It is illegal to post this copyrighted PDF on any website. A Systematic Review and Meta-Analysis of Brief Versus Ultrabrief Right Unilateral Electroconvulsive Therapy for Depression

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ABSTRACT

Objective: Electroconvulsive therapy (ECT) is an effective depression treatment, but it has potential cognitive side effects. Ultrabrief pulse (UBP) right unilateral (RUL) ECT is an increasingly used treatment option that can potentially combine efficacy with lesser cognitive side effects. However, current trials are underpowered or have conflicting results. A systematic review and meta-analysis was conducted to evaluate the relative efficacy and cognitive effects of brief pulse (BP) and UBP RUL ECT.

Data Sources: MEDLINE, EMBASE, PsycINFO, CENTRAL, DARE, and the International Clinical Trials Registry Platform were searched with the search terms *ECT, electroconvulsive therapy, electroconvulsive shock, electroconvulsive shock therapy, electrical stimulation, electroconvulsive* combined with *brief, ultra*, pulse,* and *trial* in English, all fields including title, abstract, subject heading, and full text up to June 20, 2013, for studies comparing BP and UBP RUL ECT in depressed patients that reported formalized mood ratings for depression.

Study Selection: Six studies met the inclusion criteria, comprising a total of 689 patients.

Data Extraction: Efficacy, cognitive, response, and remission outcomes were extracted from each publication or obtained directly from authors.

Results: BP RUL ECT was significantly more efficacious in treating depression than UBP RUL ECT (standardized mean difference = 0.25; 95% Cl, 0.08–0.41; P = .004) but showed significantly more cognitive side effects in all cognitive domains examined (global cognition, anterograde learning and recall, retrograde memory) (P < .01). The mean number of treatment sessions given was 8.7 for BP ECT and 9.6 for UBP ECT (P < .001). UBP had a lower remission rate (OR = 0.71; 95% Cl, 0.51–0.99; P = .045), with a number needed to treat of 12.1.

Conclusions: BP compared with UBP RUL ECT was slightly more efficacious in treating depression and required fewer treatment sessions, but led to greater cognitive side effects. The decision of whether to use BP or UBP RUL ECT should be made on an individual patient basis and should be based on a careful weighing of the relative priorities of efficacy versus minimization of cognitive impairment.

J Clin Psychiatry 2015;76(9):e1092–e1098 dx.doi.org/10.4088/JCP.14r09145 © Copyright 2015 Physicians Postgraduate Press, Inc.

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Electroconvulsive therapy (ECT) is a highly efficacious¹ treatment for depression. However, cognitive side effects are an important limitation of ECT.^{2,3} Bitemporal ECT has been traditionally used, but in recent decades, right unilateral (RUL) electrode placement has been proposed to decrease the cognitive side effects of ECT.⁴⁻⁶ More recently, it has been further proposed that altering the type of electrical stimulus used in ECT may impact the efficacy and cognitive outcomes.⁷ Brief pulse (BP) square wave, vis-à-vis sine wave ECT, had been recognized as a more efficient and physiologic stimulus for inducing seizures with lesser cognitive side effects.⁸ However, these brief pulse widths (0.5–1.5 ms) still exceed optimal pulse widths for depolarizing neurons.⁹ Thus, interest has turned to the use of an ultrabrief pulse (UBP) (0.3 ms). Theoretically, UBP stimulation should have lesser cognitive side effects than BP stimulation due to less direct stimulation of brain tissue by the electrical current¹⁰ and less stimulation of neuronal tissue during the refractory period.¹¹ UBP stimulation has been applied to both bitemporal and RUL ECT. However, in the only randomized controlled trial (RCT) that compared BP and UBP stimulation for bitemporal as well as RUL ECT, the combination of bitemporal electrode placement and UBP stimulation led to a substantive reduction in efficacy, whereas the efficacy of RUL ECT was not affected when combined with UBP stimulation.¹²

More studies have compared BP and UBP RUL ECT^{13,14} in treating depression, mostly finding that efficacy was similar.^{12,15–18} However, limitations of these trials include small sample sizes^{12,16} and nonrandom assignment to treatment type.^{15,18} Although most studies found lesser cognitive side effects with UBP stimulation,^{12,15,16,18} the largest RCT to date failed to find a cognitive advantage for UBP stimulation.¹⁷ In addition, a recent analysis of speed of response suggested that the rate of improvement may be slower with UBP than BP RUL ECT.¹⁹ To date, there has been no meta-analysis of the available trial data examining the relative efficacy and cognitive side effects of BP versus UBP RUL ECT. Hence, we performed a systematic review and meta-analysis of the efficacy and cognitive side effects of BP versus UBP RUL ECT for patients with depression.

