Journal of Affective Disorders 167 (2014) 235–243

Contents lists available at ScienceDirect

Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad

Research Report

A long-term follow-up of clinical response and regional cerebral blood flow changes in depressed patients treated with ECT

Åke Berggren [a,b,c,*,1], Lars Gustafson [d,1], Peter Höglund [e,1], Aki Johanson [a,c,1]

[a] Department of Psychology, Lund University, Lund, Sweden
[b] Department of Anaesthesia, Blekinge Hospital, SE-371 85 Karlskrona, Sweden
[c] Department of Psychiatry, Clinical Sciences, Lund University, Lund, Sweden
[d] Department of Geriatric Psychiatry, Clinical Sciences, Lund University, Lund, Sweden
[e] Department of Laboratory Medicine, Clinical Chemistry & Pharmacology, Lund University, Lund, Sweden

ARTICLE INFO

Article history:
Received 6 March 2014
Received in revised form
2 June 2014
Accepted 4 June 2014
Available online 12 June 2014

Keywords:
Major depression
Follow-up
Electroconvulsive therapy
Clinical response
Regional cerebral blood flow

ABSTRACT

Background: Depression is the leading cause of disability worldwide and electroconvulsive therapy (ECT) is the most potent therapy. We investigated the clinical response and regional cerebral blood flow changes in depressed in patients treated with (ECT) in a repeated longitudinal study.

Method: Forty-nine patients (21 men and 28 women) with a mean age 61 years underwent ECT. Forty-one patients grading improvement after the initial ECT-series (responder group) were compared with eight, grading no improvement (non-responder group). The patients underwent neuropsychiatric ratings, measure of clinical response (defined as $\geq$ 50% reduction of pre-treatment depression score) and measure of regional cerebral blood flow (rCBF).

Results: The responder group had an initial 60–82%, and the non-responder group a 30–64% clinical response throughout the follow-up. The non-responder group showed more reported depression ($p=.003$), and vegetative anxiety ($p=.024$), with a generally higher left temporal rCBF ($p=.045$).

Limitations: The retrospective approach and the small sample-size.

Conclusion: Patients with no subjective improvement after ECT had lesser objective clinical response, more sustained reported depression with anxiety features, and higher left temporal rCBF.

1. Introduction

Electroconvulsive therapy (ECT) is, besides pharmacological treatment and psychotherapy, an important alternative in the treatment of major affective disorders. Strong arguments for ECT are melancholic states with imminent risk of suicide, depressive stupor and depression not responding to drug treatment and delirious mania (Fink, 1999).

Some patients, however, have a poor or short-acting response to ECT (Prudic et al., 1996; Tominaga et al., 2011). Several factors influence the clinical response. There may be differences between treatment response as estimated by the patients and the by professionals, due to different perspectives. The perceived benefits are probably based on other considerations than just relief of certain symptoms, for example patient's experience of anxiety or memory impairment, especially impaired autobiographical memory (Coleman et al., 1996; Rose et al., 2003). Also the level of different symptoms and medication may affect the mental and physical well-being of the patients (Freeman et al., 1980). The severity of depressive symptoms has furthermore been strongly associated with patient reports of memory dysfunction (Coleman et al., 1996).

Poorer subjective response to ECT has been seen in bipolar depression versus unipolar depression (Hallam et al., 2009) although fewer ECT treatments may be required in bipolar patients compared to unipolar patients to achieve similar clinical benefit (Agarkar et al., 2012).

Studies have found melancholic depression, older age, the presence of psychotic symptoms, psychomotor change, suicidal ideations, catatonia or manic episodes, to be predictors of positive objective response to ECT (Gupta et al., 2000; Hatta et al., 2007; Hickie et al., 1996; Mukherjee et al., 1994; Nordenskjöld et al., 2012; O'Connor et al., 2001; Tominaga et al., 2011). On the contrary, comorbidity of major depression with personality disorder, especially borderline personality disorder, schizoaffective disorder, or medial temporal lobe atrophy, may predict poor response to ECT (DeBattista and Mueller, 2001; Feske et al.,

* Corresponding author at: Department of Anaesthesia, Blekinge Hospital, SE-371 85 Karlskrona, Sweden. Tel.: +46 455 735310.
E-mail addresses: ake.berggren@ltblekinge.se, akebe100@gmail.com (Å. Berggren), lars.gustafson@med.lu.se (L. Gustafson), peter.hoglund@skane.se (P. Höglund), aki.johanson@med.lu.se (A. Johanson).
[1] All authors read and approved the manuscript.

http://dx.doi.org/10.1016/j.jad.2014.06.005

2004; Nordenskjöld et al., 2012; Oudega et al., 2011; Prudic et al., 2004).

Cerebral blood flow (CBF) and metabolism have been studied in different psychiatric conditions with a variety of two and three-dimensional techniques. A regional cerebral blood flow (rCBF) technique has been shown to differentiate between different types of dementia, mood disorder and non-organic psychosis (Risberg, 1980). Measurement of rCBF level and distribution in patients with affective disorders may show contradictory results depending on factors such as symptomatology, patient age, and psychopharmacological treatment. Often, normal to reduced global CBF and rCBF abnormalities are seen pre-ECT (Iidaka et al., 1997; Mathew et al., 1980; Milo et al., 2001; Navarro et al., 2004; Silfverskiöld and Risberg, 1989) and in objective ECT-responders contradictory short-term results have been seen. Some studies have shown decreases, also associated with positive clinical outcome (Nobler et al., 1994, 2001; Silfverskiöld et al., 1986), and others have found increases in frontal regions (Milo et al., 2001; Vangu et al., 2003) A 12-month follow-up study after ECT showed normalisation in frontal rCBF in remitted elderly patients (Navarro et al., 2004).

