Journal of Psychiatric Research 45 (2011) 770–780

Contents lists available at ScienceDirect

Journal of Psychiatric Research

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

Unilateral brief-pulse electroconvulsive therapy and cognition: Effects of electrode placement, stimulus dosage and time

Maria Semkovska [a,b], Deborah Keane [b], Oyemi Babalola [a], Declan M. McLoughlin [a,b,*]

[a] Department of Psychiatry, Trinity College Dublin, St Patrick's University Hospital, James's Street, Dublin 8, Ireland
[b] Trinity College Institute of Neuroscience, Trinity College Dublin, St Patrick's University Hospital, James's Street, Dublin 8, Ireland

ARTICLE INFO

Article history:
Received 17 June 2010
Received in revised form
28 September 2010
Accepted 1 November 2010

Keywords:
Electroconvulsive therapy
Cognition
Depression
Electrode placement
Meta-analysis

ABSTRACT

To clarify advantages of unilateral electrode placement as an optimisation technique for electroconvulsive therapy (ECT) for depression, aims were to meta-analyse unilateral ECT effects on cognitive performance relative to: (1) bitemporal electrode placement, (2) electrical dosage, and (3) time interval between final treatment and cognitive reassessment.

Relevant electronic databases were systematically searched through May 2009, using the terms: "electroconvulsive therapy" and ["cogniti*", "neuropsycholog*", "memory", "attention", "executive", "spatial", or "intellectual"]. Inclusion criteria were: independent study of depressed patients receiving unilateral or bitemporal brief-pulse ECT; within-subjects design; use of objective cognitive assessments; available mean electrical dosage for unilateral samples. Standardized pre-post ECT weighted effect sizes were computed and pooled within 16 cognitive domains by a mixed-effects model.

Thirty-nine studies (1415 patients) were meta-analysed. Up to three days after final treatment, unilateral ECT was associated with significantly smaller decreases in global cognition, delayed verbal memory retrieval, and autobiographical memory, compared to bitemporal ECT. Significant publication bias was found for autobiographical memory, favouring reporting of larger percentage loss. Higher unilateral ECT electrical dosage predicted larger decreases in verbal learning, delayed verbal memory retrieval, visual recognition, and semantic memory retrieval. When retested more than three days after completing ECT, no significant differences remained between the two electrode placements; for unilateral ECT, electrical dosage no longer predicted cognitive performance whereas increasing interval between final treatment and retesting predicted growing improvement in some variables. This interval is a more useful long-term predictor of cognitive function than electrode placement or electrical dosage following unilateral ECT.

1. Introduction

Electroconvulsive therapy (ECT) is a well-established and highly effective treatment for severe depression (American Psychiatric Association, 2001). However, its use remains limited mainly because of concerns about cognitive side-effects, especially effects upon both short- and long-term memory function. Several modifications of ECT technique have been introduced to minimise these side-effects. These include: using unilateral, instead of bilateral, electrode placement; moving from sine wave electrical stimulus to more efficient brief-pulse stimuli; and adjustment of stimulus intensity to the individual patient's seizure threshold (ST, the minimum charge required to induce a generalised seizure that is needed for therapeutic effect). While moderately suprathreshold stimulation (e.g. 1.5 x ST) is effective for bitemporal ECT (Eranti et al., 2007), substantially higher charges are required for right unilateral ECT to approach the antidepressant effectiveness of bitemporal ECT (Little et al., 2003; Sackeim et al., 2000). Although unilateral ECT is associated with less cognitive side-effects than bitemporal ECT, higher charges of unilateral ECT may result in more deficits than lower charges (UK ECT Review group, 2003).

A major focus of recent research has therefore been to determine if, at higher dosage, unilateral ECT keeps its potential advantage over bitemporal ECT with regards to cognitive side-effects. Reports on this possible optimisation technique are inconsistent – some studies do not find significant differences between high-dose unilateral ECT and standard bitemporal ECT with regards to cognitive side-effects (McCall et al., 2002; Schweitzer et al., 2004) while others demonstrate less severe effects following high-dose unilateral ECT (Sackeim et al., 2000, 1993). The UK ECT review group (2003) systematically reviewed randomised controlled trials that

* Corresponding author. Department of Psychiatry and Trinity College Institute of Neuroscience, Trinity College Dublin, St Patrick's University Hospital, James's Street, Dublin 8, Ireland. Tel.: +353 1 2493343; fax: +353 1 2493428.
E-mail address: d.mcloughlin@tcd.ie (D.M. McLoughlin).

0022-3956/$ – see front matter
doi:10.1016/j.jpsychires.2010.11.001

assessed effect of electrical stimulus dose on cognitive functioning. Data at end of treatment from only five studies were described, but not meta-analysed. Conclusions were that there was no difference between high-dose and low-dose unilateral ECT on personal memory, with some indication that anterograde memory might be more impaired in the high-dose group. Findings on the Mini-mental State Examination (MMSE) described from two studies were inconsistent. No short- or long-term follow-up data were included in this systematic review.