METHOD

Data Sources

We searched MEDLINE, EMBASE, PsycINFO, CENTRAL, DARE, and the International Clinical Trials Registry Platform

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Tor et al

- Current evidence supports the efficacy of right unilateral (RUL) electroconvulsive therapy (ECT) given with an ultrabrief pulse width in the treatment of depression.
 - Ultrabrief pulse RUL ECT leads to lesser cognitive side effects than traditional forms of ECT.
- Ultrabrief pulse RUL ECT may be slightly less effective than traditional forms of ECT.

with the search terms *ECT*, *electroconvulsive therapy*, *electroconvulsive shock*, *electroconvulsive shock therapy*, *electrical stimulation*, *electroconvulsive* combined with *brief*, *ultra**, *pulse*, and *trial* in English, all fields including title, abstract, subject heading, and full text up to June 20, 2013.

Searches were combined and duplicates removed. The results were screened for relevance to BP versus UBP RUL ECT. For papers of uncertain relevance, the full text was obtained. The reference lists of the sourced papers were hand-searched for other relevant studies, and SCOPUS was used to further identify relevant studies that referenced sourced papers. Two e-mails were sent out to members of international professional ECT societies, the International Society for ECT and Neurostimulation and the European Forum for Electroconvulsive Therapy, to solicit relevant published and unpublished studies. The first author (P.C.T.) and second author (A.B.) separately evaluated the inclusion of papers in the review. Disagreements were resolved via consensus (see Figure 1).

Data Extraction

Clinical Points

We included all randomized, controlled, and naturalistic prospective studies of BP versus UBP RUL ECT for patients with depression that had formalized mood ratings at more than 1 time point. The inclusion criteria were deliberately broad to avoid missing any studies in a small field. Studies not in English were excluded. Mood ratings, cognitive test scores, response/remission outcomes, and patient demographics were extracted from the papers. The first author (P.C.T.) extracted relevant data from the selected papers, and, if additional data were required, the authors of the relevant papers were contacted. Outcome data were obtained for baseline, a predetermined point during the study (6–8 ECT sessions, ie, same number of treatment sessions in BP and UBP groups), and the end of the acute ECT treatment course (which may involve different numbers of treatment sessions in the BP and UBP groups).

Statistical Analysis

The first outcome investigated was efficacy, the primary outcome being change in mean mood scores from pre-ECT baseline scores. Separate analyses were performed for efficacy measured at 2 endpoints: 1 at the end of 6–8 ECT sessions and the other at the end of acute ECT treatment. Per-protocol analyses data were used with the exception of the 1 study¹² that only reported intention-to-treat data. As the included studies measured depressive symptoms **control PDF on any website**, using different psychometric scales (Montgomery-Asberg Depression Rating Scale [MADRS] or Hamilton Depression Rating Scale [HDRS]), standardized mean differences (SMDs)²⁰ were calculated to represent effect sizes. SMD corresponds to the posttreatment standardized difference in mean depressive scores between the BP and UBP RUL ECT groups; a positive SMD suggests that the UBP RUL ECT had superior effects on depression compared to BP RUL ECT. Weighted mean difference (WMD) was calculated to compare the difference between the mean number of ECT sessions for BP versus UBP RUL ECT.

