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Electroconvulsive Therapy and Schizophrenia: A Systematic Review

Sana A. Ali[a] Nandita Mathur [a] Anil K. Malhotra[a–c] Raphael J. Braga[a, c]

[a]Division of Psychiatry Research, The Zucker Hillside Hospital, Northwell Health, New York, NY, USA; [b]Center for Psychiatric Neuroscience, The Feinstein Institute for Medical Research, Manhasset, NY, USA; [c]Department of Psychiatry, The Donald and Barbara Zucker School of Medicine at Northwell/Hofstra, Hempstead, NY, USA

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Abstract
Electroconvulsive therapy (ECT) is a remarkably effective treatment for major depressive disorder, but is less commonly utilized for treatment of psychotic disorders. Recent literature indicates that ECT can be a useful strategy for a wide range of psychotic disorders, including treatment-resistant schizophrenia. The purpose of this review is to examine the extant literature on ECT in schizophrenia with a primary focus on its efficacy, its impact on cognitive function, the role of maintenance ECT, and the potential role of neuroimaging biomarkers to provide more precise ECT treatment strategies. We evaluated the available literature, with a particular focus on prospective, randomized trials. Our review suggests that ECT can be an effective treatment strategy in this severely ill patient population. Studies suggest that while ECT in schizophrenia is a safe treatment modality, the potential for cognitive impairment must always be carefully weighed. The use and investigation of new biomarker strategies for the pharmacological treatment of schizophrenia, and the extension of these approaches to ECT are also discussed.
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Introduction

Schizophrenia is considered as one of the most debilitating psychiatric disorders [1], which occurs in all countries, irrespective of culture or socioeconomic class [2]. Electroconvulsive therapy (ECT) was introduced as a suitable treatment for schizophrenia and other psychotic disorders in 1938 [3]. However, the introduction of chlorpromazine in the 1950s and continued successful development of new pharmacological agents since led to a considerable decline in the utilization of ECT, particularly in the United States and Europe [4]. This decline can predominantly attributed to the convenience and better social acceptance of pharmacologic treatment, and the results of early studies suggesting that antipsychotics have comparable efficacy to ECT [5, 6].

Despite the remarkable developments of pharmacological agents, a significant proportion of individuals with schizophrenia still do not achieve satisfactory treatment response with current available medications. As many as 30% of patients with schizophrenia respond poorly to standard treatment with antipsychotic medications [7]. Clozapine is the only medication shown to be effective in antipsychotic-refractory patients, however, it benefits only about 30–55% of this population [8, 9]. Recent meta-analysis [10] and treatment guidelines recommend [11]

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E-Mail karger@karger.com
www.karger.com/mnp

Raphael J. Braga
Division of Psychiatry Research, The Zucker Hillside Hospital
75-59 263rd Street
Glen Oaks, NY 11004 (USA)
E-Mail rbraga@northwell.edu

ECT as an augmentation strategy for medication-resistant schizophrenia, and in recent years, a number of studies have focused on the potential role of ECT in patients that failed to respond to clozapine, the only antipsychotic agent approved for treatment-resistant schizophrenia (TRS) [12]. In this review, we will discuss the extant literature on ECT in schizophrenia, with focus on efficacy, adverse events, and ECT techniques. We will also discuss new results from brain imaging research that may provide a method to identify biomarkers of ECT response in schizophrenia.

Methods

A computerized search was performed on the literature published on PubMed in English language using the search query (ECT [Title/Abstract] OR Electroconvulsive Therapy [Title/Abstract] OR Electroconvulsive Treatment [Title/Abstract]) AND (Psychosis [Title/Abstract] OR Schizophrenia [Title/Abstract]). The search results totaled to 983 articles. Each reference was inspected to ensure that only studies containing information exclusively regarding the use of ECT in schizophrenia were included. References cited in each study were also screened manually, to assure that no study was left out of the search. The study design characteristics, demographic data, and ECT techniques and medication status are included in Tables 1 and 2, respectively.

