Clinical Effectiveness and Cognitive Impact of Electroconvulsive Therapy for Schizophrenia:
A Large Retrospective Study

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ABSTRACT

Objective: To determine the clinical effectiveness and cognitive impact of electroconvulsive therapy (ECT) in a large clinical sample of patients with schizophrenia and explore factors associated with treatment response and transient cognitive impairment.

Methods: We examined the clinical records of 144 patients with a *DSM-IV* diagnosis of schizophrenia or schizoaffective disorder who were treated at an academic mental health hospital from October 2009 to August 2014. These patients received 171 acute courses of ECT; we attempted to determine their treatment response and transient cognitive impairment from ECT. We explored the impact of various factors including ECT indication, clinical characteristics, medication during ECT, and technical parameters on treatment response and transient cognitive impairment.

Results: Treatment with ECT resulted in a 76.7% response rate. Factors associated with a better response to ECT were absence of treatment with antiepileptic medication (17.9% vs 3.9%, $P = .007$), a previous good response to ECT (36.4% vs 15.4%, $P = .017$), and primary indication for ECT referral other than failed pharmacotherapy (89.7% vs 69.8%, $P = .012$). Factors not associated with treatment response included age, clozapine treatment, and benzodiazepine treatment ($P > .05$). Treatment with ECT caused transient cognitive impairment in 9% of treatment courses; no demographic or clinical factors were associated with cognitive impairment.

Conclusions: This work demonstrates the effectiveness of ECT for schizophrenia treatment and several factors associated with treatment response. The rate of transient cognitive impairment is lower than expected based on the rate of cognitive impairment seen in ECT for depression. ECT appears to be an effective treatment option for schizophrenia that is tolerated by the majority of patients.

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Schizophrenia is an illness that affects approximately 1% of the population.[1] Although the mainstay of treatment for patients with schizophrenia is antipsychotic medication, up to 25% of patients do not respond to first-line antipsychotics, and up to 83% of patients do not respond to second-line antipsychotics.[2] The current standard of care for patients who have failed 2 trials of antipsychotics is to start clozapine treatment.[3] However, up to 25% of these patients do not respond to clozapine,[2] and there are no guidelines for treatment after clozapine failure.[3] Furthermore, the risk of serious adverse effects and need for frequent blood monitoring limit clozapine's widespread use.[4]

One option for patients who do not respond to clozapine or who cannot take clozapine due to adverse effects is electroconvulsive therapy (ECT).[5] The most recent Cochrane review concluded that "ECT combined with treatment with antipsychotic drugs may be considered an option for people with schizophrenia, particularly when rapid global improvement and reduction of symptoms is desired."[5(p2)] Furthermore, recent evidence has shown ECT to be effective for treating psychotic symptoms in patients who are nonresponsive to clozapine.[6] Despite promising evidence supporting the effectiveness of ECT in schizophrenia, the current literature has several limitations. First, previous studies[7–9] have often used typical, rather than atypical, antipsychotics in conjunction with ECT. Second, these studies[7–9] have often included small numbers of patients, and, to date, the largest study[10] of patients with schizophrenia receiving ECT with atypical antipsychotics was a retrospective study that included 72 patients with schizophrenia and schizoaffective disorder. Third, there has been only 1 study using ultrabrief pulse width ECT, a technology designed to reduce cognitive side effects, for the treatment of schizophrenia.[11] Last, cognitive impairment resulting from ECT for patients with schizophrenia remains unclear because the use of disparate cognitive scales has led to conflicting results.[5]

The goal of this study was to address these limitations and to describe the clinical effectiveness and cognitive impact of ECT in a large clinical sample of patients with schizophrenia using modern pharmacotherapy and ECT techniques. In addition, we sought to explore clinical characteristics that may predict treatment response and transient cognitive impairment.

METHODS

Study Design and Subjects

This study was conducted at the Centre for Addiction and Mental Health, a large academic mental health hospital in Toronto, Ontario, Canada. We completed a retrospective chart review including all patients referred to the hospital's ECT treatment program from October 2009 to August 2014. Any patient with a *DSM-IV* diagnosis of schizophrenia or schizoaffective disorder who received at least 1 acute course of ECT was included in this study.