Differences between response and remission rates were quantified using odds ratios (ORs), and the BP RUL ECT group was used as the reference group in all analyses. An OR of less than 1 indicates that the UBP RUL ECT had a lower response or remission rate, while an OR of more than 1 indicates that the UBP RUL ECT had a higher response or remission rate. The ORs were calculated using the following equation:

 $OR = [P_{UB} (1 - P_B)] / [P_B (1 - PU_B)]$

where P_{UB} is the response or remission rate of the UBP RUL ECT group and P_B is the response or remission rate of the BP RUL ECT group. The ORs were log transformed for the calculation of standard errors.²¹ The pooled OR estimates were used to calculate the number needed to treat (NNT) for remission when using BP RUL rather than UBP RUL ECT. Calculating NNTs directly from pooled absolute risk differences in a meta-analysis may be misleading due to variation in the baseline risks in the different included trials.²² It is recommended that in order to avoid this difficulty, calculations of NNT from a meta-analysis should utilize the pooled relative effect size in combination with known outcome prevalence rates.^{22,23} In line with this advice, we used the pooled estimate for OR of remission to calculate an absolute risk difference for remission between BP RUL and UBP RUL ECT. The NNT formula used was

 $NNT = 1/(P_B - EP_{UB})$

where P_B is the known rate of remission with BP RUL ECT and EP_{UB} is the estimated rate of remission with UBP RUL ECT (based on the pooled OR estimate).

Cognitive functioning was assessed as a second main outcome and categorized into 4 domains (retrograde memory, anterograde memory [learning], anterograde memory [delayed recall], and global cognitive functioning) (see Supplementary eTable 2), each of which was analyzed individually. SMDs were also computed as described above using the cognitive domain scores, with a negative SMD indicating better posttreatment cognitive functioning in the UBP RUL ECT group relative to that of patients that received BP RUL ECT. Sufficient data were available only for calculation of cognitive outcomes at the end of acute ECT treatment. If a study collected 2 or more measures for the same domain of cognitive functioning, the SMDs of



Abbreviations: BP = brief pulse, ECT = electroconvulsive therapy, RUL = right unilateral, UBP = ultrabrief pulse.

these measures were averaged to ensure that all studies were represented only once in the meta-analysis.

RESULTS

The meta-analyses were performed in Stata, Version 12.0,²⁴ using the metan command. The pooled effect sizes for efficacy and cognitive outcomes are expressed as SMDs with 95% confidence intervals. The studies were weighted by the inverse-variance method. To test for heterogeneity, we calculated the I^2 statistic,²⁵ which estimates the percentage of outcome variability that can be attributed to heterogeneity across studies. Where there was low heterogeneity, the fixed-effects model was used to calculate the pooled SMD estimates. As considerable heterogeneity was expected for the cognitive outcomes due to methodological diversity across the studies, the more conservative random-effects model that produces wider confidence intervals²⁶ was applied to obtain the pooled cognitive effect sizes.

To evaluate whether or not methodological design affected the summary effect size estimates at both endpoints, we performed stratified analysis by study design (RCT or non-RCT) and ECT dosage relative to seizure threshold (DRST).

Publication bias²⁷ was assessed through examination of a funnel plot and, quantitatively, through the application of the Egger test for small-study effects.²⁸

A total of 7 studies were assessed as suitable for inclusion in the meta-analysis (Figure 1). In addition to 4 previously published papers,^{12,15,16,29} 2 more papers that were in press at the time of systematic review^{14,18} were assessed as suitable for inclusion. One dataset had additional data due to both continued data collection after publication and pooled data from a related study.^{15,30} One study was later excluded²⁹ due to the use of left rather than exclusively right unilateral electrode placement, as disclosed by the authors during the data request process. Data from a recently completed RCT at our site were also included.³¹ Therefore, 4 double-blinded RCTs and 2 nonrandomized prospective trials remained for analysis.

Brief vs Ultrabrief Right Unilateral ECT for Depression

The pooled results from all studies included data from 689 patients, with 261 receiving BP RUL ECT and 428 receiving UBP RUL ECT. The mean age was 50.7 years (range, 16.1–93 years). Of the sample, 36.1% were male, 20.3% had depression of psychotic subtype, and 25.1% had bipolar disorder. Patients receiving BP RUL ECT had a mean of 8.7 ECT sessions in an acute course, while those receiving UBP RUL ECT had a mean of 9.6 ECT sessions (WMD=1.12; 95% CI, 0.64–1.59; P < .001) (see Supplementary eTable 1). The included trials were similar, with all but 1 study¹⁴ administering ECT sessions

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Figure 2. Forest Plot of Efficacy of Brief Versus Ultrabrief Right Unilateral Electroconvulsive Therapy (ECT) in Depression at End of Acute ECT Course^a



Abbreviation: SMD = standardized mean difference

Figure 3. Forest Plot of Remission Rates for Brief Versus Ultrabrief Right Unilateral Electroconvulsive Therapy (ECT) in Depression at End of Acute ECT Course^a



3 times a week. MADRS was used to rate mood, and pulse widths for BP and UBP RUL ECT were 1 ms and 0.3 ms, respectively, in all but 1 study.¹² Most studies used the Mini-International Neuropsychiatric Interview (MINI)³² for assessment of diagnoses and the MADRS³³ or HDRS³⁴ to assess the severity of depression.