Results

Efficacy

The impact of ECT in the treatment of schizophrenia can be inferred from large datasets. Lin et al. [13] conducted the largest study to date to explore the effectiveness of ECT augmentation on long-term clinical outcomes. They completed a retrospective mirror-image study utilizing data from the National Health Insurance Research Database in Taiwan. They identified 2,074 individuals hospitalized for schizophrenia who were receiving ECT for the first time and compared their outcomes to a randomly selected and carefully matched comparison group. The authors found that patients treated with ECT had significantly reduced rates of psychiatric hospitalization during the posttreatment period. This effect was more pronounced in patients treated with higher doses of antipsychotics or with clozapine.

Initial controlled studies conducted with typical antipsychotics suggest that ECT is a valid augmentation strategy in schizophrenia, although the results are ambiguous. These discrepancies arise partly due to methodological variabilities, particularly regarding the populations studied and the number of ECT sessions. Moreover, few studies are truly randomized controlled double-blind trials, using sham ECT as a control condition, since the use of sham ECT presents significant ethical issues as the risks of anesthesia without treatment are considerable.

Through our search, we identified 2 single-blinded studies that evaluated ECT augmentation in patients treated with typical antipsychotics. Janakiramaiah et al. [14] randomized 60 patients with a diagnosis of schizophrenia and no previous treatment to either chlorpromazine alone or chlorpromazine plus ECT. The patients had an average of 10 bilateral ECT sessions. Results indicate that despite a faster initial response, the addition of ECT did not result in further improvement. It should be noted that first-episode schizophrenia patient cohorts are usually found to have high treatment response rates, making the observation of a significant difference between treatment groups less likely.

We also identified 7 studies on the efficacy of ECT compared to sham ECT. All studies randomized patients with schizophrenia to ECT versus a sham intervention as an add-on to treatment with first-generation antipsychotics. Three of the studies [15–17] reported superiority of acute ECT over sham treatment, while the other 4 [18–21] failed to detect an advantage for this treatment strategy. None of the studies showed significant posttreatment difference between groups after 1 month. Of note, most studies used only 6 intervention sessions, and none allowed for more than 12. More recent studies on ECT and schizophrenia use up to 20 sessions, and it is possible that a larger number of sessions would result in more significant group differences [22]. Finally, none of the sham studies were specifically focused on TRS with the exception of one. Goswami et al. [23] conducted a double-blind study to compare the efficacy and safety of ECT in TRS patients (n = 15 ECT group, n = 10 sham ECT group) and found that the ECT group showed a significant decline in the Brief Psychiatric Rating Scale (BPRS) compared with the sham ECT after 6 ECT sessions. The authors suggest that ECT is associated with significant impact and lower rehospitalization of this patient population.

Chanpattana et al. [24] evaluated the usefulness of ECT augmentation for TRS, as defined by the Kane et al. [8] and Miller et al. [25] criteria. One-hundred and one patients were started on flupenthixol up to 24 mg a day and received bilateral ECT 3 times a week. After a minimum of 20 treatments, 57% of the patients were considered responders. Although no control group was includ-

