



A new early cognitive screening measure to detect cognitive side-effects of electroconvulsive therapy?



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ARTICLE INFO

Article history:

Received 10 April 2013

Received in revised form

8 August 2013

Accepted 29 August 2013

Keywords:

Electroconvulsive therapy

Side-effects

Cognition

Memory

ABSTRACT

Cognitive side-effects from electroconvulsive therapy (ECT) can be distressing for patients and early detection may have an important role in guiding treatment decisions over the ECT course. This prospective study examined the utility of an early cognitive screening battery for predicting cognitive side-effects which develop later in the ECT course. The screening battery, together with the Mini Mental Status Examination (MMSE), was administered to 123 patients at baseline and after 3 ECT treatments. A more detailed cognitive battery was administered at baseline, after six treatments (post ECT 6) and after the last ECT treatment (post treatment) to assess cognitive side-effects across several domains: global cognition, anterograde memory, executive function, speed and concentration, and retrograde memory. Multivariate analyses examined the predictive utility of change on items from the screening battery for later cognitive changes at post ECT 6 and post treatment. Results showed that changes on a combination of items from the screening battery were predictive of later cognitive changes at post treatment, particularly for anterograde memory ($p < 0.01$), after controlling for patient and treatment factors. Change on the MMSE predicted cognitive changes at post ECT 6 but not at post treatment. A scoring method for the new screening battery was tested for discriminative ability in a sub-sample of patients. This study provides preliminary evidence that a simple and easy-to-administer measure may potentially be used to help guide clinical treatment decisions to optimise efficacy and cognitive outcomes. Further development of this measure and validation in a more representative ECT clinical population is required.

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1. Introduction

Electroconvulsive therapy (ECT) is widely considered an essential treatment for severe major depression, with research showing robust efficacy, even in treatment resistant patients (Husain et al., 2004; Heijnen et al., 2010). Despite such clear evidence for effectiveness, there is still much controversy and public misunderstanding about the treatment (Chakrabarti et al., 2010), driven at least in part by the risk of cognitive side-effects. Although cognitive side-effects are frequently evident immediately after ECT, particularly for memory for newly learned information (i.e., anterograde

memory), research studies have consistently demonstrated that these are mostly short lived and tend to resolve in the months following treatment (Semkovska and McLoughlin, 2010; Verwijk et al., 2012). Nevertheless, there remain concerns regarding the risk of longer term cognitive effects, with some studies showing persistent subjective memory complaints (Squire and Slater, 1983; Berman et al., 2008) and deficits in autobiographical memory (Ng et al., 2000; McCall et al., 2002; Sackeim et al., 2007) after treatment has ended. Variation in the severity and duration of cognitive side-effects has been shown to be contingent upon the ECT treatment approach used (Sackeim et al., 2007; Semkovska and McLoughlin, 2010; Loo et al., 2012), with more effective treatment approaches (e.g., higher dosage, bilateral electrode placement) tending to result in poorer outcomes. Early detection of emerging cognitive side-effects during the ECT course is, therefore, important so adjustments to the treatment approach (e.g., the

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wider spacing of treatments) can be made to minimize later side-effects.

Routine assessment of cognition during a course of ECT has been suggested in the practice guidelines of many professional organizations (American Psychiatric Association, 2001; Scott, 2004). Despite such guidelines, there is currently no consensus regarding the cognitive measures that should be used, or when they ought to be administered to best monitor cognitive effects of treatment. Impediments to widespread, routine, formal assessment in clinical practice include time restraints, lack of adequate training for administration of neuropsychological measures, and patient attrition and resistance. For example, the administration of a standardized neuropsychological test of anterograde memory (i.e., word list learning task), typically involves at least 30 min administration time (including 20–25 min delay) and formal administrator training. In the absence of consensus for appropriate measures and the aforementioned constraints in clinical practice, important treatment decisions made during the ECT course, including switching of electrode placement, changes in electrical dose, and spacing of treatments, are often made without formal assessment or at best with brief “bedside” cognitive tests, such as, the Mini Mental State Examination (MMSE; Folstein et al., 1975). The concern is that these measures may be effective in detecting gross cognitive impairment but may not be sensitive to early cognitive changes which are predictive of later cognitive impairment (Porter et al., 2008). The development of a brief, simple, easy-to-administer measure, which is sensitive to early cognitive changes following ECT, would therefore be of significant utility for clinical practice in informing such decisions.

