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## Lorazepam provocation test in purported schizophrenia with lack of treatment response

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### **Abstract**

Some patients with severe mental disorders are refractory to psychotherapeutic or psychopharmacological interventions. We present a patient who at the age of 19 developed several schizophrenia - suspect symptoms. Soon inexplicable general seizures where observed. He was treated with antipsychotics, but had two bouts of malignant neuroleptic syndrome. Electroconvulsive therapy (ECT) gave some symptom relief and he continued on maintenance ECT for years with weekly intervals. Interruption of this treatment pattern rapidly increased symptom load. After seven years a lorazepam provocation test was performed as he had a new relapse after 3 weeks without ECT. In the ensuing hours his aggressiveness and nonsense speaking rapidly diminished. Kahlbaums observation of seizures as part of a catatonia was not understood in this case. The publication of the new DSM-V diagnosis of catatonia may hopefully reduce the probability of treating a patient for schizophrenia for years without access to a more targeted medication and ECT plan.

## Introduction

Patients not responding to psychotropic medication are a challenge for psychiatrists and facility staff. The burden on the families of the patients is not only emotional, but also a financial one.1,2 Some of these patients, with affective symptoms and more schizophreniform symptoms as part of the primary diagnostic entity, may be helped by electroconvulsive treatment (ECT). This was already shown in a paper penetrating the medical records of the first series of patients treated by Meduna in Budapest, albeit with camphor.3 Rabheru and Persad reviewed the literature on continuation and maintenance electroconvulsive therapy in different patient groups in 1997.4 The efficacy of maintenance ECT has recently been shown in a study of major depression.5 They concluded that both continuation and maintenance

electroconvulsive therapy were efficacious, safe, well tolerated, and also cost-effective for patients with major psychiatric disorders with depression. The procedure in itself is deemed extremely safe according to Nuttal *et al.* who studied 2279 patients given 17,394 ECT treatments.<sup>6</sup> No deaths were observed, and only transient cardiac complications (arrhythmias and one cardiac arrest) in 9 patients. The adverse effects of ECT are related to the anaesthesia, which today is very short and practically without any danger of mortality. Headache and nausea occur in some patients, and transient memory impairment is usual during the time of a series of ECTs.

The indications for ECT around the world differ, although the main indication is severe depression, uni- or bipolar or as part of other mental illnesses. Also manic episodes and catatonia without schizophrenia do respond favourably to ECT. Thus it would be of interest to report on the treatment of a patient with severe mental illness, purportedly diagnosed as schizophrenia, given ECT for more than seven years.

## **Case Report**

We describe a patient with severe symptoms from the age of 20. His illness started during military service in 1973. The military doctor observed that he suddenly one day was sitting under military training staring, answering only yes or no. He was referred to the psychiatric asylum on chlorpromazine 50 mg twice daily. In the asylum his illness was described as catatonic episodes or a parkinsonistic crisis. Shortly after arrival he had a general seizure and later minor seizures. The first week he was mute with a stupor. After one week he responded to other people and after three weeks he was sent home on 4 mg haloperidol. For 12 years he lived a fairly normal life with work and non-resident contact with a psychiatrist. Some episodes of depression were observed. He was maintained on small doses of different antipsychotics. Before the next resident stay he had taken contact with Hare Krishna groups, giving him a state of incoherent speech and agitation. Again he had general seizures of 2-3 minutes duration. EEG was normal. This time he was treated with the following medication: Haloperidol 40 mg, levomepromazin 300 mg, perfenazin 32 mg and orfenadrin 200 mg per die. In 1995 he probably had neuroleptic malignant syndrome (NMS) and was treated in a somatic department. 2006 he had several grand mal seizures and a new serious episode of NMS. After this episode ECT was started and already at the 6th treatment he was deemed to be normal. He showed no sign of a psychotic disease.