Table 1. Study design

Citation	Randomized control	Blinded	Design
Abraham et al. [17], 1987*	1	1	ECT + trifluoperazine vs. Sham ECT + trifluoperazine
Abhishekh et al. [44], 2014	0	0	Bifrontal vs. bitemporal ECT
Agarwal et al. [18], 1985*	1	1	ECT vs. Sham ECT
Bansod et al. [36], 2017	1	0	High dose right unilateral ECT vs. threshold bifrontal ECT vs. threshold bitemporal ECT
Brandon et al. [16], 1985*	1	1	ECT vs. Sham ECT
Chanpattana et al. [24], 1999	1	1	ECT alone vs. flupenthixol alone vs. ECT and flupenthixol
Chanpattana et al. [40], 2000	1	1	Just above seizure threshold vs. 2-times threshold vs. 4 times threshold
Vuksan Ćusa et al. [29], 2018	0	0	–
Goswami et al. [23], 2003*	1	1	ECT vs. Sham ECT
Janakiramaiah et al. [14], 1982	1	0	ECT-CPZ combination vs. CPZ alone
Kaster et al. [45], 2017	0	0	Retrospective chart review – efficacy of ECT
Kristensen et al. [32], 2011	0	0	Chart review – efficacy of ECT
Lin et al. [13], 2017	1	0	Mirror-image study
Petrides et al. [22], 2015	1	1	ECT + clozapine vs. clozapine alone
Phutane et al. [35], 2013	1	1	Bifrontal ECT vs. bitemporal ECT
Pisvejc et al. [37], 1998	1	1	Brief vs. ultra-brief stimuli
Rami et al. [28], 2004	0	0	Atypical antipsychotic drugs + ECT vs. atypical antipsychotic drugs alone
Ravanić et al. [46], 2009	0	0	Sulpiride + ECT vs. risperidone + ECT vs. olanzapine + ECT bilateral
Sarita et al. [20], 1998*	1	1	ECT vs. unilateral ECT vs. Sham ECT
Sarkar et al. [19], 1994*	1	1	ECT vs. Sham ECT
de la Serna et al. [27], 2011*	1	0	ECT vs. no ECT group
Shelef et al. [31], 2015	0	0	Retrospective chart review – Eeficacy of maintenance ECT
Tang et al. [47], 2003	0	0	ECT vs. patients who refused ECT
Taylor and Fleminger [15], 1980*	1	1	ECT vs. Sham ECT
Tor et al. [30], 2017	0	0	Bitemporal ECT with age-based dosing vs. right unilateral ECT with seizure threshold-based dosing vs. bitemporal ECT seizure threshold-based dosing vs. bifrontal ECT seizure threshold-based dosing
Ukpong et al. [21], 2002*	1	1	ECT vs. simulated ECT
Wessels [34], 1972	1	1	Bilateral vs. unilateral
Yang et al. [33], 2016	1	1	Maintenance ECT with risperidone vs. risperidone only

* Studies that included Sham ECT.

RCT, indicates randomized controlled trials; RCD, research diagnostic criteria; SCZ, schizophrenia; SAD, schizoaffective disorder; SSD, schizophrenia spectrum disorder; PSE, present state examination; FEP, first-episode psychosis.

