# Maintenance Electroconvulsive Therapy for a Neuroleptic-Intolerant Patient with Disorganized Schizophrenia

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## Abstract

Owing to unresolved questions concerning the efficacy and safety of electroconvulsive therapy (ECT) in the treatment of schizophrenia, and widespread negative attitudes toward ECT, maintenance ECT (mECT) is generally considered only as a last resort. Nevertheless, in some clinical situations, the advantages of mECT may outweigh the risks and associated concerns. We report the case of a patient suffering from disorganized schizophrenia who had life-threatening hematological side effects to treatment with antipsychotic agents. Long-term mECT was administered and the patient achieved remission with no notable side effects. He was able to maintain a peaceful daily routine and improved functioning. Considering the lack of controlled trials in this area, this case and other similar cases reported in the literature add support to a possible benefit of mECT in disorganized schizophrenia, particularly when pharmacotherapy is insufficient or contraindicated

**Key Words:** mECT, cECT, Drug Resistance, Schizophrenia

## Introduction

As in other fields of medicine, it is a common practice to continue successful psychiatric therapies for chronic conditions beyond stabilization in order to sustain the achieved clinical benefit. In contrast, electroconvulsive therapy (ECT) is routinely halted once the clinical objective is accomplished, resulting in high relapse rates (up to 84%) (1-3). The cessation of ECT among patients with a history of drug resistance or intolerance is even more problematic since pharmacotherapy maintenance is inapplicable (4).

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Maintenance ECT (mECT) is the long-term therapeutic use of ECT in a lower adjusted frequency (e.g., monthly), with the aim of preventing disease recurrence (2, 5). Historically, the use of mECT has fluctuated considerably. Shortly after ECT was introduced, mECT was commonly applied beyond the acute phase in order to maintain remission. The emergence of psychotropic medications in the late 1950's and the unfavorable reputation ECT gained resulted in declined interest. Due to advances in ECT technology and practice and an emerging awareness of the limitations of pharmacotherapy, interest in mECT has been rekindled (2).

An earlier review of mECT literature (2) reported high efficacy and manifold advantages in psychiatric disorders. Specifically, the role of ECT in the treatment of schizophrenia has been debated over the past decade, as reflected in contradictory recommendations and guidelines (6). The benefit of ECT in the treatment of chronic schizophrenia subtypes—particularly in patients lacking significant affective or catatonic symptoms (7, 8)—is controversial. Nev-

ertheless, case series reports have demonstated benefits of mECT in "hard-to-treat" patients such as those with drug-resistant disorganized schizophrenia (9, 10) or clozapine nonresponders (11). A retrospective report of a cohort of 19 treatment-refractory schizophrenic and schizoaffective patients documented mECT's substantial efficacy in improving symptoms' intensity and in reducing mean duration of yearly hospitalization (by 80%) (12). In a prospective, open-label study of 21 schizophrenic patients, a combination of bilateral mECT and antipsychotic pharmacotherapy (flupenthixol) lead to marked clinical improvement (70% reduction in Brief Psychiatric Rating Scale scores; 91% increase in Global Assessment of Functioning scores) with zero relapses during a one-year follow-up (13).

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Aside from relatively minor side effects such as transient headaches and confusion following sessions (2), a major concern shared by patients and clinicians is ECT-associated memory impairment. Overestimated by some and minimized by others, the extent and severity of memory deficit after ECT are yet to be clarified (14). In several studies, cognitive functions were found to improve after ECT, but the interpretation of such results is difficult because of the "biased baseline" obstacle (2, 15). A possible transient, short-term memory impairment during the six months post-ECT has consistently been reported (5, 15). A subjective sustainable memory deficit that may also affect long-term memory was argued, but it tended to correlate with patient dissatisfaction and nonresponse to treatment, independent of objective measures of dysmnesia (15). One prospective study used a comprehensive neuropsychological battery to assess cognitive functions of ten schizophrenic patients treated with mECT compared to ten schizophrenic patients who never received ECT. There were no between-group differences on any cognitive measure (9). Similar results were demonstrated in studies of patients with affective disorders (16). The longer inter-treatment interval in mECT further reduces the risk for cognitive side effects (5). Nevertheless, mECT is often stigmatized and rarely prescribed (14, 6).

We present the case of a patient with severe disorganized schizophrenia who developed serious side effects to treatment with antipsychotic agents. ECT was prescribed as an acute and then as maintenance therapy.