1.1. Aim of the study

The aim is to study the long-term effects of ECT on clinical measures and rCBF in patients from graded estimation of the clinical outcome. We will also investigate the long-term outcome in relation to the initial treatment response.

2. Methods

2.1. Participants and procedure.

Forty-nine consecutive inpatients that presented long-term data are included in the study. They were suffering from major depression (in 1980 diagnosed according to DSM III) (DSM-III, 3rd ed.., 1980), several with deceptions and delusional traits. They were referred to ECT in accordance with current guidelines for the time (Fink, 1999). All patients were under voluntary care at the Psychiatric Department at the Lund University Hospital, and gave their informed consent to participate in this study of acute and long term effects of ECT. The study was approved by the local Ethics and Radiation Safety Committees at the University of Lund. The patients were included in the study from 1976 to 1983. They did not show any major neurological deficits, and were not suffering from severe somatic disorder, chronic psychosis, or addiction.

We have earlier studied the clinical and neurophysiological effects of ECT in depression (Silfverskiöld et al., 1986; Silfverskiöld et al., 1987a; Silfverskiöld and Risberg, 1989) and the long-term outcome in patients who were still alive after 25 years follow-up (Johanson et al., 2005). At the end of the follow-up investigation year 2002, ten patients were still alive.

The medical reports include neuropsychiatric investigation and rCBF before and after ECT and at repeated follow-up investigations. The study covers a median duration of 3.6 years of follow-up investigations with sufficient numbers of patients in the groups.

2.2. Electroconvulsive therapy (ECT)

A conventional ECT equipment, (Siemens Konvulsator 622®) and procedure were used. The equipment produced a peak current of 0.8 A, and intermittent volleys of four unidirectional pulses of 5 ms. The frequency of the pulses was 50 per sec. and the interval between the volleys 95 ms. The electrode placement was either bifronto-temporal (BL) or right non-dominant uni-lateral (RUL) as described by d Èlia (1970). The choice of electrode placement during the treatments was made on both experimental and clinical grounds. For inducing anaesthesia we used Atropine (0.5 mg), methohexital (1 mg/kg), and suxamethone (0.5 mg/kg) which were injected intravenously. After anaesthesia was induced, 100% oxygen was given to the patient during average 30 s prior to the electric stimulus and resumed immediately after cessation of the visible convulsion and continued until the patient's spontaneous respiration sufficed. The amount of muscle relaxant was chosen so as to make the switch from the tonic to the clonic phase visible on the patient's feet. This moment was selected as the starting point for measuring the seizure duration. The electric stimulus was kept as low as possible to achieve an adequate (20–60 s) grand mal seizure (Siemens Joule indicator range between 4 and 9 was used). The starting point was set as low as possible and increased by one step when more than 4 s were needed to elicit an adequate seizure. The treatments were given 2–3 times weekly initially. When the decision to give ECT was made most non-vital medications were discontinued (usually three days or more in advance). Most psychotropic drugs known to interfere with ECT or CBF pattern were omitted (Silfverskiöld et al., 1987b).

2.3. Neuropsychiatric investigation

The psychiatric evaluations were carried out by the same psychiatrist at all the investigations. At each follow-up occasion (II–VI), the treatment result was scored in 7 grades: score 0=no improvement; 1=doubtful improvement; 2=some improvement; 3=modest improvement; 4=moderate improvement; 5=better than moderate but not clearly improved; and 6=clearly improved/restored (full effect of the ECT treatment). We compare the patients rating of improvement to a measure of clinical response defined as a $\geq$50% reduction of the total pre-treatment score on the reported and observed rating of depression on a rating-scale for affective symptoms. Patients with improvement (score 1–6) after the first ECT series were defined as responders, and patients with no improvement (score 0) were defined as non-responders.

We also assessed the number of remissions at each follow-up occasion. We defined remission as the case when both the observer and the patient reported relief of depressive symptoms.

The psychiatrist used a semi-structured interview with a specially designed rating scale, the Rating scale for Affective Symptoms (RAS scale), developed at the Psychiatric Department (Eberhard et al., 1965; Nilsson and Smith, 1965).

The RAS scale consists of two sub scales, the depression–mania scale and the anxiety scale, with reported as well as observed items. We used the intensity of each symptoms scored in 7 grades: score 0=no signs of the symptom, to score 6=constant presence of the symptom. In this study the clinical analysis was based on 15 items covering both a depressive and a manic/agitated clinical dimension of the symptoms reported by the patient and observed during the interview. In addition there were seven items covering reported and observed *anxiety related symptoms* as well as various items describing reported orientation. The three qualities describing *orientation* were: temporal orientation, spatial orientation, personal orientation (own identity) (the intensity was scored in 7 grades from: none, difficulties, over partial to total disorientation).

For each group of symptoms (reported and observed depressive dimension, reported and observed manic/agitated dimension, anxiety groups: vegetative, psychomotor and observed symptoms, and groups of disorientation) the mean values of the frequency scores were calculated.

Reported qualities of amnesia for recent events for the time before the first ECT (scored as: none, to more than a week) and anterograde amnesia from the first ECT (scored as: none, to for most events) were graded after the first ECT-series at investigation II (Table 1).