Table 2. ECT technique and medications

Citation	Mean *n* of ECT sessions	Placement	Medications	Anesthetic agent	Titration
Abhishekh et al. [44], 2014	Not reported	Bifrontal vs. Bitemporal	Not reported	Thiopental	ST titration
Agarwal et al. [18], 1985	8	Bitemporal	Chlorpromazine (600–1,200 mg/day)	Thiopental	Not reported
Bansod et al. [36], 2018	8	RUL, Bifrontal or Bitemporal	Not controlled	Propofol	Not reported
Chanpattana et al. [24], 1999	14	Bitemporal	Flupenthixol up to 24 mg/day	Thiopental	Fixed stimulus
Chanpattana et al. [40], 2000	20	Bitemporal	Flupenthixol (18–24 mg)	Thiopental	ST Titration
Vuksan Ćusa et al. [29], 2018	10.2	Bitemporal	Olanzapine, Clozapine, Risperidone, Haloperidol, or Fluphenazine	Propofol	Not reported
Goswami et al. [23], 2003	6	Bitemporal	Chlorpromazine (up to 100 mg), intravenous diazepam, and promethazine (PRN)	Thiopental	Not reported
Janakiramaiah et al. [14], 1982	12	Not reported	Chlorpromazine (300 mg/day)	Not reported	Not reported
Kaster et al. [45], 2017	171	Bitemporal or RUL	Not controlled	Methohexital	Not reported
Petrides et al. [22], 2015	20	Bitemporal	Clozapine (~842.18 ng/mL)	Methohexital	ST titration
Phutane et al. [35], 2013	7.5	Bifrontal vs. Bitemporal	Not reported	Thiopental	ST titration
Pisvejc et al. [37], 1998	8	RUL	Perphenazine (4–20 mg/day)	Not described	Not reported
Rami et al. [28], 2004	27.2	Bitemporal	Not controlled	Thiopental	Not reported
Ravanić et al. [46], 2009	6	RUL	Sulpiride (*n*=17, 100–400 mg/day), Risperidone (*n*=26, 2–8 mg/day), Olanzapine (*n*=27, 5–10 mg/day)	No anesthesia	Not reported
Sarita et al. [20], 1998	~12	Bilateral vs. Unilateral vs. Sham ECT	Haloperidol (>10 mg/day)	Not reported	Not reported
Sarkar et al. [19], 1994	6	Bitemporal	Haloperidol (15 mg)	Thiopental	Fixed stimulus
de la Serna et al. [27], 2011	13	Bitemporal	Not reported	Not reported	Not reported
Shelef et al. [31], 2015	92.8	Not reported	Not reported	Not reported	Not reported
Tang et al. [47], 2003	15.9	Bitemporal	Olanzapine (max 2.5 mg/day); Risperidone (max 2 mg/day)	Thiopental	ST titration
Taylor et al. [15], 1980	~10	7 Bitemporal, 3 RUL	Chlorpromazine (300 mg daily), Trifluoperazine (15 mg daily), Flupenthixol (40 mg monthly), Fluphenazine (25 mg monthly)	Methohexital	Not reported
Tor et al. [30], 2017	9.8	Bitemporal, RUL, Bifrontal	Not controlled	Propofol	ST titration or age based method
Ukpong et al. [21], 2002	6	Bitemporal placement	Chlorpromazine (up to 300 mg/day)	Thiopental	Not reported
Wessels [34], 1972	8	49 Bitemporal, 51 RUL	Thioridazine (200 mg)	Not reported	Not reported
Yang et al. [33], 2016	16	Bitemporal	Risperidone	Propofol	Not reported

RUL, right unilateral; ST, seizure threshold; ECT, electroconvulsive therapy.

ed in this study, the results compare favorably with those of other studies targeting treatment refractory patients.

According to modern treatment guidelines, individuals with schizophrenia can only be considered truly treatment resistant if they have failed a trial of clozapine. Data from retrospective studies and open trials suggest a potential benefit of ECT augmentation for patients who have failed clozapine [26]; however, no controlled RCTs had been conducted until recently. Petrides et al. [22] published a prospective, randomized study highlighting the synergistic effects of ECT plus clozapine. In this randomized, single-blind study, 39 patients with schizophrenia who were being treated with clozapine were recruited. For inclusion into the study, patients had to have significant psychotic symptoms despite clozapine treatment. Patients were assigned to one of 2 groups: ECT plus clozapine versus clozapine only. ECT was performed bilaterally 3 times a week for the first 4 weeks then twice a week for the last 4 weeks. Clozapine dosages remained constant throughout the study. Response was defined as a 40% or more reduction in the BPRS psychosis subscale, a Clinical Global Impression (CGI) rating of <3, and a CGI improvement rating <2. The results were quite compelling as 50% of the ECT plus clozapine group met the a priori response criteria, while none of the patients in the clozapine only group experienced improvement. This data remain the strongest evidence for the role of ECT in treatment-resistant schizophrenia.

Cognitive Side Effects

A frequently reported side effect of ECT is a transient cognitive impairment, and this may be especially germane in patients with schizophrenia, as it is commonly associated with cognitive problems. Data on cognition and ECT in schizophrenia were collected in the aforementioned Taylor and Fleminger [15] study. The authors studied 20 patients with a diagnosis of schizophrenia who were treated with the equivalent of 300 mg chlorpromazine a day for 2 weeks, and those who showed no improvement were included in the final study. Patients were randomly assigned to receive up to 12 procedure sessions of either real or sham ECT as an adjunct to their drug treatment. Twenty-four hours after the last treatment, and only at this point, the patients in the ECT group rated themselves as subjectively more impaired than those in the sham ECT group. Nurses' rating, which were not blinded, showed a similar difference. No specific details were provided regarding rating scales used. Objective testing conducted via the Wechsler Memory Scale showed a tendency toward improvement in the ECT group after 6 treatments, some deterioration at the end of the course, but full recovery one month after completing treatment. However, the differences between the groups on these memory scores were not significant.