Clinical Points

- Electroconvulsive therapy (ECT) results in a clinically significant response in approximately three-fourths of treatment courses for patients with schizophrenia.
- ECT results in clinically significant transient cognitive impairment in a minority of treatment courses (approximately one-tenth).
- Several factors are associated with treatment response including being referred for ECT due to failure of pharmacotherapy, prior good response to ECT, and antiepileptic drug treatment.

Data for this study were obtained from referrals to the ECT service with the referring clinician providing information on the patient's diagnosis, indication, and previous medications. Subjects included in this study were patients identified on the referral form as suffering from "schizophrenia" or "schizoaffective disorder." The information provided by the referring physician was verified by a thorough review of the patient's electronic medical record.

For patients who were found by the treating physician to lack capacity to consent to ECT treatment due to their mental illness, a substitute decision-maker was appointed. *Lack of capacity* is specific to the proposed treatment in the province of Ontario and is defined as the inability to understand and appreciate information relevant to making an informed decision. Once an individual has been determined to lack capacity, he or she is notified with a legislatively defined form. The individual is then informed of his or her right to challenge the finding of incapacity by an independent advisor. If the individual chooses, that patient can challenge this finding at the Consent and Capacity Board, which is an independent government panel, composed of a psychiatrist, lawyer, and community member. For the Consent and Capacity Board hearing, the individual is provided with legal representation at no cost. If the finding of incapacity is upheld, or if the individual does not challenge the finding of incapacity, then informed consent is provided by a substitute decision-maker. The identity of the substitute decision-maker is defined by provincial legislation and follows a hierarchy whereby individuals appointed by the courts are top of the hierarchy, followed by family members, and lastly government-employed health care trustees. No patient in this study received court-ordered ECT.

The study was approved by the ethics board at the Centre for Addiction and Mental Health.

ECT Technique

The ECT machine used for this study was a MECTA spECTrum 5000Q. A 1.0-millisecond (ms) pulse width with 800 milliamps (mA) was used for bilateral (BL) and right unilateral (RUL) electrode placement. For the RUL setting, the pulse width was set to an ultrabrief pulse width of 0.3–0.37 ms in the more recent treatment courses, while the remainder received RUL with a pulse width of 1.0 ms. The choice of electrode placement was determined by the consultant ECT psychiatrist based on variables such as risk of cognitive side effects, need for rapid response, and previous treatment protocols. In general, BL electrode placement was recommended based on the prevailing reports in the literature.[12] The stimulus titration method was used to determine the seizure threshold. After threshold was achieved, the stimulus intensity was set at 1.5 times the seizure threshold. An adequate seizure for determination of threshold was defined as a seizure lasting at least 15 seconds of the peripheral motor manifestation to ensure that the seizure had generalized. The anesthetic agent used was methohexital 0.75–1.0 mg/kg IV, and the muscle relaxant was succinylcholine 0.3–0.6 mg/kg IV. For hypertension, labetalol IV was used as needed, and granisetron IV or ondansetron IV was used for severe nausea associated with treatment.

Assessment of Treatment Response

Chart review technique. All patients who received at least 1 ECT treatment were eligible for the assessment of treatment response. ECT treatment response was assessed by chart review using a 4-point scale similar to the one described by Kristensen et al.[10] The 4-point scale was used to estimate the Clinical Global Impression-Improvement scale (CGI-I),[13] and we have referred to this scale as the clinical note CGI (c-CGI). The c-CGI scale was determined as follows:

1. Excellent: The patient chart demonstrated dramatic benefit from ECT treatment. Examples of this level of response include rapid discharge after treatment, reduction in need for medications, resolution of target symptoms, and statements such as "dramatic response" or "greatly improved."
2. Good: The patient chart indicated that the patient responded well. Examples of this level of response include referral for maintenance ECT, significant reduction in severity of target symptoms, and statements such as "responded well" or "good response."
3. Moderate: The patient chart indicated that the patient had some amount of benefit. Examples of this level of response include slight to moderate reduction in severity of target symptoms and statements such as "improved somewhat" or "partial response."
4. Poor: The patient chart indicated that the patient had minimal to no benefit. Examples of this level of response include treatment stoppage after 1 to 2 sessions due to side effects and documentation of no benefit to the patient with statements such as "no symptom changes" or "no improvement noted."
5. *Treatment response* was defined as a c-CGI score of 1 or 2, and *treatment nonresponse* was defined as a c-CGI score of 3 or 4.

