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Unravelling Autobiographical Retrograde Amnesia Following Bitemporal Electroconvulsive Therapy: Effect of Treatment versus Effect of Time

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Abstract

Objective: To reliably quantify the autobiographical retrograde amnesia directly attributable to the effect of electroconvulsive therapy (ECT) independent from normal and depression-associated changes in autobiographical memory consistency. Method: By use of retrospective case-control study design, 19 severely depressed inpatients never treated with ECT who received pharmacotherapy (noECT group) were individually matched to similarly depressed 19 patients treated with standard, bitemporal electrode placement, ECT (B-ECT). The two groups were compared at Pre-Treatment, at Post-Treatment and at three months Follow-Up on their performance on the Semantic, Episodic-Extended and Episodic-Specific Components of the Columbia Autobiographical Memory Interview-Short Form (CAMI-SF). Effects of treatment group and time on the three components were tested with 2 × 3 repeated-measures analyses of variance. Depression severity, assessed using the Hamilton Depression Rating Scale, was investigated as possible covariate. To explore the results' clinical significance, individual CAMI-SF performances were compared to available normative data. Results: At Pre-Treatment, the two groups were comparable on all three CAMI-SF components. In both groups, a significant effect of time explained decreased performance at Post-Treatment and Follow-Up on all components (p-values < 0.0001). No significant effect of treatment was observed on the Semantic and Episodic-Extended components ($p > 0.16$). The B-ECT retrieval consistency on the Episodic-Specific component was significantly worse at both Post-Treatment ($p = 0.009$) and Follow-Up ($p = 0.012$) relative to the noECT group. Ratios of im-

paired retrieval consistency were higher in the B-ECT group than in the noECT group at Post-Treatment only. On individual level, bitemporal ECT was associated with a clinically significant decrease in Episodic-Specific autobiographical memory recall at Post-Treatment in 37% of participants and, for about 26%, this specific impairment persisted for at least three months after end of treatment. Depression severity did not influence observed results. Conclusion: ECT-associated autobiographical amnesia is limited to specific personal episodes, does not affect all patients and is reversible for some.

Keywords

Autobiographical Memory, Retrograde Amnesia, Depression, Electroconvulsive Therapy

1. Introduction

Electroconvulsive therapy (ECT) is widely recognized as the most acutely effective treatment for severe depression (Sackeim et al., 2007; UK ECT Review Group, 2003). Systematic reviews identify autobiographical memory (AM) difficulties as the ECT side-effect that is of most concern to patients (Dybedal et al., 2014; Fraser et al., 2008; Goodman, 2011; Rose et al., 2003). These reviews also agree that, due to the complexity of AM function, reliably measuring its loss following treatment represents a methodological challenge. This difficulty is further compounded by depression-associated AM impairments. Indeed, according to other systematic reviews and meta-analyses (King et al., 2010; Van Vreeswijk & De Wilde, 2004), experiencing depression correlates with a decreased ability to recall specific AMs that persists in the euthymic phase of recurrent depression (Bergouignan et al., 2008; Kohler et al., 2015). Despite these systematic observations, relatively few studies have sought to isolate the specific effect of ECT on AM independent of mood-associated changes over time. Consequently, the nature, extent and possible persistence of AM deficits specifically caused by ECT remain unclear.

During the last forty years, several modifications of ECT technique have been introduced to minimize cognitive side-effects, such as moving from sine-wave to brief-pulse ECT or using unilateral rather than bilateral electrode placement (UK ECT Review Group, 2003). In the case of AM, this corresponded to favouring the technique associated with the highest preservation of consistency in personal memories recall. Autobiographical memory consistency refers to the use of test-retest procedure where the patient is asked to generate personal memories before the treatment phase and following its completion and where AM preservation is quantified as percentage of consistent with pre-treatment information responses obtained following treatment. In line with this preferred methodology, the majority of ECT research on AM equals autobiographical amnesia to any inconsistency noted after ECT relative to the observed pre-treatment recall of

personal memories (e.g., McElhiney et al., 1995; Sackeim et al., 2007, 2009; Sobin et al., 1995). However, loss in consistency with the passage of time is a normal process in AM functioning (Conway, 2009; Semkovska & McLoughlin, 2013). This should be taken into account while interpreting AM assessments based on consistency. For example, the largest percentages consistency loss that have been reported in the ECT literature fluctuate between 28% and 40% for reassessments taking place one to two months after a pre-ECT assessment (Sackeim et al., 1993, 2000). However, these percentages are equivalent to the extent of loss in AM consistency observed in healthy individuals over similar time frames (e.g. Anderson et al., 2000; Talarico & Rubin, 2003).