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Maintenance ECT was not started and after some months he was again referred to the hospital and was in need of 10 ECT treatments before he remitted. 2007 he started with regular ECT at two weeks intervals, later the intervals have changed and before the latest referral he was on ECT once weekly. He recently dropped out of the regular, scheduled ECT for three weeks and he relapsed with involuntary movements and incoherent speech. His agitated stait precluded an orderly ECT procedure.

A lorazapam challenging test with only 1 mg orally was given because the department did not have injectables. His motor unrest and incoherent speech improved after a couple of hours. He was put on lorazepam 1 mg thrice daily and ECT could again be given after two days. He was after four/five treatments again able to communicate and respond normally. When asked about his memory he had no complaints after all these years with ECT. He maintained he recalled as well as his compatriots at home.

# Electroconvulsive treatment: procedure

ECT is performed in dedicated rooms in the acute psychiatric department with an anaesthesiologist and anaesthetic nurse present. The treatment is given with a Thymatron IV<sup>TM</sup> device. Two EEG leads and pulse oxymeter readings are registered together with ECG and the calculated output from the Thymatron device. A nurse surveys the patient after the treatment. Most of his treatments have been as a non-resident patient coming to the hospital only for the sessions. The treatments have been given with right unilateral stimulating electrode placement with 90-100% stimulation





level. He has to date received 350 ECT treatments.

#### Anesthesia

Three hundred mg thiopental and 60 mg succinylcholine has been used over the years. Premedication with glycopyrron 0.2 mg.

## **Discussion and Conclusions**

The present case demonstrates the importance of a thorough clinical diagnosis in patients with changing stupor and mutism, florid megalomanic and muscular symptoms. The seizures as observed already by Karl Ludwig Kahlbaum after 1863 may be a signal of the disease of catatonia in an early stage.8 The use of lorazepam is both a diagnostic tool and a treatment supplement besides ECT when the patient suffers from catatonia.9 Treatment with ECT over many years may influence memory and cognition, but the severity differs greatly. Malignant neuroleptic syndrome in this patient reduced the possible cognitive reduction from medication.10 His definite improvement would be a positive input in the vivid on-going discussion by lay people and psychologist/psychiatrists on cognitive deficits after ECT.11-17 It is still disputed in the literature, less among clinicians, whether ECT as a maintenance option is effective. The NICE guidelines (National Institute of Clinical Excellence, technology appraisal 59) from 2003 are negative, but their conclusion is based on mostly retrospective reports, and not the following study. In a prospective, controlled study Swoboda et al. studied a group of patients (N=42) with affective or schizoaffective disorder.18 They got either maintenance ECT + pharmacotherapy or pharmacotherapy alone. At 12 months the former group had a rehospitalisation rate of 33% whereas the latter had 67%. Time to relapse was also longer in the ECT group. The results were somewhat poorer for the schizoaffective cases. Frequent maintenance ECT, as in our patient, may keep the incumbent out of hospital. The NICE guidelines conclusion may thus be irrelevant in these special patients as mentioned in the most recent textbook on ECT.19 And in a case as the present, with catatonia, evidence for the positive effect of ECT with or without the use of lorazepam is forthcoming.

The outcome years after a series of ECT may in many cases not be very different from other short-term treatment options as pharmacotherapy and/or psychotherapy for depressions.<sup>20</sup> Our patients are influenced by social, economic and emotional factors after successful ECT. These factors would mostly not be related to the ECT as such. Helping patients develop skills to cope with lifea and are necessary would be a task for other health professionals than those administering the treatment. In a small follow up study after ECT some patients committed suicide long time after the end of the series.21 The patients had serious problems with coping in life as assessed by the Sense of Coherence test of Antonovsky.<sup>22</sup> Long-term maintenance treatment may thus contribute to a lower mortality rate in severely depressed patients. The present patient finally got a proper diagnosis after experiencing NMS twice and thus forcing his clinicians to offer him ECT. This could have been realised at a much earlier time point in his illness

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