Validation of technique. Although attending psychiatrists were encouraged to complete the CGI-I after an ECT

Table 1. Potential Clinical and Treatment Features Associated With ECT Response

Referral indications
Failed pharmacotherapy
Prior good response to ECT
Suicidality
Failed continuation maintenance pharmacotherapy
Violent behavior
Intolerance of adequate pharmacotherapy
Patient preference
Demographic/clinical
Age[a]
Diagnosis (schizophrenia vs schizoaffective disorder)
Catatonia
Medications
Clozapine
Mood stabilizers[a]
Antiepileptic drugs
Lithium
Benzodiazepine use and dose[a]
ECT characteristics
First vs subsequent (second/third) treatment course of ECT
Number of acute treatments[a]
≤6 vs >6 treatment sessions[a]
Electrode placement (BL vs RUL)[a]

[a]Indicates that a clinical feature was examined for association with cognitive impairment.
Abbreviations: BL = bilateral, ECT = electroconvulsive therapy, RUL = right unilateral.

Table 2. Patient Demographic and Treatment Features of the Treatment Cohort (N = 144; no. of ECT courses = 171)[a]

Demographic/clinical	
Age, mean ± SD [min–max], y	45 ± 14.0 [20–83]
Male gender	105 (61.4)
Schizophrenia diagnosis	100 (58.5)
Schizoaffective diagnosis	71 (41.5)
Lacked capacity to consent to ECT	102 (59.6)
Medications	
Oral/depot antipsychotic	169 (98.8)
Depot antipsychotic	56 (32.7)
Clozapine antipsychotic	82 (48.0)
Benzodiazepine use[b]	33 (19.3)
Antidepressant treatment	51 (29.8)
Mood stabilizer/AED treatment	24 (14.0)
Treatment setting	
Inpatient	163 (95.3)
Voluntary inpatient[c]	82 (50.3)
Outpatient	8 (4.7)

[a]Values are number (%) of ECT courses, unless otherwise stated.
[b]Includes both regular and intermittent use.
[c]Percentage is calculated based on total number of ECT courses during status as an inpatient (no. of ECT courses = 163).
Abbreviations: AED = antiepileptic drug, ECT = electroconvulsive therapy, SD = standard deviation.

treatment course, this information was available for only a subset of treatment courses in the study (89 treatment courses). Therefore, we used this subset of treatment courses to validate the c-CGI technique and have reported the results in Supplementary eTable 1. c-CGI was measured by the main author (T.S.K.); when there was a disagreement with the CGI-I scale, an experienced ECT psychiatrist (D.M.B.) reviewed the treatment response, and this score was used. The strength of interrater agreement was quantified using the linearly weighted κ and interpreted using established standards.[14] When comparing c-CGI with CGI-I and their classification of treatment response (score of 1 or 2) versus nonresponse (score of 3 or 4), there was found to be a good agreement between techniques (κ = 0.7597).

Cognitive Impairment

The subset of treatment courses with an available CGI-I score for treatment response (89 treatment courses) also had a similar scale rating the level of their transient cognitive impairment following the ECT treatment course. Cognitive impairment was rated as "none," "mild," "moderate," or "severe" by the treating clinician. Similar to our review of treatment response, a chart review of transient cognitive impairment was attempted; however, in 106 of the acute ECT courses (62%), no reference was made in clinical notes to cognitive impairments. Therefore, we were able to assess transient cognitive impairment in only the subset of patients with completed rating scales. Based on the 4-point clinician-rated transient cognitive impairment scale, "none" or "mild" was considered to lack clinical significance while "moderate" or "severe" was considered to be clinically significant for the purposes of statistical analysis.