To date, instruments most frequently used in ECT for AM assessment have not sought to demonstrate the specific treatment effect independent from normal or depression-associated loss in consistency (e.g., Loo et al., 2008; Sackeim et al., 2007), thus precluding the identification and research on possible preventive or remedial strategies. With the aim to dissociate normal from depression-associated loss in AM consistency over time, Semkovska & colleagues (2012) have validated an alternative scoring system for one such instrument, the Columbia Autobiographical Memory Interview-Short Form (CAMI-SF; McElhiney et al., 2001). Previous to this validation study, the CAMI-SF has been exclusively used in ECT research on AM. The authors distinguished three theoretically-based CAMI-SF sub-components: a Semantic component (containing decontextualised information regarding one's past), an Episodic-Extended component (containing information regarding personal, extended in time, events) and an Episodic-Specific component (containing information regarding personal, specifically situated in time and place, events). The results suggested that, at initial assessment, depressed patients never treated with ECT recalled less Episodic-Specific AMs than healthy controls (Semkovska et al., 2012). However, both groups showed equivalent amounts of consistency loss over a two-month interval on all AMs components. Moreover, following this reassessment interval, remitted patients were comparable to healthy controls on Episodic-Specific AMs retrieved, while patients with persisting depressive symptoms continued to show an impaired Episodic-Specific AM recall. This study also demonstrated that, over a six-month interval, large decreases in retrieval consistency were observed in healthy volunteers on all AM components, with Episodic-Specific AMs showing significantly greater consistency loss than Semantic AMs. Therefore, a natural loss in consistency occurs with the passage of time and this fact needs to be taken into account when interpreting CAMI-SF results obtained following ECT before concluding on the occurrence of autobiographical retrograde amnesia.

The present retrospective case-control study was designed to attempt dissociating the specific effect of ECT on AM from normal and mood-associated changes observed through the course of depression using the validated CAMI-SF scoring system and to determine the clinical significance of this ECT-associated effect. Specific aims were to: 1) evaluate, in patients who were hospitalised for severe depression, the effect of ECT on the consistency of AM recall relative to

the simple effect of pharmacological treatment and the passage of time; 2) determine if this treatment effect was different depending to the AM type (Semantic, Episodic-Extended, Episodic-Specific); and 3) assess the clinical significance of observed results by comparing, at both post-treatment and three-month follow-up, the treatment groups (ECT, pharmacotherapy) on their ratios of patients scoring within the normal versus impaired range in AM consistency relative to published normative data.

In light of existing literature, we hypothesised that both treatment groups would show a decline in performance between pre-treatment and post-treatment, on all types of AM, which would be at least partially attributed to the normal effect of time on AM. With regards to the remaining research aims, our study was exploratory given the absence (to our knowledge) of published research that has specifically addressed the ECT effect on the semantic and episodic components of AM.

2. Methods

2.1. Participants and Procedure

Anonymised records of patients hospitalised in an Irish mental health care institution between October 2008 (date of anonymised records introduction) and January 2013 (date of current study design) were searched that fulfilled the following inclusion criteria: 1) age of 18 or older; 2) hospitalised and treated for a major depressive episode, according to Structured Clinical Interview for DSM-IV disorders (First et al, 1994); 3) depression severity was assessed before treatment (Pre-Treatment) with the 24-item Hamilton Rating Scale for Depression (HRSD-24, ECDEU version; Beckham & Leber, 1985); 4) presented with severe depression, determined by a score of 21 or higher (Kearns et al., 1982) on the HRSD-24; 5) record contained a complete verbatim of answers on the Columbia Autobiographical Memory Interview-Short Form (CAMI-SF; McElhiney et al., 2001) for all of the following time points: Pre-Treatment, Post-Treatment and three to four months Follow-up; and 6) English was the participant's first language. Exclusion criteria were: neurological disorder, co-morbid (other than mood) psychiatric disorder, major sensory deficit and alcohol and/or other substance abuse in previous six months.