## Case Report

Mr. B was born in Ethiopia in 1979 and his early development is described as normal. He suffered from bronchial asthma treated with inhaled β-agonists. At age 12, Mr. B immigrated to Israel with his uncle and was sent to a boarding school. His family arrived in Israel soon after. At age 14, Mr. B was referred for psychiatric evaluation by the school counselor who reported behavioral disturbances, truancy, unexplained smiles and odd ideas. In 1994, a child and adolescent psychiatrist diagnosed him with disorganized schizophrenia and treatment was initiated with perphenazine 16 mg/day. Monthly injections of fluphenazine decanoate 12.5 mg were soon added because of nonadherence. Combined treatment was continued through 2001 in an outpatient setting.

Mr. B was first hospitalized in 2001. In the letter of referral, a switch to risperidone due to the emergence of acute extrapyramidal side effects was mentioned as the reason for the exacerbation. On admission he appeared distressed and unkempt. Suspicious scanning glances and inappropriate facial expressions implied perceptual disturbances. Thought process was disorganized and tangential. Thought content included idiosyncrasies and paranoid delusions but no systematic narrative could be elicited. Mr. B met *DSM-IV-TR* (17) criteria for disorganized schizophrenia. Endangering command hallucinations along with impulsive aggressive behaviors necessitated admission to a protected ward. Routine blood screens on admission—electrolyte levels, liver, renal and thyroid functions, HIV, VDRL—were all unremarkable. Complete blood count (CBC) was normal excluding low granulocyte counts: white blood cells (WBC) count was 3,300/mm$^3$ (normal range 4,000–11,000), neutrophils (NE) count was 1,500/mm$^3$ (normal range 2,000–8,000). Hematologic consultation led to the diagnosis of "benign ethnic neutropenia," a condition characterized by low baseline white line count that usually requires no medical intervention (often found in Israeli patients of Ethiopian origin) (18). Treatment was switched to low-dose haloperidol (3 mg/d), augmented with lithium (dose up to 1.5 g/d, blood levels 0.69 mEq/L). Aside from its augmenting antipsychotic properties, lithium is known to stimulate the white blood cell lines (19). On this regimen the patient's WBC count improved (4,500/mm$^3$) as did his mental state, and he was discharged.

As an outpatient Mr. B did not adhere to treatment. Two years later Mr. B was readmitted, presenting with a similar clinical picture. A trial of olanzapine (20 mg/d) resulted in severe acute leucopenia: WBC count was 2,800/mm$^3$, neutrophil count was 630/mm$^3$. A month-long course of oral prednisone 5 mg/d was used to rapidly demarginate WBC. Within a week, WBC count successfully rose up to 6,000/mm$^3$, but Mr. B's mental state further deteriorated. Through-

out 2003–2004 a variety of antipsychotic drugs were tried, including zuclophenthixol (20 mg/d), chlorpromazine (300 mg/d), clotiapine (120 mg/d), amisulpiride (300 mg/d) and ziprasidone (80 mg/d), usually combined with lithium and anxiolytics. Unfortunately, reaching therapeutic doses was consistently limited by a decline in the granulocytes count. Clozapine could not be considered for the same reason. Therapeutic doses of antipsychotic drugs could not be administered and the clinical picture continued to exacerbate. Disorganized, judgment-lacking behaviors such as asking for money from strangers and endangering himself on the highway warranted repeated hospitalizations, and unsafe behaviors such as drinking cleaning fluid necessitated admission to a protected ward. Mr. B seemed dominantly responsive to his inner-world stimuli, his behavioral responses became impulsive and aggressive leading to frequent necessity for seclusion and restraints in order to prevent him from harming himself and others. Precatatonic states—alternating between psychomotor excitement and stupor with stare—became more common.