Treatment Subgrouping and Statistical Analysis

Subgroup analyses compared treatment response and transient cognitive impairment rates by various referral indications and clinical and treatment features (Table 1). The differences in these clinical/treatment features between treatment responders and nonresponders were calculated to determine their association with treatment response. A similar procedure was performed for patients with and without significant transient cognitive impairment. For continuous data, Student *t* test was used to compare means, and for categorical data, Fisher exact test was used to compare frequency distributions of clinical/treatment features. All statistical procedures were 2-tailed, and significance was set at an α level of .05. All analyses were computed using SPSS 20.0 (IBM Corporation, Armonk, New York).

RESULTS

Demographics and ECT Details

This study included 144 patients who received a total of 171 courses of acute ECT (Table 2). During a course of ECT, the typical patient who received ECT was hospitalized (95.3% of treatment courses), was taking antipsychotics (98.8%), lacked capacity to consent to ECT treatment (59.6%), had been referred because of failed pharmacotherapy (73.1%), and received approximately 12 sessions of ECT with BL electrode placement (86.0%) (Table 3). Of the 24 treatment courses in which a patient received ECT with RUL electrode placement, 9 of these (37.5%) were with an ultrabrief pulse width of 0.3–0.37 ms. Furthermore, 19 treatment courses started with RUL ECT, of which 8 eventually switched to BL ECT (42.1%). There were 152 treatment courses that started with BL ECT, of which 5 eventually switched to RUL ECT (3.3%). Considering all treatment courses, 40 patients (23.4%) required more than 16 treatments, and

Table 3. ECT Treatment Details of the Treatment Cohort (N = 144; no. of ECT courses = 171)[a]

ECT indication[b]	
Failed pharmacotherapy	125 (73.1)
Prior good response to ECT	54 (31.6)
Suicidality	28 (16.4)
Failed continuation maintenance pharmacotherapy	26 (15.2)
Violent behavior	23 (13.5)
Intolerance of adequate pharmacotherapy	20 (11.7)
Patient preference	16 (9.4)
ECT electrode placement	
BL	147 (86.0)
BL → RUL	5 (2.9)
RUL	11 (6.4)
RUL → BL	8 (4.7)
Multiple treatment courses	
Two courses	23 (13.5)
Three courses	4 (2.3)
Other	
Number of treatments, mean ± SD [min–max]	12.2 ± 6.5 [1–38]
Previous ECT	72 (42.1)
Referred for maintenance treatment	77 (45.0)
Discharged within 31 days of treatment completion[c]	73 (44.8)

[a]Values are number (%) of ECT courses, unless otherwise stated.
[b]Total percentages are greater than 100% because some patients may had multiple indications for ECT.
[c]Only includes inpatient ECT courses.
Abbreviations: BL = bilateral, ECT = electroconvulsive therapy, RUL = right unilateral, SD = standard deviation.

Table 4. Factors Associated With Treatment Response to ECT (N = 144; no. of ECT courses = 168)[a]

Variable	Treatment Response (129 courses)	Treatment Nonresponse (39 courses)	*P* Value[b]
Referral indication			
Failed pharmacotherapy	90 (69.8)	35 (89.7)	**.012**
Prior good response to ECT	47 (36.4)	6 (15.4)	**.017**
Suicidality	20 (15.5)	8 (20.5)	.47
Failed continuation maintenance pharmacotherapy	21 (16.3)	5 (12.8)	.80
Violent behavior	19 (14.7)	4 (10.3)	.60
Intolerance of adequate pharmacotherapy	14 (10.9)	6 (15.4)	.41
Patient preference	12 (9.3)	4 (10.3)	1
Demographic/clinical			
Age, mean, y	46.9	43.1	.13
Schizophrenia diagnosis	72 (55.8)	26 (66.7)	.27
Catatonia	7 (5.4)	3 (7.7)	.70
Medications during ECT			
Clozapine	62 (48.1)	20 (51.3)	.85
Mood stabilizer/AED	14 (10.9)	10 (25.6)	**.034**
AED	5 (3.9)	7 (17.9)	**.007**
Lithium	9 (7.0)	5 (12.8)	.32
Benzodiazepine use	23 (17.8)	9 (23.1)	.49
Benzodiazepine dose ≥ 2 mg lorazepam equivalent	8 (6.2)	4 (10.3)	.48
ECT characteristics			
First treatment course	105 (81.4)	36 (92.3)	.14
Number of treatments, mean	12.62	11.38	.30
≤ 6 treatments	25 (19.4)	9 (23.1)	.65
BL treatment	114 (88.4)	39 (100)	**.02**

[a]Values are number (%) of ECT courses, unless otherwise stated.
[b]Bold indicates statistical significance.
Abbreviations: AED = antiepileptic drug, BL = bilateral, ECT = electroconvulsive therapy.

the maximum number of ECT treatments delivered was 38. There were 3 patients who received benzodiazepine doses greater than 6 mg of lorazepam equivalent during their ECT treatment.