de la Serna et al. [27] published a 2-year follow-up study of cognitive function in schizophrenia spectrum disorders among adolescent patients treated with ECT. The sample consisted of 9 adolescent patients in the ECT group and 9 adolescent subjects matched by age, socioeconomic status, diagnostic and Positive and Negative Syndrome Scale (PANSS) total score at baseline. Clinical and neuropsychological assessments were administered at baseline pre ECT and again at a 2-year follow-up. The study showed no significant differences over time in clinical (as assessed by the PANSS) or cognitive (as assessed by the Neuropsychological Examination Scale) variables between the ECT group and the non-ECT group at 2-year follow-up. Similarly, Rami et al. [28] followed ten patients with TRS, as per the Kane et al. [8] criteria. Patients were treatment with maintenance ECT for over a year, with bitemporal placement and a mean intersession interval of 37 days. When compared to matched controls, the authors found no significant differences between groups in terms of cognition as measured by the Wechsler Memory Scale, Rey Auditory Verbal Learning Test, Wechsler Adult Intelligence Scale, and Tails Tower of Hanoi and FAS-test. They were unable to find any correlation between the number of previous ECT treatments and any cognitive measure. This may be due to the small sample size of the study likely under powering statically significance.

Cusa et al. [29] published a prospective, open study to evaluate the effects of ECT augmentation of antipsychotics on cognitive functions in patients with TRS. Thirty-one patients were included and evaluated on both clinical (PANSS and CGI) and cognitive (California Verbal Learning Test Second Edition, Benton Visual Retention Test, Wechsler Adult Intelligence Scale and Stroop) measures before and after completion of a course of ECT. Overall, none of the neurocognitive domains showed a significant decline after ECT. In fact, some domains such as immediate and delayed verbal memory and executive functioning showed statistically significant improvements.

Tor et al. [30] compared the symptomatic and cognitive outcomes of patients with schizophrenia receiving one of 4 ECT modalities: bitemporal ECT with age-based dosing, right unilateral (RUL) ECT with seizure threshold (ST)-

based dosing, bitemporal ECT with ST-based dosing, or bifrontal ECT with ST-based dosing. The Montreal Cognitive Assessment and BPRS were administered to 62 patients before and after a course of ECT. Overall, there was significant improvement in both the clinical and cognitive measures across the patients after their ECT course. The response rates did not differ significantly across the 4 modalities. This finding suggests that there may be some cognitive benefits during the acute course of ECT.

Maintenance

The risk of relapse after a successful acute course of treatment is a clinical challenge in electroconvulsive (ECT) practice, particularly in cases with a history of marked resistance to previous treatments. Retrospective studies indicate that the use of continuation and maintenance ECT (C-ECT) is effective in terms of reducing the risk of relapse and readmission rates [31, 32]. Unfortunately, few prospective studies regarding maintenance in schizophrenia are available.

In the aforementioned Chanpattana et al. [24] study, 58 patients who met stringent remitter criteria during the acute phase were further followed and included in a single-blind 6 months continuation treatment study (phase II). Patients were randomized to 3 treatment groups: C-ECT and flupenthixol combined, C-ECT alone, and flupenthixol alone. After 6 months of continuation treatment, relapse rates were 40% for the combination group, as opposed to 93% for both other monotherapy groups, suggesting that continued maintenance ECT in combination with an antipsychotic may be a worthwhile strategy in this patient population.

Yang et al. [33] conducted a randomized open trial with 62 patients considered as responders to an acute course of ECT for schizophrenia. Patients were assigned to either receive risperidone alone or risperidone and ECT augmentation. Maintenance ECT was done once a week in the first month, once every 2 weeks in the second month and once a month afterwards, for 1 year. Patients assigned to ECT augmentation had a probability of being relapse free 0.86 ± 0.07, compared to 0.49 ± 0.1 for the risperidone only group, a significant difference.