Two waves of searches were performed. An additional inclusion criterion only for the first wave of searches was: no history of previous ECT or ECT during hospitalisation or Follow-Up which formed the noECT group. Then, for the second wave of searches, each participant from the noECT group was individually matched on gender, age (±5 years) and level of education (completed or reached) to a patient who, after an initial assessment, was treated with standard bilateral brief-pulse (1.0 msec pulse width) ECT (B-ECT group) at 1.5 seizure threshold. Bilateral standard ECT was chosen as this is the most frequently administered electrode placement for treatment of depression (Leiknes et al., 2014). Additional exclusion criterion for the B-ECT group was having received ECT within the six months preceding the initial assessment.

2.2. Data Collection

2.2.1. Sociodemographic, Depression Severity and Treatment Data

Data were collected relative to three time points, with respect to treatment received: 1) Pre-Treatment, 2) Post-Treatment: five to eight weeks after Pre-Treatment, and 3) Follow-Up: three to four months after Post-Treatment. For the pharmacologically treated patients (noECT group), Pre-Treatment occurred within the first two weeks after hospital admission for depression, while for the B-ECT group, it was completed during the week preceding the first ECT treatment.

Pre-Treatment age, gender and educational level sociodemographic data were collected. Where available, pre-morbid intellectual quotient (IQ), estimated using the National Adult Reading Test (Nelson & Willison, 1991) was also extracted. Depression severity, using the HRSD-24, was extracted for all time points. Information regarding pharmacological treatment was collected for all participants at Pre-Treatment and at Follow-Up. For the B-ECT group, number of ECT treatment sessions received was also extracted.

2.2.2. Autobiographical Memory Assessment

Originally, the CAMI-SF (McElhiney et al., 2001) was designed for use in depressed patients receiving ECT with the primary aim of quantifying retrograde amnesia for autobiographical information observed following this particular treatment. However, until recently, this instrument has not been validated and it has been previously demonstrated that its original scoring (from McElhiney et al., 2001) does not allow distinguishing ECT-related amnesia from normal or mood-associated loss in AM consistency (e.g., McClintock et al., 2014; Semkovska et al., 2011). To answer our research questions, namely dissociating the specific effect of ECT on AM from normal and mood-associated changes observed through the course of depression, the current study proposed to apply the validated by Semkovska & colleagues (2012) scoring system on existing CAMI-SF verbatims. This system differentiated theoretically based AM components, provided normative data for AM consistency loss with the passage of time across components and resolved ceiling effect issues imposed by the original scoring system.

The CAMI-SF (McElhiney et al., 2001) contains 30 questions covering six personal themes (Family Member, Last Major Trip, Last New Year's Eve, Last Birthday, Last Employment, and Last Physical Illness). Five questions gather specific details within each theme. At initial assessment (Pre-Treatment), all 30 questions are asked. At reassessment (both Post-Treatment and Follow-Up), only questions that have elicited specific memories are re-administered with the aim to quantify their consistency in recall with the passage of time. As per the above-described inclusion criteria, only participants with complete CAMI-SF verbatims at all three time points (Pre-Treatment, Post-Treatment and Follow-up) were considered for the study.

The validated scoring system of the CAMI-SF (Semkovska et al., 2012) was

then applied for quantifying the AM functioning. Following it, each separate specific personal detail provided in response to individual questions within a theme was given 1 point at Pre-Treatment. The score given per item can be limited given the nature of the question. For example, the item "What was your title when last working at this job?" (Last Employment theme, Q.1) can elicit only a score of 1 or 0 points. However, the total score on a given theme is unlimited as the score cumulated on other questions is determined by the number of specific AMs produced (e.g. "Describe what you did when you celebrated your last birthday?" from Last Birthday theme, Q.3). Items which, at Pre-Treatment, did not elicit a specific memory (e.g. from the Last Birthday theme, for the item "What did you receive at your last birthday?", the reply: "I don't remember") or were answered with a guess based on previous experiences (e.g., from the Last New Year's Eve theme, for the item "what did you do at midnight?", the reply: "I guess I watched TV, as I was at home, but I don't have a clear memory") receive a Pre-Treatment nil score and are not considered for scoring at Post-Treatment or Follow-Up. Three component scores are recorded; Semantic: total of AM specific details provided on themes Family Member and Last Employment, Episodic-Extended: total of specific AM details provided on themes Last Major Trip and Last Physical Illness, and Episodic-Specific: total of specific AM details provided on themes Last New Year's Eve and Last Birthday. Only information consistent with initial assessment was analyzed for retest scoring and any additional information was ignored (see Semkovska et al., 2012 for more scoring details).

