider four points.

1. In psychotic patients who have failed two medication trials, psychiatrists now often offer

clozapine therapy. Should the clozapine trial fail, various alternative treatments and combinations are considered (Christison et al. 1991). Adding ECT to continued neuroleptic medications has merit and should probably be undertaken before other alternative treatments.

Many psychiatrists express concern that the benefits of ECT in the short-term treatment of schizophrenia do not last. Certainly, high relapse rates following ECT would limit its utility. Three alternatives should be considered, however. First, comparative studies of ECT and neuroleptic medications reported that advantages for ECT were maintained or emerged over long-term followup (Smith et al. 1967; May et al. 1981). The possibility that ECT alters the course of illness, allowing continued benefit from neuroleptic drugs, should not be dismissed out of hand.

Second, in mood disorders, the most common practice is to follow the response to ECT with continuation and then maintenance pharmacotherapy. The assumption is that pharmacological strategies will sustain the improvement achieved with ECT. Similarly, when it is established that ECT alone or in combination with neuroleptic medication can produce a more rapid or profound remission in certain patients with schizophrenia, determining whether the remission can be sustained by neuroleptic medication alone becomes a central research and clinical issue.

Third, there is a long history of using continuation or maintenance ECT to prevent relapse and recurrence in schizophrenia (Moore 1943; Geoghegan and Stevenson 1949; Stevenson and Geoghegan 1951; Karliner and Wehrheim 1965; Asnis and Gabriel 1976). Conceptually, there are strong grounds for assuming that intermittent use of ECT will sustain the action that ECT produced in treating the psychotic episode. However, the experience with continuation ECT in schizophrenia is entirely anecdotal, and rigorous examination of its role and optimization is needed.

2. In patients with catatonia, trials of sedatives (lorazepam or barbiturate) are considered first. For those who fail to recover within 5 to 10 days, a trial of ECT is recommended (Fink 1994; Philbrick and Rummans 1994).

3. Young adults with first-break psychosis present an interesting dilemma. The episode may be a manifestation of schizophrenia but is as likely to be the consequence of drug toxicity, systemic disorder, or onset of an affective psychosis. The cross-sectional picture is often ambiguous as to the long-term course of the illness. For clinicians who view the illness as one of schizophrenia, the immediate response is to administer high-potency neuroleptic drugs. Such an approach exposes the patient to the risks of acute dystonia, dyskinesia, akathisia, and the neuroleptic malignant syndrome, as well as to tardive dystonia and tardive dyskinesia if use is prolonged. For young adults with affective illnesses, neuroleptic drugs may have a low efficacy and may prolong illness. When it is unclear whether a case is "true" schizophrenia or an affective illness, a detailed benefit-risk analysis comparing the relative safety of ECT and of high-potency neuroleptic drugs should lead to the conclusion that an ECT trial may be safer than, and probably as effective as, neuroleptic drugs.

4. Other conditions occasionally seen in the severely mentally ill warrant experimental trials. The recent report that tardive dyskinesia secondary to neuroleptic use is less frequent in male patients who had a course of ECT than in those who did not, suggests that the intercession of ECT has a protective effect on neuroleptic-induced persistent brain changes (Schwartz et al. 1993).

Research Considerations

The risk that inadequate or incomplete early treatment of psychosis may lead to incapacitating negative symptoms is frustrating and disturbing. As Wyatt (1991) asks, "Is there something about being psychotic that is toxic to the individual beyond the immediate psychotic episode?" (p. 347). His answer:

> While it is far from clear what kind of scar prolonged or repeated psychoses might leave (some possibilities include biochemical alterations, gross pathological or microscopic scars, and changes in neuronal connections), there is ample evidence that some patients have structural brain changes. . . . While in some patients these brain alterations appear to precede evidence of psychosis (Weinberger et al. 1980) . . . in others there may be progressive brain changes associated with changes in symptoms (Woods and Wolf 1983). . . . Glial scarring, while not universally found in the brains of schizophrenic patients, has been described on a number of occasions. [p. 347–348]

Given that patients with schizophrenia, especially those who have not yet reached the illness's various debilitating stages, may improve with ECT or ECT combined

with neuroleptic drugs, might it not be reasonable to undertake systematic prospective studies? Christison et al. (1991), Wyatt (1991), and Krueger and Sackeim (1995) argue that ECT warrants reassessment, both as a primary treatment for patients with first-break psychosis and those with "pharmacotherapy-resistant psychosis."

Krueger and Sackeim (1995) also argue for ECT as a primary treatment of first-break psychoses. Such treatment would be particularly useful in the malignant variety, which appears in young adults of intelligence and promise, often precipitated by alcohol, cannabis, or hallucinogens. From the very earliest experience with ECT, observers reported its efficacy in first-break psychoses. In recent studies, 85 percent of patients in their first episode of illness present a syndrome that can be classified confidently at 6 months as either schizophrenia or severe affective illness. Examining the 6-month diagnoses for stability revealed that 43 percent had changed at 1 year from initial diagnosis (Fennig et al. 1994). Separating a case of mania with psychosis from a case of schizophrenia with overactivity is clinically difficult in any cross-sectional examination; the longitudinal course remains the only way to ensure a stable diagnosis.

Difficulties in separating patients with schizophrenia from those with affective disorders with psychosis has led some authors to suggest that these disorders are not separate entities with individual genetic bases or individual pathophysiologies but that the phenotypic form seen in the clinic may reflect a single continuum of disorders, the so-called "unitary psychoses." Given ECT's success in patients with psychoses associated with prominent affective symptoms, is it not reasonable to encourage consideration of ECT in patients with psychoses in whom the affective symptoms are less prominent? In the range of first-episode psychoses, an ECT trial gives the patient the opportunity for immediate relief, regardless of the underlying pathology. This recommendation is especially compelling in patients with catatonia or schizoaffective (cycloid) psychoses.

These arguments for greater attention to ECT in the study of schizophrenia are not limited to these reviewers. Similar points have been presented by van Valkenburg and Clayton (1985), Christison et al. (1991), Hertzman (1992), and Saju and Jacob (1993), all of whom argue that the potential efficacy and safety of ECT in schizophrenia has been largely ignored.

Conclusions

Before the advent of neuroleptic drugs, ECT was considered an effective treatment for dementia praecox. The main reason for discarding ECT was not its lack of efficacy, nor even the risks of its use, but the convenience, ease of administration, lower cost, and political and social acceptance of neuroleptic drugs.

This review argues for the use of ECT early in the treatment of acutely psychotic patients, especially of first-break patients with excitement, overactivity, delusions, or florid delirium, and of young patients, to avoid the debilitating effects of chronic illness. We believe that if patients are treated effectively early in the course of illness, the risks of the illness becoming chronic and a deterioration of personality can be avoided.

There is need for prospective studies comparing the effects of ECT, alone and combined with neuroleptic drugs, with neuroleptic drugs alone in patients with schizophrenia. Since combined medication and ECT is probably more effective than ECT alone, combined therapy should be favored in prospective assessments.

And finally, ECT should be considered early in patients with psychosis with catatonia, including the varieties of neuroleptic malignant syndrome, malignant catatonia, and manic delirium.

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Acknowledgments

The authors are grateful for the comments of Jan-Otto Ottosson, M.D., and Richard J. Wyatt, M.D., on early drafts of this review.

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