ECT was considered appropriate for Mr. B in March 2004. Although not absolutely contraindicated (20), the lithium was stopped in order to reduce the risk of cognitive side effects. Anesthesia was induced using IV propofol, and muscle relaxation with IV succinylcholine. A constant current (0.9A) Thymatron-DGx machine (Somatics, LLC) was used to produce brief pulse stimuli. The acute sessions were carried out three times weekly, with bilateral electrode placement. The dose was set using age-based formula. Seizures were 35 seconds on average (range 25–40) and terminated abruptly and spontaneously. Dose adjustments were guided by the observed motor response and electroencephalogram recording parameters. Response to treatment was good, with clear waning of positive signs and symptoms and no reported complications. After receiving 28 treatments, maintenance options were discussed. In light of the contraindications for pharmacological maintenance therapy, ECT was continued as maintenance with the same electrode placement and dosing. A baseline frequency of once weekly was reached by monitoring clinical signs and symptoms. On relapse, 2–3 sessions at the initial frequency were used with good response. Every six months, psychiatric assessment was performed, including risk-benefit analysis for continuing mECT. Owing to the positive results of the treatment, Mr. B and his family supported its continuation.

During the following years, Mr. B's clinical state remained stable, positive signs were controlled and only minimally influenced his affect and behavior. He seemed calm, more involved and enjoyed the ward activities offered. Aggressive impulses were rarely observed and restraint or seclusions were not required. For the past eight years mECT constituted Mr. B's main therapy. In 2007, an attempt was made to withdraw mECT treatment. Mr. B's mental state deteriorated within weeks as reflected in PANSS (22) values: total score was 161, positive scale score was 57, negative scale score was 27, general pathology scale score was 77; and the Clinical Global Impression (CGI) scale score was 5 (markedly ill). On resumption of ECT, all values improved dramatically: 79, 25, 16, 38, and 3 (mildly ill), respectively. Mini-Mental State Examination score was 14/30 on remission, a low score characteristic of schizophrenia patients (9). In 2008, impressed by several successful home visits, Mr. B's family requested his discharge. Ongoing ambulatory mECT was offered; however, due to logistic difficulties in bringing the patient to the hospital for mECT, he missed sessions, and signs of relapse reemerged. Such circumstances are considered exclusion criteria for ambulatory ECT (5). Two months later, Mr. B's family could no longer contain his deteriorating behavior and he was readmitted to the hospital. Until 2011, Mr. B received over 240 ECT treatments, and he continues mECT as an inpatient in a long-term psychiatric unit (chronic psychiatric departments are currently available in Israel).

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Occasionally the therapeutic effect wanes during the days before the next treatment. Low-dose perphenazine (8 mg/d) was used for up to several days with strict monitoring of the blood counts. This treatment plan seems to control his illness with no notable side effects.

## Discussion

Our case adds support to the benefit of ECT in achieving and maintaining remission in patients suffering from disorganized schizophrenia. Maintenance ECT successfully treated debilitating positive signs and subjective distress in our patient, enabling him to engage in rehabilitation activities. Attempts to stop mECT consistently led to symptom recurrence and, in the absence of suitable alternatives, resuming mECT was warranted. Difficultes in bringing Mr. B to the hospital precluded ambulatory mECT and were the obstacle to hospital discharge.

Questions rise concerning the necessity of an upper limit to mECT duration. Is it clinically and ethically appropriate

to continue mECT for an undetermined period of time? The answer should reflect mECT's long-term risk/benefit balance. Repeated examinations failed to reveal ECT-associated brain damage (23, 24), even when hundreds of ECT sessions were administered (25, 26). Nonetheless, cultural and emotional influences possibly lead to over emphasizing the potential risks compared to more culturally neutral biological therapies (e.g., surgical procedures, long-term pharmacotherapy) (27).

In many chronic illnesses therapies aim to maintain stability and control symptoms rather than offer a cure; for example, relapse of psychosis following termination of pharmacotherapy in schizophrenia, and the development of hyperglycemia when skipping insulin therapy in diabetes mellitus. In such circumstances, the side effects of long-term continuation therapy should be weighed against the adverse consequences of continued disease activity. In light of the commonly argued deleterious effects of durable psychosis on the brain (28) and the non-apparent mECT-associated brain damage or cumulative cognitive impairment, long-term mECT seems justifiable in certain cases.

## Conclusions

The literature and the presented case suggest a possible role for mECT in the treatment of disorganized schizophrenia, especially in the context of nonresponse or intolerance to pharmacotherapy. When mECT is justified, the current literature neither excludes its long-term use nor sets a fixed maximum number of treatments (29). A recently published review of the mECT literature (30) describes emerging evidence for its effectiveness and safety; however, methodological limitations in the studies reviewed precluded generalization of the results to clinical recommendations. As long as large controlled studies evaluating the efficacy and risks of mECT are absent, small studies and case descriptions remain a valuable guide to clinical decisions.

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