2.2.3. Statistical Analyses

Effects of treatment group (noECT; B-ECT) and time (Pre-Treatment; Post-Treatment; Follow-Up) on the three CAMI-SF components were tested with 2 × 3 repeated measures analyses of variance (ANOVAs). Depression severity was investigated as possible covariate of CAMI-SF performance. For this, the two groups were compared on depression severity at all assessment time points using paired t-tests. Additionally, at all time points, Pearson correlations explored the possible association between depression severity and CAMI-SF performance. ANCOVAs with depression severity as covariate were planned if either paired t-tests or Pearson correlations reached significance level, fixed at $\alpha = 0.01$, given the number of statistical testing involved.

All patients were individually compared to published CAMI-SF normative data (Semkovska et al., 2012) on both initial CAMI-SF performance (Pre-Treatment) and AM retrieval consistency at re-assessments (Post-Treatment, Follow-Up). Then, the two groups (noECT, B-ECT) were compared on ratios of normal/borderline/impaired performance using the Contingency Coefficient of association with the significance level fixed at $\alpha = 0.05$. In line with conventional guidelines for defining clinically meaningful change in comparison to normative data (McGlinchey et al., 2002; Moleiro & Beutler, 2009), normal performance was defined as the participant scoring within 1.5 standard deviation (SD) from the mean of his/her reference age group, borderline performance was defined as

the participant scoring between 1.5 and 1.96 SD from the mean of his/her reference age group, and impaired performance was defined as the participant scoring below 1.96 SD from the mean of his/her reference age group.

3. Results

3.1. Sociodemographic, Treatment and Depression Severity Descriptives

Nineteen individuals (10 women, 9 men) with no history of ECT met the inclusion criteria of the first wave searches. They all have received only pharmacotherapy, as prescribed by their treating psychiatrist (noECT group). Each participant from the noECT group was individually matched, through the second wave of searches, on gender, age (±5 years) and level of education (completed or reached) to an inpatient who, after an Pre-Treatment assessments, received standard bitemporal ECT (B-ECT group). The delay, in days, between the Pre-Treatment and Post-Treatment assessments was comparable between the groups (noECT: Mean = 44.6, SD = 6.72; B-ECT: Mean = 41.7, SD = 7.44, $t(36) = 0.82$, $p = 0.23$). Depression severity data were available for all participants at all time points. Estimated NART IQ data were available for 84% participants of the noECT group (n = 16) and for 95% participants of the B-ECT group (n = 18). Table 1 presents sociodemographic and depression severity data for all participants.

There were no significant differences on depression severity between the two groups at any assessment time point. However, patients from the B-ECT group received a significantly higher number of psychotropic medications at Pre-Treatment than patients from the NoECT group ($t(36) = 5.44$, $p < 0.001$). This was true across all psychotropic classes with three exceptions. The groups were equivalent in hypnotics and noradrenergic and specific serotonergic antidepressants use, while the selective serotonin re-uptake inhibitors antidepressants were more frequently prescribed in the NoECT group ($p = 0.015$). At Follow-Up, all classes of psychotropic medications were prescribed equally frequently in both groups (all $p > 0.17$) (See Table 2 for detailed treatment information). In the B-ECT group, no significant correlations were found between number of ECT sessions and CAMI-SF components at any time point (all $p > 0.24$).

3.2. Association among CAMI-SF Performance, Depression Severity, and Estimated Intelligence

Table 1 presents the results on participants' CAMI-SF performance and between-group comparisons at the three assessment time points. Before conducting the between-groups ANOVAs, Pearson correlations explored the possible association between depression severity and CAMI-SF performance on each component at each time point. No significant correlations were found: at Pre-Treatment, all p-values were above 0.19, at Post-Treatment: $p > 0.17$, while at Follow-Up, for the Semantic, Episodic-Extended and Episodic-Specific component, these p-values for correlations with depression severity were respectively: 0.18,

0.052 and 0.82, thus also non-significant α = 0.01. Overall, as depression severity was not found to relate significantly with CAMI-SF performance, it was not used as a covariate in the subsequent ANOVAs. In both groups, no significant correlations were found between the NART and CAMI-SF outcomes at any time point (all $p > 0.10$).