ECT Technique

Electrode placement in ECT is thought to affect efficacy and the adverse events profile of the treatment. Three placements, bitemporal (also referred to as "bifrontotemporal" or "bilateral"), RUL, and bifrontal placement are commonly used by clinicians. The choice is usually based on studies with patients with depression, which suggest that bitemporal and bifrontal placements might be slightly better in terms of efficacy, at the expense of slightly worse cognitive adverse events.

The effects of electrode placement on ECT's efficacy in schizophrenia have been observed in several studies. For example, Wessels et al. [34] found that bilateral and unilateral ECT are equally effective in the treatment of schizophrenia when combined with thioridazine. However, this study used ECT parameters that are not comparable to modern standards, including no anesthesia.

More recently, Phutane et al. [35] conducted a double-blind randomized controlled study showing symptomatic and cognitive superiority of bifrontal over bitemporal electrode placements during ECT for patients with schizophrenia. A total of 122 patients were assigned to either the bifrontal (n = 62) or the bitemporal (n = 60) group. The clinical instruments included the BPRS, Bush-Francis Catatonia Rating Scale, Nurse Observation Scale for Inpatient Evaluation, and CGI. At the end of 2 weeks (after 6 ECT sessions), 63% of patients assigned to bifrontal placement and 13.2% assigned to bitemporal had met the response criterion of 40% reduction in BPRS scores. Moreover, the patients in the bifrontal group had significantly better memory performance than the bitemporal group. The authors hypothesized that bifrontal ECT avoids direct electrical stimulation to the temporal lobes, which may contribute to the decreased cognitive side effects.

Two studies compared all 3 placements in schizophrenia. Bansod et al. [36] enrolled 82 patients diagnosed with schizophrenia in a randomized, nonblinded comparison of a fixed course of 8 moderately high-dose RUL (n = 24), threshold bifrontal (n = 27), and threshold bitemporal (n = 31) ECT. Results suggest that RUL was less effective in reducing positive symptom, while BT was associated with greater memory impairment. The authors note that the differences reported were small and perhaps clinically insignificant. In the aforementioned Tor et al. [30], the efficacy of 3 different placements was compared. No single placement showed significant superiority. It should be noted that in this study, 62 patients were randomized to 4 different groups, and therefore the chance of a type 2 error should be considered.

One of the reviewed studies evaluated the impact of pulse width in efficacy and cognitive side effects. In a double-blind, randomized, comparative study, Pisvejc et al. [37] compared the efficacy and side effects of brief and ultrabrief pulse stimuli for unilateral ECT in 48 patients, most diagnosed with schizophrenia (n = 42). After 8 sessions, the authors concluded that both pulse widths ap-

pear to be associated with significant reduction in BPRS scores, with no difference between groups. Furthermore, neither group showed any significant change in memory performance.

Modern ECT techniques seek to maximize efficacy and minimize side effects by using the lowest possible dosing charges. Studies targeting patients with depression suggest that an electrical charge above the ST is associated with increased cognitive adverse effects. ST is determined via the method of titration, where repeatedly increasing stimuli are applied until a full seizure is elicited – the last charge used becomes a proxy for the ST. RUL ECT requires stimuli much higher than the ST for effective treatment of depression samples [38], while with bilateral ECT requires stimuli just above the ST [39]. In our review, one study suggests that higher stimuli might accelerate bilateral ECT results with no additional adverse events. Chanpattana et al. [40] assigned 63 patients diagnosed with schizophrenia to 3 treatment groups: just above ST (1 × ST), twofold ST (2 × ST), and fourfold ST (4 × ST). At the end of the study, all groups exhibited similar response rates (52% for the 1 × ST, 52% for the 2 × ST, and 55% for the 4 × ST). However, the higher stimulus groups (2 × ST and 4 × ST) required 3 fewer treatments to achieve a BPRS score of 25 when compared to the 1 × ST group.