A recent meta-analysis of cognitive outcomes following ECT confirmed that electrode placement is a significant moderator of performance, with unilateral ECT being associated with less cognitive side-effects than bitemporal or mixed treatments (e.g. unilateral followed by bitemporal) in some cognitive domains (Semkovska and McLoughlin, 2010). However, because of methodology restrictions, the effect of electrode placement was not systematically meta-analysed and its contribution was not examined independently from stimulus waveform, which also was found to be a significant moderator of cognitive performance. In addition, that meta-analysis included only studies that assessed cognition using standardised and validated neuropsychological tests. This stringent inclusion criterion precluded the meta-analysis of retrograde amnesia. In fact, the accompanying systematic review of the ECT literature revealed that there was a significant paucity of standardised instruments used in assessment of retrograde amnesia and thus could not provide an estimate of its importance and resolution over time. As retrograde memory deficits are a major concern to patients (Rose et al., 2003), possible impairment of this cognitive function following ECT still needs to be quantified despite the limitations of available instruments. Therefore a less stringent inclusion criterion with regards to potentially suitable objective cognitive tests needed to be adopted in order to be able to include retrograde amnesia assessments.

To clarify the effects of unilateral ECT for depression upon cognitive function, the aims of the present meta-analysis are: (1) to compare the pattern, extent and post-treatment resolution of cognitive side-effects following right-sided brief-pulse unilateral ECT with those observed following brief-pulse bitemporal ECT and (2) to examine the effects of both electrical stimulus dosage and reassessment time interval on cognitive outcomes following right unilateral brief-pulse ECT.

2. Methods

Standard guidelines for reporting meta-analyses of observational studies were followed (MOOSE criteria, Stroup et al., 2000).

2.1. Search strategy and selection criteria

The electronic databases MEDLINE, EMBASE, PsycARTICLES, PsychINFO, and PsychLIT were searched from their commencements to May 2009, using the terms "ECT" or "electroconvulsive therapy" and ["cogniti*", "neuropsycholog*", "memory", "attention", "executive", "spatial", or "intellectual"]. Reference lists of reviews and relevant articles were manually searched for additional studies. Only published reports, including non-English language ones, were searched.

Study inclusion criteria were as follows:

1. Independent sample(s) of subjects older than 18 years, treated with contemporary brief-pulse ECT for a diagnosis of Major Depressive Episode according to DSM-III, DSM-III-R, DSM-IV, ICD-9 or ICD-10; or Primary Depression according to the Research Diagnostic Criteria (Feighner et al., 1972).
2. At least one objective measure of cognitive performance was used with results reported as means and standard-deviations (SD): cognitive data should have been collected at baseline and at least at one post-treatment assessment point on the same test(s) used at baseline. Studies that collected only post-ECT measures in between-subjects research designs were therefore excluded.
3. Alternative versions for tests of anterograde memory must have been used to control for practice effect (Lezak et al., 2004).
4. Quantitative information regarding time interval between final ECT and post-ECT assessment must be provided.
5. Electrode placement details must be provided. Only studies using bitemporal, right unilateral d'Elia, or right unilateral Lancaster positions were included. Mixed samples (e.g. including patients that received either bitemporal or unilateral ECT) were excluded if the corresponding author could not provide subgroup data.
6. Mean charge of electrical dosage per session in millicoulombs (mC) should be provided.

To maintain statistical independence of effect sizes, a "study" was delineated as a published article with no obvious sample and test redundancy with other articles. When redundancy was found, the most recent study with the largest sample size was coded. Case reports, self-reported measures and assessments of cognition by qualitative clinical observation were excluded.

2.2. Data extraction and recorded variables

Two assessors (DK and OB) independently reviewed the titles and abstracts generated by the initial literature search and retained possible eligible articles. Discrepancies about inclusion of studies were resolved by arbitration and consensus following discussion with a third investigator (MS). Before discussion, inter-rater agreement regarding classification of papers was 94%. Two investigators (DK, MS) then independently reviewed retained articles, and extracted and cross-checked data. Disagreements were again resolved by consensus. When reported results were insufficiently detailed, but studies fulfilled remaining inclusion criteria, corresponding authors were contacted for missing information; authors who did not initially reply were re-contacted.

The neuropsychological test data were pooled into composite measures of different cognitive functioning domains. For example, outcomes from all verbal learning tests were jointly meta-analysed (Table 1). When, in a given study, more than one neuropsychological test was administered within a particular domain, the corresponding cognitive effect size was calculated using test mean scores weighted by number of subjects and pooled standard deviations (McDermott and Ebmeier, 2009).

From each study, the following variables were coded for each independent sample in a standard fashion: number of participants at each assessment point; cognitive domain assessed; results for calculating standardised mean pre-post ECT differences for each cognitive variable; interval between final ECT course and test administration; electrode placement; and mean electrical charge dose. As age has been related to higher electrical dosage needed to achieve seizure (Benbow, 2005) and is associated with decline in performance on several cognitive tests (Lezak et al., 2004), mean age was also extracted to explore its moderator effect.

2.3. Statistical analysis

Statistical analyses were done with SPSS (version 15.0) and Comprehensive Meta-analysis software (version 2.2, Biostat™, Englewood, New Jersey). Effect sizes (ES) were computed for each cognitive variable using Cohen's d index of individual effect: $d_i = (M_{2i}-M_{1i})/SD_{pi}$, where d is effect size, i individual sample, M_{1i}