Treatment Response

Data on treatment response to calculate c-CGI were available for 168 treatment courses. Based on c-CGI (168 treatment courses), 76.7% of ECT courses resulted in patient response; and based on CGI-I (89 treatment courses), 82.0% of ECT courses resulted in patient response (Supplementary eTable 2). Table 4 presents the analysis of clinical/treatment features associated with ECT treatment response. Of note, there were no significant differences in the following features between treatment responders and nonresponders: age ($t = 1.5_{166}$, $P = .13$), clozapine treatment ($P = .85$), and benzodiazepine treatment ($P = .49$). However, there were significant differences in the following features between treatment responders and nonresponders: antiepileptic drug treatment (17.9% of treatment courses with nonresponding patients received treatment with antiepileptic drugs compared to 3.9% of treatment courses with responding patients, $P = .007$), a previous good response to ECT (36.4% of treatment courses with responding patients compared to 15.4% of treatment courses with nonresponding patients, $P = .017$), and a referral indication of failed pharmacotherapy (69.8% of treatment courses with responding patients compared to 89.7% of treatment courses with nonresponding patients, $P = .012$).

Cognitive Impairment

Table 5 presents the analysis of clinical/treatment features associated with transient cognitive impairment for the subset of treatment courses with available cognitive impairment data (89 treatment courses). Overall, cognitive impairment was observed in 9.0% of treatment courses (8 courses). We did not find any significant differences in clinical/treatment features between patients with and without transient cognitive impairment secondary to ECT.

DISCUSSION

Clinical Implications

This study suggests that ECT can be a clinically effective treatment for patients with severe forms of schizophrenia. Using a clinically representative population and modern ECT technology and pharmacotherapy, we found that ECT treatment resulted in a clinically significant response for 76.7% of treatment courses, with clinically significant transient cognitive impairment in only 9% of treatment courses. While the cognitive impairment rate is lower than expected, based on literature on the use of ECT for depression,[12] it still remains an important task to appropriately select patients likely to benefit from ECT.

To determine clinical/treatment factors associated with response to ECT, we compared these factors between responders/nonresponders and discovered several clinically relevant findings. The first is that treatment with antiepileptic drugs during an acute ECT course was associated with lower response rates to ECT, as we found that a significantly higher

Table 5. Factors Associated With Cognitive Impairment After ECT (N = 71; no. of ECT courses = 89)[a]

Variable	No Cognitive Impairment (81 courses)	Cognitive Impairment (8 courses)	*P* Value
Demographic/clinical			
Age, mean, y	47.7	45.0	.62
Medications			
Mood stabilizer/AED	10 (12.3)	0 (0)	.59
AED	4 (4.9)	0 (0)	1
Lithium	8 (9.9)	0 (0)	1
Benzodiazepine use	15 (18.5)	0 (0)	.34
Benzodiazepine dose ≥ 2 mg lorazepam equivalent	7 (8.6)	0 (0)	1
ECT characteristics			
Number of treatments, mean	12.4	13.2	.66
≤ 6 treatments	12 (14.8)	0 (0)	.59
BL treatment	71 (87.7)	8 (100)	.59

[a]Values are no. (%) of ECT courses, unless otherwise stated.
Abbreviations: AED = antiepileptic drug, BL = bilateral, ECT = electroconvulsive therapy.

percentage of ECT nonresponders received treatment with antiepileptic drugs than responders. Previous work has suggested that patients receiving antiepileptic drug treatment during an ECT treatment course have a significantly higher seizure threshold, higher incidence of failed seizure induction, and shorter duration of motor seizures.[15] We also hypothesize that the quality of induced seizures may be adversely impacted by antiepileptic drug treatment during ECT; however, this hypothesis will require future studies examining EEG seizure quality.

