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Research report

Retrograde amnesia after electroconvulsive therapy: A temporary effect?

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ABSTRACT

Objective: Although electroconvulsive therapy (ECT) is generally considered effective against depression, it remains controversial because of its association with retrograde memory loss. Here, we assessed memory after ECT in circumstances most likely to yield strong retrograde amnesia

Method: A cohort of patients undergoing ECT for major depression was tested before and after ECT, and again at 3-months follow-up. Included were 21 patients scheduled to undergo bilateral ECT for severe major depression and 135 controls matched for gender, age, education, and media consumption. Two memory tests were used: a verbal learning test to assess anterograde memory function, and a remote memory test that assessed memory for news during the course of one year.

Results: Before ECT the patients' scores were lower than those of controls. They were lower again after treatment, suggesting retrograde amnesia. At follow-up, however, memory for events before treatment had returned to the pre-ECT level. Memory for events in the months after treatment was as good as that of controls.

Limitations: The sample size in this study was not large. Moreover, memory impairment did not correlate with level of depression, which may be due to restriction of range.

Conclusions: Our results are consistent with the possibility that ECT as currently practiced does not cause significant lasting retrograde amnesia, but that amnesia is mostly temporary and related to the period of impairment immediately following ECT.

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1. Introduction

Electroconvulsive therapy (ECT) is generally considered to be an effective treatment for severe depression (Sackeim et al., 1993, 2000, 2009; Reisner, 2003), but that has not stopped it from being controversial. Most criticism, from outsiders and from patients that have undergone ECT, centers on the purported loss of memory (Rose et al., 2003). ECT is reported to cause anterograde amnesia (an inability to form new memories), but this is usually restricted to the period

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immediately following the ECT. On the other hand, retrograde amnesia (loss of remote memories) has been argued to be both significant and permanent (reviewed in Fink, 2001).

Earlier studies have documented large memory deficits after a course of ECT. For example, in a seminal study, Squire et al. (1976) found that memories from the last 6 years were severely affected by a course of ECT. In the last decades, however, new techniques (such as the switch from sinusoidal to brief pulse current) have resulted in fewer cognitive side-effects. Anterograde amnesia, which in the 1970s could be as severe as that of dense amnesics (Cohen and Squire, 1981), has recently been shown to be relatively mild (Brodaty et al., 2001; Sackeim et al., 2009). Moreover, it tends to be restricted to a period of confusion immediately following ECT. Studies that include a follow-up of 2–3 months after treatment report

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better memory at follow-up than immediately after ECT or even before the treatment (Sackeim et al., 1993). These improvements over and above the pretreatment level are correlated with the lifting of depression (Brodaty et al., 2001).

However, retrograde amnesia is still reported after ECT, even in more recent studies. It is often severe for memories laid down directly prior to treatment (O'Connor et al., 2008) while remote memories are to some extent spared (Lisanby et al., 2000). In some cases the amnesia partially lifts during the months of recovery (Lisanby et al., 2000; Sackeim et al., 2000, 2007) whereas in others it does not (Sackeim et al., 1993). At follow-up years after ECT, some retrograde amnesia relative to matched controls is still found (Kho et al., 2006). Retrograde amnesia is particularly marked for bilateral, as opposed to unilateral, electrode placement (Sackeim et al., 1993, 2000, 2007, 2009).

However, the actual extent of retrograde amnesia is not yet established. After the seminal work of Squire and colleagues (Squire et al., 1976; Cohen and Squire, 1981) ECT research has rarely focused on retrograde amnesia. Therefore, few studies have, for example, included a control group. Moreover, many studies have relied on autobiographical memory tests (Sackeim et al., 1993, 2000, 2009) which are known to be sensitive to confabulation (Meeter et al., 2006), do not allow memories to be precisely dated and, since such tests tend to rely on free recall by the participant, are very sensitive to the recall deficits typically found in depression (Taconnat et al., 2010).