3.3. Effects of Treatment Group and Time on the Semantic, Episodic-Extended and Episodic-Specific CAMI-SF Components

For each individual CAMI-SF component, a mixed between-within subjects ANOVA was conducted to assess the treatment (noECT, B-ECT) effect on participants' performance across three time periods (Pre-Treatment, Post-Treatment, Follow-Up).

Table 1. Sociodemographic, depression severity and Columbia autobiographical memory interview-short form results presented as means and standard deviations.

Variable	Pharmacotherapy group (noECT, n = 19)	Bilateral ECT group (B-ECT, n = 19)	Between-group differences
Age (years)	47.2 (12.0)	47.8 (12.3)	$t(36) = 0.16$, $p = 0.87$
Sex (% female)	52.6	52.6	χ^2 (1, n = 38) < 0.001, $p = 1.00$
Educational level* (% 1 - 2 - 3 - 4)	0% - 36.8% - 53.6% - 10.5%	10.5% - 47.4% - 26.3% - 15.8%	χ^2 (3, n = 38) = 4.12, $p = 0.25$
NART IQ	113.1 (7.1)	110.2 (8.9)	$t(32) = 1.06$, $p = 0.30$
Pre-Treatment HRSD-24	31.2 (6.1)	29.4 (5.7)	$t(36) = 0.91$, $p = 0.37$
Post-Treatment HRSD-24	19.0 (9.5)	15.6 (9.3)	$t(36) = 1.11$, $p = 0.28$
Follow-Up HRSD-24	19.5 (10.0)	16.4 (9.8)	$t(36) = 0.99$, $p = 0.33$
CAMI-SF Semantic component			
Pre-Treatment	14.61 (4.3)	13.97 (3.8)	$F(1, 36) = 1.87$, $p = 0.18$
Post-Treatment	13.47 (4.1)	11.13 (3.6)	
Follow-Up	13.53 (4.2)	11.32 (4.0)	
CAMI-SF Episodic-Extended component			
Pre-Treatment	12.63 (4.0)	12.03 (3.5)	$F(1, 36) = 2.09$, $p = 0.16$
Post-Treatment	10.03 (3.8)	8.34 (2.9)	
Follow-Up	9.53 (3.3)	7.42 (2.9)	
CAMI-SF Episodic-Specific component			
Pre-Treatment	14.87 (9.2)	12.95 (5.8)	$F(1, 36) = 4.43$, $p = 0.042$
Post-Treatment	10.26 (7.8)	4.82 (3.7)	
Follow-Up	8.32 (6.7)	3.76 (3.4)	

Note. CAMI-SF: Columbia Autobiographical Memory Interview-Short Form (McElhiney et al., 2001; Semkovska et al., 2012); HRSD-24: Hamilton Rating Scale for Depression-24 items (from Beckham & Leber, 1985); NART IQ: National Adult Reading Test Intellectual Quotient (Nelson & Willison, 1991); *Percent participants from sample whose maximal completed educational level was 1) Primary school, 2) Secondary school, 3) Under-graduate University studies or 4) Post-graduate University studies.

Table 2. Treatment characteristics of the studied sample and between-group comparisons on the type and number of psychotropic medications received.