The second finding of our work is that certain ECT referral indications are associated with different response rates to ECT. If a patient is referred for ECT because of a previous good response to ECT, our results suggest that the patient is more likely to respond subsequently. Our results also suggest that when a clinician refers a patient for ECT primarily because of failed pharmacotherapy rather than for other reasons (ie, prior good response to ECT, suicidality, violent behavior, catatonia, etc) then the patient may be less likely to respond to ECT. One possibility is that these patients represent a more refractory form of illness that is less responsive to both antipsychotics and ECT. This finding is consistent with the literature on the use of ECT for depression, with a recent meta-analysis[16] finding that the rate of ECT response was significantly lower in patients with medication failure compared to those without. Benzodiazepines are also known to raise the seizure threshold; however, our results did not find an association between benzodiazepine use and ECT response. This negative finding may be due to the fact that only 3 patients received doses of benzodiazepines greater than 6 mg of lorazepam equivalents, which was the threshold for study inclusion in the recent prospective trial of ECT in schizophrenia.[6] Additionally, our standard procedures of holding benzodiazepine doses after 5 PM the evening prior to treatment quite likely mitigated the anticonvulsant effects of those taking low doses. Determining the interaction between benzodiazepines and ECT response remains an important area for future work.

The third finding of our work is that clozapine treatment was not associated with a different response rate to ECT compared to nonclozapine antipsychotic treatment. This suggests that ECT can be used as an augmentation treatment for patients who have not adequately responded to clozapine. This finding is consistent with a recent prospective randomized controlled trial[6] that demonstrated a response rate of approximately 50%, using ECT for patients with persistent psychotic symptoms despite clozapine treatment. These results suggest that ECT offers an incremental therapeutic benefit in treatment-resistant schizophrenia not seen with other adjunctive[17] or augmentation[18] therapies.

While there was a significantly higher nonresponse rate to BL ECT than RUL ECT, this finding is likely an artifact of clinical decision-making. If a patient is not responding quickly enough to RUL ECT, then the clinician will most likely switch to BL ECT given that clinical guidelines for treatment of depression suggest RUL ECT should be switched to BL ECT if there is minimal response.[19] This preference for BL ECT in our study is demonstrated by the fact that 42.1% of treatment courses (8/19) starting with with RUL ECT switched to BL ECT, in contrast to only 3.3% of treatment courses (5/152) starting with with BL ECT that switched to RUL ECT. Therefore, this means that treatment nonresponders are more likely to remain on BL ECT until the end of their treatment course. Recent work found no difference in final response rates between BL and RUL ECT for the treatment of depression, but did find that BL ECT resulted in more rapid symptom reduction than RUL ECT.[12] The high levels of switching from RUL to BL ECT in our study suggests that rapid symptom reduction is critical for patients with severe schizophrenia who are referred for ECT.

While BL ECT results in quicker response than RUL ECT, it has also been associated with greater transient cognitive impairment than RUL ECT.[20] Despite the frequent use of BL ECT in the current study, our results suggest that transient cognitive impairment in patients with schizophrenia is not as prominent as cognitive impairment in patients with depression who are treated with ECT.[21] We found that clinically significant cognitive impairment was observed in only 9.0% of treatment courses in our study, and severe cognitive impairment was not observed in any treatment course. While there were no statistically significant differences in clinical/treatment features between patients with/without transient cognitive impairment, this may be a result of the small sample size of patients who developed cognitive impairment (n = 8). However, we note that every patient who developed cognitive impairment received at least 6 ECT sessions and was treated with BL ECT, both of which (greater number of treatments and BL electrode placement) are known risk factors for transient cognitive impairment.[22,23] Furthermore, only 3.3% of patients treated with BL ECT were switched to RUL ECT, which is a change often made due to cognitive impairment.