1.1. Objectives of the study

In the current study, we investigated the utility of individual items from a screening battery to detect early cognitive changes from ECT in a large sample of patients drawn from three multi-site research studies, conducted across three hospitals. We hypothesized that change in performance on items from this battery after three ECT treatments would be predictive of later cognitive changes during the treatment course. Analyses were conducted to determine which items in the battery best predicted later cognitive changes during the treatment course. Lastly, a scoring method for these items was developed and tested in a sample of patients drawn from one of the trials.

2. Methods and materials

2.1. Participants

Participants were 123 inpatients treated with ECT at three hospitals in Australia: The Northside Clinic, Wesley Hospital Kogarah, and The Melbourne Clinic. Participants were drawn from three trials. The studies were a non-randomized, prospective, single-blind trial of types of ECT (Study 1: $N = 21$), a double-blind randomized trial of ECT with either ketamine or saline placebo added to barbiturate anaesthesia (Study 2: $N = 23$; NCT00680433), and a double-blind, randomized trial of ultrabrief versus brief pulse ECT (Study 3: $N = 79$; NCT00870805). Studies 1 and 2 were conducted across two hospitals, Study 3 across all three hospitals. Inclusion criteria common to all three studies were: age ≥ 18 years, DSM-IV Major Depressive Episode, no diagnosis of schizophrenia, schizoaffective disorder or rapid cycling bipolar disorder, no ECT in the last 3 months, and no drug or alcohol abuse in the last six months. Participants with current psychotic symptoms were additionally excluded in Study 2.

The above trials and current study were approved by the Human Research Ethics Committees of the University of New South Wales, The Northside Clinic, and The Melbourne Clinic. All participants had been prescribed ECT by their own treating psychiatrist and had given informed consent for ECT treatment and participation in the research trials. Demographic and clinical characteristics of participants were obtained in semi-structured interviews conducted by a psychiatrist or research psychologist. Out of the 123 participants initially included in the study, 3 were removed from the analysis as they had received their first suprathreshold ECT treatment on or after their third ECT session, leaving a final sample of 120 for analysis.

2.2. ECT treatment

Participants were anaesthetised with either thiopentone (3–5 mg/kg) or propofol (1–2 mg/kg), followed by succinylcholine (1 mg/kg). For Study 2, approximately half of the participants received adjunctive ketamine 0.5 mg/kg with their regular anaesthetic. ECT was given three times per week with a bitemporal (BT), bifrontal (BF), or right unilateral (RUL) (d’Elia placement) electrode placement. ECT was also given at a range of pulse widths (0.3–1.0 ms). For each participant, seizure threshold (ST) was established by titration at the first ECT session. Out of the 120 participants, 81 received their first suprathreshold treatment in their first ECT session and 39 in their second ECT session. Subsequent ECT treatments were given at $5 \times ST$ for brief pulse RUL ECT; 6 or $8 \times ST$ for ultrabrief pulse RUL ECT; $1.5 \times ST$ for brief pulse BT and BF ECT; and $3 \times ST$ for ultrabrief pulse BT and BF ECT. ECT dose increases were made over the treatment course if there was a decline in EEG seizure quality (Study 1 and 2) or if retitration of seizure threshold at treatment 6 indicated changes in the threshold (Study 3).

2.3. The screening battery

This screening battery was constructed for this study with the aim of detecting cognitive changes early in the treatment course, that are predictive of later cognitive side-effects during and following the full ECT treatment course. The tasks chosen included a global cognitive screening measure (i.e., MMSE), as well as several simple and easy-to-administer items chosen to assess anterograde memory, executive function, and processing speed, as these are the areas of cognition commonly affected by ECT (Ingram et al., 2008). These items included the first and second recall items of the Modified Mini-Mental State Examination (3MSE; Teng and Chui, 1987) and several mental control items. The mental control items were: 1) counting backwards from 20 to 1; 2) saying the alphabet (forwards); 3) counting forwards in 3 s starting with 1, ending after 14 responses; 4) saying the days of the week backwards, starting with ‘Sunday’; and 5) saying the months of the year backwards, starting with ‘December’. For each item, outcome measures included the total time taken (seconds) and total number of errors. The screening battery was administered 1–3 days before the first ECT treatment, and the day after the third treatment (i.e., post ECT 3).

2.4. The detailed cognitive battery

The detailed cognitive battery comprised the following tests: Medical College of Georgia Complex Figure Test (MCG; Meador et al., 1993), Hopkins Verbal Learning Test-Revised (HVLT-R; Benedict et al., 1998), Letter Fluency (COWAT; Benton and Hamsher, 1976), Animal Fluency (Spreen and Strauss, 1998), Cross Out task (90 s for Studies 1 and 2; 120 s for Study 3; Woodcock and Johnson, 1989); Symbol Digit Modalities Test (SDMT; Smith, 1991) and the

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