Treatment variable	NoECT group	B-ECT group	Between-group differences
Selective serotonin re-uptake inhibitors			
Pre-Treatment	53% (n = 10)	11% (n = 2)	CC = 0.41, p = 0.005
Follow-Up	32% (n = 6)	32% (n = 6)	CC < 0.001, p = 1.00
Serotonin and norepinephrine reuptake inhibitors			
Pre-Treatment	42% (n = 8)	58% (n = 11)	CC = 0.16, p = 0.33
Follow-Up	26% (n = 5)	37% (n = 7)	CC = 0.11, p = 0.49
Tricyclic antidepressants			
Pre-Treatment	5% (n = 1)	37% (n = 7)	CC = 0.36, p = 0.017
Follow-Up	16% (n = 3)	26% (n = 5)	CC = 0.13, p = 0.43
Noradrenergic and specific serotonergic antidepressants			
Pre-Treatment	16% (n = 3)	16% (n = 3)	CC < 0.001, p = 1.00
Follow-Up	11% (n = 2)	21% (n = 4)	CC = 0.14, p = 0.37
Lithium			
Pre-Treatment	5% (n = 1)	42% (n = 8)	CC = 0.40, $p = 0.008$
Follow-Up	26% (n = 5)	16% (n = 3)	CC = 0.13, $p = 0.43$
Anticonvulsants			
Pre-Treatment	5% (n = 1)	42% (n = 8)	CC = 0.40, p = 0.008
Follow-Up	16% (n = 3)	16% (n = 3)	CC < 0.001, p = 1.00
Benzodizepines			
Pre-Treatment	26% (n = 5)	68% (n = 13)	CC = 0.39, p = 0.009
Follow-Up	32% (n = 6)	26% (n = 5)	CC = 0.06, p = 0.72
Nonbenzodiazepine hypnotics			
Pre-Treatment	53% (n = 10)	53% (n = 10)	CC < 0.001, p = 1.00
Follow-Up	26% (n = 5)	26% (n = 5)	CC < 0.001, p = 1.00
Antipsychotics			
Pre-Treatment	21% (n = 4)	63% (n = 12)	CC = 0.39, p = 0.009
Follow-Up	26% (n = 5)	47% (n = 9)	CC = 0.21, p = 0.18
Total number of psychotropic medication			
Pre-Treatment	Mean = 2.37; SD = 0.96	Mean = 4.47; SD = 1.39	$t_{(36)} = 5.44$, p < 0.001
Follow-Up	Mean = 2.21; SD = 0.79	Mean = 2.36; SD = 1.57	$t_{(36)} = 0.39$, p = 0.70
Number of ECT treatments	-	Mean = 8.58; SD = 2.36	-

Note. CC: contingency coefficient; SD: standard deviation.

For the Semantic component, there was a significant effect of time, Wilks Lambda = 0.32, $F(2, 35) = 37.68$, $p < 0.0001$, partial $\eta 2 = 0.68$, but not a significant effect of group, $F(1, 36) = 1.87$, $p = 0.18$. A significant group * time interaction on the Semantic component was also observed: Wilks Lambda = 0.72, $F(2, 35) = 6.89$, $p = 0.003$, partial $\eta 2 = 0.28$. This significant interaction was explored via one-way repeated-measure ANOVAs within each of the treatment groups. In both groups, the effect of time on performance was the same – there was a significant decrease between Pre-Treatment and Post-Treatment (in the NoECT group, mean difference = −1.13, $p = 0.001$, 95% Confidence Interval (CI) [−1.67; −0.59]; in the B-ECT group, mean difference = -2.84, $p < 0.00001$, 95%CI [−3.71; −1.97]), and also a significant decrease between Pre-Treatment and Follow-up (in the NoECT group, mean difference = −1.08, $p = 0.001$, 95%CI [−1.59; −0.56]; in the B-ECT group, mean difference = −2.66, $p < 0.0001$; 95%CI [−3.57; −1.74]). In both groups, the slight increase in performance between Post-Treatment and Follow-up was non-significant (mean differences of 0.053 and 0.13, respectively, in the NoECT and B-ECT group, both $p > 0.99$). Post hoc t-tests did not demonstrate any significant difference between the two groups at any time point. However, although at Pre-Treatment, the Semantic CAMI-SF performance of the two groups appeared similar: $t(36) = 0.48$, $p = 0.63$, at Post-Treatment, the inferior B-ECT performance (M = 11.13, SD = 3.6) almost reached significant difference with the noECT group performance (M = 13.47, SD = 4.1): $t(36) = 1.88$, $p = 0.068$. Based on the significant group*time interaction and the borderline significant post-hoc test of between group difference at Post-Treatment, we can speculate that the performance on the Semantic component also slightly decreases after ECT compared to pharmacotherapy, but then catches up at Follow-Up. The clinical significance of these results is assessed in the Individual CAMI-SF Performance analysis section below.

For the Episodic-Extended component, there was a significant effect of time, Wilks Lambda = 0.22, $F(2, 35) = 61.47$, $p < 0.0001$, partial $\eta 2 = 0.78$, but not a significant effect of group, $F(1, 36) = 2.09$, $p = 0.16$, nor a significant group*time interaction, Wilks Lambda = 0.90, $F(2, 35) = 1.98$, $p = 0.15$, partial $\eta 2 = 0.048$.