Neuroimaging Biomarkers of ECT Response

An emerging area of inquiry is the relevance of neuroimaging biomarkers to treatment response in schizophrenia. With ECT, a number of studies have suggested that structural MRI measures, such as hippocampal volume, may be predictive of treatment response in depression, although the most recent and largest study to date did not find a relationship between ECT-induced changes in hippocampal volume and clinical response. With schizophrenia, however, there has been a dearth of studies examining neuroimaging biomarkers of ECT treatment response.

A potential avenue for the identification of neuroimaging biomarkers of ECT response is the use of resting state MRI (rsMRI). rsMRI assesses the level of activity in regions across the brain; the regions where activities are correlated with each other are assumed to functionally connected, and may define networks of functional connectivity. As schizophrenia has been hypothesized to be a dysconnectivity syndrome, it seems plausible that effective treatments may work via effects on connectivity and that baseline connectivity patterns could represent a biomarker of treatment response.

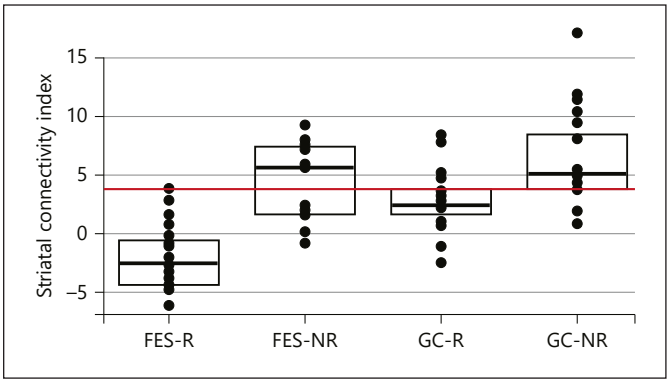

Fig. 1. The relationship between the striatal connectivity index and clinical response to treatment in four groups (first episode schizophrenia-responders; first episode schizophrenia-non-responders; generalizability cohort-responders; generalizability cohort-non-responders).

Data in support of this hypothesis have been reported by several groups who have found that baseline connectivity predicted response to second-generation antipsychotic agents. For example, our group has conducted a study in which first-episode schizophrenia patients underwent rsfMRI scanning at the initiation of a 12-week trial of randomized, double-blind controlled treatment with risperidone or aripiprazole [41]. This study found that an index of striatal connectivity predicted response to antipsychotic treatment in 2 cohorts of subjects, including a cohort of first-episode schizophrenia patients (Fig. 1). Receiver operator characteristic curves demonstrated potential clinical utility with 80% sensitivity and 75% specificity for prediction.

Data of this kind are now being collected in schizophrenia patients treated with ECT. Thomann et al. [42] observed an ECT-induced increase in the right amygdala and hypothalamic functional connectivity in a group of patients with major depression and schizophrenia. Huang et al. [43] reported that increased connectivity in one particular network, the default mode network, was associated with ECT treatment. Further studies, however, that assess baseline neuroimaging predictors of ECT response are needed, however, to truly identify biomarkers of ECT response in schizophrenia.

Discussion

The primary purpose of this review was to examine the literature of the effectiveness of ECT augmentation on treatment refractory schizophrenia. To date, several

studies have suggested that ECT augmentation is a safe, efficacious treatment option for this severely ill patient population, which results in minimal cognitive side effects and in some cases improved cognition. Although most controlled studies used bilateral placements, available literature is still inadequate to make definitive statements regarding specific techniques for ECT in schizophrenia. Further research, particularly large randomized controlled trials, focused on the effectiveness of ECT in combination with antipsychotic treatment as well as potential neuroimaging biomarkers of treatment response is encouraged.

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Statement of Ethics

The authors have no ethical conflicts to disclose.

Disclosure Statement

Dr. Anil K. Malhotra receives consulting fees as a consultant for Genomind, Inc.

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