The present study therefore tests remote memory after ECT using a design that is maximally sensitive to lasting retrograde amnesia. This included testing patients on three occasions, compared with a matched non-depressed control group. Moreover, an objective questionnaire was used with questions focusing on memories previously shown to be most sensitive to ECT, i.e. those from up to one year prior to ECT (Squire et al., 1976; Cohen and Squire, 1981).

2. Method

2.1. Participants

A total of 21 patients at the Erasmus Medical Center (EMC) participated in the study, which was approved by the medical ethical committee of the EMC. Each subject was diagnosed with depression according to the DSM-IV criteria using the SADS (Schedule for Affective disorders and Schizophrenia, Endicott and Spitzer, 1978). Nineteen of 21 patients suffered from major depression with melancholic features; in four of these the depression also had psychotic features. From patients deemed competent to consent by their treating psychiatrist, written informed consent was obtained after providing a complete description of the study. For those whose competence to consent was in doubt, written consent was obtained (after providing a complete description of the study) from the patient and from the family or legal guardian (s). All patients were observed during a medication-free period of 5 days before treatment started.

Grounds for exclusion were alcohol or drug dependence, a diagnosis of dementia or other neurological conditions, endocrinologic conditions and, for participants aged 65 years

or older, a Mini-Mental State Examination (MMSE, Folstein et al., 1975) score of 24 or lower.

A sample of 131 adults from the general population was used as a control group. The control group was matched with the patient group for gender, age, level of education and the number of newspapers read over the course of one week (as estimated by the participants). The controls were recruited via an unrelated study on epilepsy, but did not themselves suffer from epilepsy.

2.2. Design

Patients were tested on three occasions: the day before the start of treatment, within 3 days after treatment had ended, and 3 months after treatment. These three occasions are referred to as pre-ECT, post-ECT and Follow-up. On each occasion, patients were administered the 10-Word Test (10-WT) for anterograde memory function, and the Daily News Memory Test-ra (DNMT-ra) for retrograde memory. Both tests were administered via a computer. Moreover, the two research psychiatrists rated the participants' state with the Hamilton Depression Rating Scale (HDRS, Hamilton, 1960). During the trial, interrater sessions with the investigating psychiatrists took place once every month (from these sessions an interrater reliability of $\kappa = 0.95$ was computed). The MMSE (Folstein et al., 1975) was administered before treatment only, and only to the four participants older than 65.

ECT was administered twice weekly and applied bilaterally with a brief pulse, constant current apparatus (Thymatron System IV, Somatics, IL, USA). Seizure threshold, defined as the stimulus dosage that elicited a seizure of at least 25 s according to the cuff method, was determined during the first session with empirical stimulus titration. If the starting stimulus dose failed to elicit a seizure of at least 25 s, stimulus charge was increased according to the titration schedule and the patient was restimulated after 30 s. For the second treatment, the stimulus dosage was set at 1.5 times the initial seizure threshold.

During the course of ECT, stimulus dosage settings were adjusted upward to maintain seizure duration of at least 25 s as measured with the cuff method. Anesthesia was achieved during the ECT sessions with intravenous administration of metoclopramide 10 mg, glycopyrrolate 0.002–0.003 mg/kg, a bolus injection of alfentanil 0.010–0.015 mg/kg and 0.2–0.3 mg/kg propofol followed by succinylcholine 0.5–1.0 mg/kg for muscle relaxation. Patients were withdrawn from all psychotropic medication at least 5 days before ECT and were maintained drug-free during the course of ECT.

Each week patients were rated with the HDRS. Treatment ended when a score below 7 had been reached, or when improvement had plateaued for 4 sessions in a row, or when no improvement was observed during the course of 10 sessions.

2.3. Measurements

The Ten-Word Test (10-WT), used as a measure of anterograde memory function, is a verbal learning test in which 10 concrete nouns are studied for 2 s each. Study is followed by a thirty-second interval of counting backwards

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