For the Episodic-Specific component, there was a significant effect of time, Wilks Lambda=0.32, $F(2, 35) = 36.69$, $p < 0.0001$, partial $\eta 2 = 0.68$, and a significant effect of group, $F(1, 36) = 4.43$, $p = 0.042$, but not a significant group*time interaction, Wilks Lambda = 0.87, $F(2, 35) = 2.54$, $p = 0.09$, partial $\eta 2 = 0.13$. Post hoc analyses using Holm's multistage Bonferroni α corrections showed that the effect of group was attributable to a significantly inferior performance of the B-ECT group relative to the NoECT group at both Post-Treatment, $t(36) = 2.75$, $p = 0.009$, and Follow-up, $t(36) = 2.63$, $p = 0.012$, while the two groups performed at similar level at Pre-Treatment, $t(36) = 0.77$, $p = 0.45$.

3.4. Individual CAMI-SF Performance Relative to Normative Data

To evaluate the clinical relevance of our results, the CAMI-SF performance of each individual participant was compared to available normative data at all as-

sessment time points. Then, the two treatment groups were compared on their respective ratios of normal/borderline/impaired performance on each CAMI-SF component at Pre-Treatment. Subsequently, they were compared on their ratios of normal/borderline/impaired performance on retrieval loss in each of the three components at both Post-Treatment and Follow-Up. Results appear in Table 3.

Table 3. Between-group comparisons on the frequency of patients scoring within the normal, borderline and impaired range on the Columbia autobiographical memory interview-short form relative to published normative data

Group	Normal	Borderline	Impaired	Contingency coefficient	p-value
Pre-Treatment					
Semantic component					
NoECT	10	0	9		
B-ECT	9	1	9	0.16	0.59
Episodic-Extended component					
NoECT	13	2	4		
B-ECT	13	1	5	0.11	0.80
Episodic-Specific component					
NoECT	17	0	2		
B-ECT	14	4	1	0.33	0.10
Post-Treatment					
Semantic retrieval loss					
NoECT	17	0	2		
B-ECT	9	0	10	0.41	0.005
Episodic-Extended retrieval loss					
NoECT	13	2	4		
B-ECT	7	2	10	0.32	0.11
Episodic-Specific retrieval loss					
NoECT	17	0	2		
B-ECT	11	0	8	0.34	0.027
Follow-Up					
Semantic recall retrieval loss					
NoECT	19	0	0		
B-ECT	17	0	2	0.23	0.15
Episodic-Extended retrieval loss					
NoECT	16	1	2		
B-ECT	14	0	5	0.25	0.30
Episodic-Specific retrieval loss					
NoECT	15	1	3		
B-ECT	14	0	5	0.20	0.46

At Pre-Treatment, no significant difference in the ratios of normal/borderline/impaired performance was observed between the two groups on any CAMI-SF component (all p-values > 0.10). However, at Post-Treatment, while the majority of patients from the NoECT group (89%) showed normal range Semantic retrieval loss, 53% of the B-ECT group showed impaired Semantic retrieval loss. Similarly, at Post-treatment, normal range on the Episodic-Specific retrieval loss was observed in a significantly higher number of participants from the noECT group (89%) relative to the B-ECT group (58%). Therefore, at Post-Treatment, having received bilateral ECT has associated with higher rates of impaired autobiographical memory consistency on both the Semantic and Episodic-Specific components compared to receiving pharmacotherapy only. At Follow-Up, ratios of normal/borderline/impaired performance were again comparable between the two groups in terms of AM consistency of recall on all CAMI-SF components (all p-values > 0.15). Furthermore, at Follow-Up, the majority of participants showed normal range retrieval loss relative to Pre-Treatment levels on all components: 95% for Semantic, 83% for Episodic-Extended and 80% for Episodic-Specific information.

4. Discussion

The present study aimed at dissociating the effect of ECT on AM consistency from the normal and depression-related changes that affect personal memory with the passage of time. Thus, we searched to quantify the extent of retrograde autobiographical amnesia specifically attributable to ECT. For this, through a retrospective case-control design, two inpatients' groups admitted for severe depression were compared on their AM consistency following treatment using the validated CAMI-SF scoring system: inpatients with no previous history of ECT who received pharmacotherapy (noECT group) and inpatients who received standard bitemporal ECT (B-ECT group).