Efficacy Outcomes

At the end of the acute treatment course, BP RUL ECT was more efficacious than UBP RUL ECT, with a small effect

size of 0.25 (P=.004; Figure 2). Sensitivity analysis conducted after removing the 2 non-RCT trials decreased the effect size, making the result nonsignificant (SMD=0.16; 95% CI, -0.10 to 0.41; P=.231). No formal analysis was performed for ECT DRST due to the small number of studies. I^2 results (0%) were also nonsignificant, indicating low heterogeneity for results.

Five studies had efficacy data at a predetermined point prior to the end of the ECT course (after 6–8 ECT sessions). There was no significant difference in efficacy between BP and

is illegal to post this copyrighted PDF on any web Figure 4. Forest Plot of Cognitive Tests for Brief Versus Ultrabrief Right Unilateral Electroconvulsive Therapy (ECT) in Depression at End of Acute ECT Course

Study	SMD (95% CI)	% Weight
Retrograde memory ^a		
Loo (2008, ¹⁴ 2012 ³⁰)	–0.52 (–0.84 to –0.20)	27.24
Loo (2014) ³¹	–0.55 (–1.01 to –0.08)	17.17
Mayur (2013) ¹⁶	-0.33 (-1.00 to 0.34)	9.89
Sackeim (2008) ¹⁵	–0.55 (–0.98 to –0.13)	19.24
Spaans (2013) ¹³	-0.03 (-0.36 to 0.30)	26.46
Subtotal (<i>I</i> ² = 36.3%, <i>P</i> = .179)	-0.38 (-0.61 to -0.15)	100.00
Anterograde memory (learning) ^b		
Loo (2008, ¹⁴ 2012 ³⁰)	–0.54 (–0.77 to –0.32)	61.71
Loo (2014) ³¹	-0.30 (-0.62 to 0.03)	38.29
Subtotal (<i>I</i> ² = 32.8%, <i>P</i> = .222)	-0.45 (-0.68 to -0.22)	100.00
Anterograde memory (delayed recall) ^c		
Loo (2008, ¹⁴ 2012 ³⁰)	–0.62 (–0.84 to –0.39)	52.62
Loo (2014) ³¹	-0.40 (-0.73 to -0.08)	25.40
Sackeim (2008) ¹⁵	-0.61 (-0.96 to -0.26)	21.98
Subtotal ($l^2 = 0.0\%, P = .546$)	-0.56 (-0.73 to -0.40)	100.00
Global cognitive function ^d		
Galletly (2013) ¹⁸	-0.31 (-0.61 to -0.00)	80.05
Sackeim (2008) ¹⁵	-0.57 (-1.17 to 0.03)	19.95
Subtotal (<i>I</i> ² = 0.0%, <i>P</i> = .444)	-0.36 (-0.63 to -0.09)	100.00
-1.2 -1.0 -0.8 -0.6 -0.4 -0.2 0 0.2 0.4 0.6 0	.8 1.0 1.2	
Favors Ultrabrief Pulse ECT Favors Brief Pulse	ECT	
^a Retrograde memory: P<.001. ^b Anterograde memory (learning): P<.001. ^c Anterograde memory (delayed recall): P<.001.		

^dGlobal cognitive function: *P* = .009. Abbreviation: SMD = standardized mean difference.

UBP groups (SMD = -0.18; 95% CI, -0.38 to 0.02; P = .077), although there was a statistical trend favoring the efficacy of BP RUL ECT. This trend remained at a nonsignificant level when a sensitivity analysis was conducted with the removal of the non-RCT trial. I^2 results (0%) were nonsignificant.