Limitations and Future Work

There are several limitations to our study. The first is that, as a retrospective study, only conclusions about associations

can be drawn rather than conclusions about causality. Because of the retrospective design of this trial, the number of ECT treatments was determined by clinical judgment. This resulted in an average of 12 ECT treatments per patient, which is less than the 16 ECT treatments delivered in a recent prospective trial[6] of ECT in schizophrenia. However, longer ECT courses were not uncommon as approximately one-quarter (23.4%) of patients required extended courses longer than 16 treatments. Future prospective studies will be required to determine the optimal number of ECT treatments to achieve the highest response rates.

Another potential weakness of this study is the crude nature of the outcome assessments. The coarse nature of the CGI-I and the measure of transient cognitive impairment used in this study meant that we were unable to characterize the domains of symptom improvement or the cognitive domains impacted by ECT. However, the strength of these assessment tools is that changes are based on clinical significance, rather than significance in the context of a rating scale. The use of the c-CGI to estimate CGI-I is another potential weakness of this study. However, support for use of the c-CGI to estimate clinician CGI-I comes from the good agreement between these 2 measures for estimating treatment response. The value of the c-CGI is that it allowed for a substantially larger patient population, and it is a technique that can be used for other studies. Furthermore, the clinician estimate of transient cognitive impairment quite likely underestimates the true cognitive burden given that ECT-related cognitive changes on neurophysiological testing may be relatively subtle, or even absent.[24] However, the advantage of this approach is that it can be done relatively quickly and incorporated into routine clinical practice.

A final limitation of this study is that including patients with schizoaffective disorder may overestimate the effectiveness of ECT, given that ECT is known to be highly effective for affective disorders.[12] However, this concern is not supported by our results as we did not find a significantly different proportion of patients with schizoaffective disorder in the treatment response or treatment nonresponse groups.

This work also highlights important areas for future study. Future studies should involve prospective trials that incorporate validated symptom rating scales such as the Positive and Negative Syndrome Scale (PANSS)[25] or Brief Psychiatric Rating Scale (BPRS)[26] in order to determine which symptom domains improve with treatment. Cognitive impairment should also be assessed in these future prospective studies using validated cognitive rating scales in patients with schizophrenia such as the Mini-Mental State Examination (MMSE)[27] or Montreal Cognitive Assessment (MoCA)[28] to determine which cognitive domains are affected. Additionally, studies should be completed to determine the role of maintenance ECT for patients with schizophrenia. While we identified several clinical and treatment predictors of clinical treatment response, future studies should examine potential biological markers of treatment response such as cortical inhibition, which has been shown to be ameliorated with antipsychotic treatment.[29] Future studies should also be directed toward optimizing ECT parameters and exploring the use of ultrabrief pulse widths.[11,30] Other avenues for future investigation include focal electrically applied seizure therapy[31] and magnetic seizure therapy[32] that retain the clinical effectiveness of ECT but minimize cognitive impairment.

CONCLUSION

This work demonstrates that ECT is clinically effective for the treatment of schizophrenia. It highlights several clinical/treatment factors associated with ECT response including antiepileptic drug treatment, medication treatment failure, and previous response to ECT. It also highlights important clinical/treatment factors that are not associated with ECT response including clozapine and benzodiazepine treatment. An unexpected finding is the relatively small number of patients who developed clinically significant transient cognitive impairment, and predictors of ECT-related cognitive impairment remain unclear. Future work should involve prospective trials, incorporation of biological markers, and development of novel stimulation technologies.

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Supplementary material follows this article.

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Supplementary Material

Article Title: Clinical Effectiveness and Cognitive Impact of Electroconvulsive Therapy for Schizophrenia: A Large Retrospective Study

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List of Supplementary Material for the article

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eTable 1. Treatment response agreement (kappa = 0.4866) between clinical note CGI and clinician CGI (n=89)

		Clinical Note CGI			
		1	2	3	4
Clinician CGI	1	**10**	13		
	2	10	**38**	1	1
	3		4	**6**	3
	4			1	**2**

eTable 2. Clinician rated CGI and clinical note CGI

Clinician CGI	**N**	**%**
1	23	25.8
2	50	56.2
3	13	14.6
4	3	3.4

Clinical Note CGI	**N**	**%**
1	27	16.1
2	102	60.7
3	19	11.3
4	20	11.9
No records	3	NA