Consistent with previous reports on the effect of time on AM stability (Anderson et al., 2000; Nadel et al., 2007; Weaver, 1993), the present study demonstrated a significant loss in AM consistency between Pre-Treatment and Post-Treatment in both groups. More specifically, in both groups, a significant effect of time explained the decreased CAMI-SF performance on all components: Semantic, Episodic-Extended, and Episodic-Specific. No significant effect of treatment group on the Semantic and Episodic-Extended CAMI-SF components was observed, suggesting that comparable AM consistency loss occurred in both groups on these components. In the ECT group, such loss can be interpreted as resulting from the combination of the effect of time and depression course on AM, but not as an evidence of autobiographical retrograde amnesia. The significant group * time interaction effect observed on the Semantic component along with the borderline significant post hoc t-test for difference between the two groups at Post-Treatment indicates a possible small effect of bitemporal ECT on Semantic AM, which appeared however reversible at Follow-Up (non-significant difference between the two groups). This main result

interpretation is supported by the relative ratios of patients scoring in the impaired range for the Semantic component: equivalent for both groups at Pre-Treatment and Follow-Up, but significantly higher in the B-ECT group at Post-Treatment than in the noECT group.

The repeated-measures ANOVAs showed a significant effect of treatment group on AM consistency only on the Episodic-Specific component. Although the two groups were comparable at Pre-Treatment in their ability to recall Episodic-Specific personal information, the B-ECT performance on this component was significantly worse at both Post-Treatment and Follow-Up relative to the noECT group. These results suggest that the retrograde autobiographical amnesia attributable to bitemporal ECT is restricted to specifically situated in time and space personal events and does not concern all recent AMs. Interestingly, although the relative ratios of patients scoring in the impaired range on Episodic-Specific consistency was significantly higher in the B-ECT group compared to the noECT group at Post-Treatment, these ratios were comparable for both groups at Follow-Up. Taken together, the group and individual results on the Episodic-Specific component suggest that bitemporal ECT specifically affects the recall of these personal memories and that for about 26% of patients this specific impairment persists for at least three months after end of treatment.

All observed treatment effects were found to be independent from depression severity – both groups appeared equally severely depressed at Pre-Treatment and their mood improved to a comparable extent at Post-treatment and Follow-Up. Moreover, this improvement was not associated with any aspect of AM performance. This result is consistent with reports suggesting that AM performance of individuals with depression history is independent of depression status (acute episode versus remission) (Bergouignan et al., 2008; Spinhoven et al., 2006). The CAMI-SF performance was not associated with level of intellectual functioning.

Our study's main limitation consists in its small sample size. A higher number of participants in each group would strengthen the power to the findings. Other limitations include retrospective design, non randomised allocation to the treatment groups, and notable variability in the psychotropic medications prescribed to both groups. Furthermore, recent studies suggest that monoamine re-uptake inhibitors, such as SSRIs and SNRIs, may improve cognitive function independently from their anti-depressant effect (e.g., Levkovitz et al., 2002). However, this is not a consistent research finding (see Greer et al., 2014, for a review) and the groups studied here were comparable in their post-treatment psychotropic use. The variety of psychotropic combinations received by each participant precludes psychotropic classes' sub-analyses of the sample.

Nevertheless, for the first time, by use of a validated AM instrument, we have quantified and qualified autobiographical amnesia following bitemporal ECT: amnesia that cannot be explained by the passage of time or depression severity and that is limited to Episodic-Specific personal information. We may speculate that, by its operation that disrupts temporarily the hippocampus's functioning bilaterally, bitemporal ECT prevents and/or interferes with the consolidation of

recent specific episodes of one's personal life or otherwise affects the fronto-temporal connections involved in AM functioning (Soderlund et al., 2014). Nonetheless, it is important to highlight that, according to our results, this amnestic effect does not appear universal as it has not affected all participants from the B-ECT group. Moreover, for some participants, the impaired at Post-Treatment AM retrieval consistency normalised at Follow-Up, which may in turn indicate that ECT only interferes with the access to sufficiently well consolidated personal memories.

The present results do not allow us to formulate a definite theoretical explanation of the specific processes that bitemporal ECT disrupts and by which it causes autobiographical amnesia. Nonetheless, this study has important clinical implications as it demonstrates the possibility to reliably quantify the extent and specify the nature of ECT-related autobiographical amnesia. Future studies, with larger samples, prospective design, and random treatment allocation, are needed to explore the type of episodic memories that are affected by ECT (e.g., are distant episodic memories impaired or is the ECT effect limited to the recent past?) and the processes through which ECT creates autobiographical amnesia (e.g., does ECT only interfere with memories access or does it prevent consolidation?).

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