Response and Remission

Studies defined response as a 50% decrease from initial depression scores with the exception of 1 study,¹² which used a cutoff of 60% reduction in depression scores. Remission was defined as a MADRS score of <10 or HDRS (24-item) score <10. At the end of acute ECT treatment, mean response and remission rates were 58.1% and 44.9% for BP RUL ECT and 55.3% and 33.8% for UBP RUL ECT (see Supplementary eTable 1). UBP RUL ECT had a significantly lower remission rate (OR = 0.71; 95% CI, 0.51–0.99; P = .045) compared with BP RUL ECT (Figure 3). This corresponds with an estimated NNT of 12.1, in favor of BP RUL ECT.

Cognitive Outcomes

Cognitive outcomes at the end of the acute course of ECT showed an advantage of UBP RUL ECT over BP

RUL ECT across all the cognitive domains, most with a moderate effect size (SMD, 0.36–0.56). The largest effect size was for anterograde memory (delayed recall), followed by anterograde memory (learning), retrograde memory, and global cognition. There was low heterogeneity for the 4 cognitive domains (Figure 4).

Publication Bias

There was no evidence of publication bias by examination of the funnel plot (Supplementary eFigure 1) or via Egger test (P=.233).

DISCUSSION

This study represents the first published systematic review and meta-analysis comparing the efficacy and side effect profiles of the increasingly used ultrabrief pulse RUL ECT with the more standard brief pulse RUL ECT. There was a small efficacy advantage for BP compared with UBP RUL ECT. The difference was seen in both mean change in mood ratings and remission rates over the ECT course, with a pooled estimate suggesting 1 additional remission for every

Tor et al It is illegal to post this con I2.1 patients treated with BP as opposed to UBP RUL EC **anted PDF on any website** These structures have been shown to subserve multiple

However, this efficacy advantage came at a cost, with BP RUL ECT having significantly more cognitive side effects in memory and global cognition.

The strengths of our conclusions are tempered by the observation that the efficacy differences observed were reduced to nonsignificant levels once the nonrandomized trials were removed. The reason for an apparently poorer response to UBP ECT in the non-RCTs is not immediately obvious. The treatment groups were not randomly assigned, and it is possible that patients assigned to receive UBP RUL ECT were less treatment responsive than those assigned to BP RUL ECT. However, a bias in this direction would not be predicted, and, based on the baseline data reported, there were no obvious differences between the groups in clinical and demographic factors that are known to affect treatment response. A consideration is that both non-RCTs had relatively large numbers of participants in the UBP group, and it is possible that these larger samples may provide a truer estimate of the effectiveness of UBP RUL ECT.

The overall average rates of response and remission were lower than those reported in some prior ECT trials^{5,6} but congruent with ECT treatment outcomes reported in community samples³⁵ and may reflect the patient populations treated. Consistent with this interpretation, the RCTs that did not find a difference in efficacy between BP and UBP RUL ECT^{12,16} had relatively high response and remission rates in both treatment groups; that is, in a highly responsive ECT sample, the difference between BP and UBP RUL ECT may be less evident.

The observation that, on average, a course of UBP RUL ECT required 1 extra treatment session, compared with BP RUL ECT, is consistent with the finding of reduced efficacy using ultrabrief pulse treatment. The number of ECT treatment sessions required, and the analysis of efficacy after 6-8 ECT sessions, supports earlier observations that the speed of response may be slightly slower with UBP ECT.¹³ Conversely, significantly less severe cognitive side effects were found with UBP RUL ECT across the 4 cognitive domains analyzed. Computer simulations of the RUL ECT stimulus in a realistic head model have shown substantial reductions in the total volume and cortical surface area directly affected with UBP compared to a BP electrical stimulus,³⁶ including the right medial and inferior frontal lobe, and temporal regions, including the hippocampus.

aspects of memory functioning.37-40

Limitations and Strengths

Strengths of this study include the systematic and detailed search strategy, with use of several techniques to identify unpublished studies and reduce publication bias. The use of separate reviewers at each stage of the systematic search and the inclusion of a broad range of efficacy and side effect measures are also important strengths. The main limitation of the study was the relatively small number of studies identified. While the finding of a statistically significant difference between the 2 evaluated treatments suggests that the power in this analysis was adequate for the main efficacy outcomes, the relatively small sample size did preclude further subgroup analysis to fully investigate the effect of factors such as DRST or to conduct a meta-regression. Furthermore, the 2 largest studies were non-RCTs, which are susceptible to practitioner treatment or patient selection bias. The main efficacy outcomes and cognitive outcomes were measured at the end of the acute course of ECT, and comments could not be made on longer term efficacy and cognitive side effects. Similarly, we did not have data on quality of life or cost-effectiveness outcomes, which could have policy implications. Finally, it was not possible to extrapolate the results of this analysis more broadly for ECT electrode placements other than RUL. Computer modeling predicts that changes in pulse width alter the spatial distribution of current in the brain,¹⁰ and the interaction between pulse width and electrode placement is likely to be complex, as also suggested in clinical trial results.¹²

CONCLUSIONS

BP and UBP RUL ECT are both efficacious treatments for depression. The results of our meta-analysis suggest that BP RUL ECT has a small efficacy advantage with a higher remission rate and, on average, 1 less session in the treatment course. However, this increased efficacy comes at a cost, with BP RUL ECT having significantly more cognitive side effects. Based on these results, we would suggest that BP RUL ECT should be considered over UBP RUL ECT in situations where urgency of response is paramount. The converse may be true for patients at higher risk for cognitive side effects but in whom an urgent clinical response is not essential.

Submitted: March 19, 2014; accepted August 13, 2014.

Published online: July 21, 2015.

Potential conflicts of interest: None reported. Funding/support: None reported.

Supplementary material: See accompanying pages.

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Supplementary material follows this article.

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Supplementary Material

- Article Title: A Systematic Review and Meta-Analysis of Brief Versus Ultrabrief Right Unilateral Electroconvulsive Therapy for Depression
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- **DOI Number:** 10.4088/JCP.14r09145

List of Supplementary Material for the article

- 1. <u>eFigure 1</u> Funnel Plot for Systematic Review of Brief Versus Ultrabrief Pulse Width Right Unilateral Electroconvulsive Therapy for Depression
- 2. <u>eTable 1</u> Characteristics of Included Studies of Brief Versus Ultrabrief Pulse Width Right Unilateral ECT
- 3. <u>eTable 2</u> Cognitive Test Grouping for Included Studies of Brief Versus Ultrabrief Pulse Width Right Unilateral ECT

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Supplementary eFigure 1. Funnel Plot for Systematic Review of Brief versus Ultrabrief pulse width Right Unilateral Electroconvulsive Therapy for Depression



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Study	Loo et al [*]	* (2008 ¹⁴ ,	Sackeim e	et al	Mayur et	al	Spaans e	t al	Galletly <i>et al</i>		Loo <i>et al</i>	
	2012)		(2008)		(2013)		(in press)	(In press ²⁰)		(under review)	
Type of study	Single blir	nded	Double bl	inded	Double b	linded	Double b	linded	Prospective non-		Double blinded	
	Prospecti	ve non-	Randomiz	ed	Randomi	zed	Randomi	zed	randomiz	ed	Randomiz	zed
	randomiz	ed trial	Controlle	d trial	Controlle	d trial	Controlle	d trial	observational trial		Controlled trial	
Group	В	UB	В	UB	В	UB	В	UB	В	UB	В	UB
n	56	129	22	22	18	17	58	58	59	155	48	47
Age (mean / SD)	49.0	45.7	45.5	53.8	43.0	43.0	60.8	60.4	50.7	50.7	51.5	47.7
	(14.7)	(14.8)	(14.1)	(16.1)	(11.0)	(12.0)	(14.6)	(16.3)	(15.4)	(15.7)	(14.0)	(14.6)
Baseline mood	34.0	34.2	30.5	30.1	40.2	43.0	28.0	31.9	30.9	33.9	34.1	33.0
rating (mean / SD)	(7.4)	(7.8)	(7.4)	(6.6)	(6.8)	(5.8)	(9.4)	(8.0)	(14)	(8.6)	(6.6)	(6.1)
Male (%)	38.0	40.0	40.9	45.5	72.2	47.1	29.3	29.3	31.0	32.0	35.0	36.0
Psychotic (%)	13.0	14.0	9.1	22.7	11.1	17.6	51.7	36.2			8.0	9.0
Bipolar (%)	24.0	31.0	36.4	22.7	11.1	29.4	25.9	19.0			19.0	23.0
No. of ECT sessions (mean	7.6 (2.9)	8.8 (3.4)	8.5 (2.5)	8.7 (2.4)	10.2 (3.3)	10.5 (3.1)	9.4 (3.1)	10.6 (2.1)	8.0 (3.1)	10.1 (4.0)	8.4 (3.2)	8.6 (3.4)
No. of ECT sessions / week	3	3	3	3	3	3	2	2	3	3	3	3
Pulse width (ms)	1	0.3	1.5	0.3	1	0.3	1	0.3	1	0.3	1	0.3
DRST	5	6	6	6	6	6	8	8	3-5	5-6	5	8
Diagnosis method	Clinician DSM	Clinician DSM	SCID	SCID	MINI	MINI	MINI	MINI	Clinician DSM	Clinician DSM	MINI	MINI
Mood rating scale	MADRS	MADRS	HRSD	HRSD	MADRS	MADRS	MADRS	MADRS	MADRS	MADRS	MADRS	MADRS
Anaesthesic	Thiopentone	Thiopentone	Methohexital	Methohexital	Thiopentone	Thiopentone	Etomidate	Etomidate	Propofol	Propofol	Thiopentone / Propofol	Thiopentone / Propofol
Response % (end of acute treatment)	56.4	52.8	72.7	77.3	83.3	76.5	51.7	53.4	66.7	54.7	45.8	48.9
Remission % (end of acute treatment)	38.2	31.2	72.7	77.3	66.7	64.7	50.0	41.4	39.4	27.3	29.2	23.4

Supplementary eTable 1. Characteristics of included studies of Brief versus Ultrabrief pulse width Right Unilateral ECT

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Key:

B – Brief pulse width UB – Ultrabrief pulse width DSRT – Dosage relative to seizure threshold DSM – Diagnostic and Statistical Manual MADRS – Montgomery Asberg Depression Rating Scale HRSD – Hamilton Rating Scale for Depression SCID – Structured Clinical Interview for DSM MINI – Mini-international Neuropsychiatric Interview * - The Loo *et al* (non RCT) sample is pooled from two studies, desired

* - The Loo *et al* (non RCT) sample is pooled from two studies, described in Loo *et al* (2008) and Loo *et al* (2012), with further recruitment of participants since the samples published. In these studies, detailed assessment of mood and neurocognitive outcomes were made prospectively by a rater blinded to treatment condition, but assignment to brief or ultrabrief RUL ECT was not randomised.

Study	Loo et al* (2008,	Sackeim <i>et al</i>	Mayur <i>et al</i>	Spaans et al	Galletly et al	Loo et al
	2012)	(2008)	(2013)	(2013)	(2013)	(under review)
Retrograde memory	Autobiographical Memory Interview – Short Form (Columbia)	Autobiographical Memory Interview (Columbia) Goldberg Remote Memory Test (Public Events)	Autobiographical Memory Interview (Kopelman)	Autobiographical Memory Interview (Kopelman) Amsterdam Media Questionnaire		Autobiographical Memory Interview – Short Form (Columbia)
Anterograde memory (learning)	Medical College of Georgia Complex Figure task (Immediate Recall) Hopkins Verbal Learning Test – Revised (Total Learning)					Medical College of Georgia Complex Figure task (Immediate Recall) Hopkins Verbal Learning Test – Revised (Total Learning)
Anterograde memory (delayed recall)	Medical College of Georgia Complex Figure task (Delayed Recall) Hopkins Verbal Learning Test – Revised (Delayed Recall)	Randt Memory Test (Story Recall, Gist 24 hr delay) Complex Figure Test (Delayed Recall) Buschke Selective Reminding Test (Delayed Recall)				Medical College of Georgia Complex Figure task (Delayed Recall) Hopkins Verbal Learning Test – Revised (Delayed Recall)
Global Cognition		Modified MMSE			MMSE	

Supplementary eTable 2. Cognitive test grouping for included studies of Brief versus Ultrabrief pulse width Right Unilateral ECT

* - The Loo *et al* (non RCT) sample is pooled from two studies, described in Loo *et al* (2008) and Loo *et al* (2012), with further recruitment of participants since the samples published. In these studies, detailed assessment of mood and neurocognitive outcomes were made prospectively by a rater blinded to treatment condition, but assignment to brief or ultrabrief RUL ECT was not randomised.