Efficacy and Cognitive Side Effects After Brief Pulse and Ultrabrief Pulse Right Unilateral Electroconvulsive Therapy for Major Depression: A Randomized, Double-Blind, Controlled Study

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ABSTRACT

Objective: To compare the efficacy and cognitive side effects of high-dose unilateral brief pulse electroconvulsive therapy (ECT) with those of high-dose unilateral ultrabrief pulse ECT in the treatment of major depression.

Method: From April 2007 until March 2011, we conducted a prospective, double-blind, randomized multicenter trial in 3 tertiary psychiatric hospitals. All patients with a depressive disorder according to *DSM-IV* criteria were eligible. Depression severity was assessed with the Montgomery-Asberg Depression Rating Scale; primary efficacy outcomes were response, defined as a score decrease ≥ 60% from baseline, and remission, defined as a score < 10 at 2 consecutive weekly assessments. Total scores on the Autobiographical Memory Interview and Amsterdam Media Questionnaire were the primary outcome measures for retrograde amnesia. Other cognitive domains included category fluency (semantic memory) and letter fluency (lexical memory). Patients received twice-weekly unilateral brief pulse (1.0 millisecond) or ultrabrief pulse (0.3–0.4 millisecond) ECT 8 times seizure threshold until remission, for a maximum of 6 weeks.

Results: Of the 116 patients, 75% (n = 87) completed the study. Among completers, 68.4% (26/58) of those in the brief pulse group achieved remission versus 49.0% (24/49) of those in the ultrabrief pulse group ($P = .019$), and the brief pulse group needed fewer treatment sessions to achieve remission: mean (SD) of 7.1 (2.6) versus 9.2 (2.3) sessions ($P = .008$). No significant group differences were found in the evaluation of the cognitive assessments.

Conclusions: The efficacy and speed of remission seen with high-dose brief pulse right unilateral ECT twice weekly were superior to those seen with high-dose ultrabrief pulse right unilateral ECT, with equal cognitive side effects as defined by retrograde amnesia, semantic memory, and lexical memory.

Trial Registration: Netherlands National Trial Register number: NTR1304

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Electroconvulsive therapy (ECT) is the most effective treatment for depression,[1–3] but its widespread use is hampered by the fear of cognitive side effects. Soon after the introduction of ECT, the stimulus techniques were modified in an attempt to reduce cognitive side effects.[4] The use of a shorter pulse width, ultrabrief pulse of less than 0.5 millisecond—instead of the standard pulse width, brief pulse of 0.5 millisecond or more—has been shown to reduce cognitive side effects.[5–8] It remains unclear, however, whether ultrabrief pulse ECT has the same antidepressant efficacy as brief pulse ECT.[7,9,10] At the same time, the practice of ultrabrief pulse ECT has increased.[11,12] In this study, we compared the efficacy and cognitive side effects of ultrabrief pulse and brief pulse right unilateral (RUL) ECT in 116 depressed patients.

We hypothesized that in depressed patients brief pulse ECT is equally effective compared to ultrabrief pulse ECT. Further, we hypothesized that ultrabrief pulse ECT has less-severe cognitive side effects.

METHOD

From April 2007 until March 2011, we conducted a prospective, double-blind, randomized multicenter trial comparing the efficacy and cognitive side effects of brief pulse and ultrabrief pulse RUL ECT (Netherlands National Trial Register number NTR1304). Patients were recruited from 3 ECT centers: Parnassia (The Hague) and GGZ Delfland (Delft) in the Netherlands and the University Psychiatric Center KU Leuven, Campus Kortenberg (Kortenberg) in Belgium. The institutional review boards (IRBs) of these hospitals approved the study, which was conducted according to the Declaration of Helsinki.

Patients

All inpatients and outpatients 18 years and older suffering from major depressive disorder or bipolar depression (with or without psychosis) according to *DSM-IV* criteria[13] who were referred for ECT were screened for inclusion in the study. The diagnosis of depression was confirmed by an experienced psychiatrist (H.-P.S., K.H.K., P.S., F.B.) using the Mini-International Neuropsychiatric Interview (MINI).[14,15] Patients who had a history of schizophrenia or schizoaffective disorder or who were diagnosed with dementia were excluded. All eligible patients were asked to participate, and baseline assessments were done after they provided informed consent.

Materials and Procedure

Concomitant medication. In accordance with daily clinical practice, antidepressants were continued during ECT, and lithium

Clinical Points

- Brief pulse and ultrabrief pulse right unilateral (RUL) ECT were shown to have equivalent cognitive effects. The results support the continued use of brief pulse RUL ECT.
- This study affirms previous findings showing ECT to be a highly effective treatment for depression.

was also continued, at plasma levels of 0.40–0.80 mmol/L.[16] Benzodiazepines were tapered to a maximum of 10 mg diazepam equivalents, 3 days prior to ECT. Psychotropic and somatic medication was kept stable until the end of the study.

Electroconvulsive therapy. Patients were randomly assigned to the brief pulse or ultrabrief pulse group. The maximum length of the randomized index phase of the study was 6 weeks. The brief pulse group received RUL ECT with a pulse width of 1.0 millisecond, and the ultrabrief pulse group received RUL ECT with a pulse width of 0.3 millisecond. All patients received ECT twice weekly according to the guidelines of the Netherlands Psychiatric Association.[17] Etomidate (± 0.25 mg/kg) and succinylcholine (1–2 mg/kg) were used as anesthetic and muscle relaxant, respectively. Seizures were induced with a square-wave, brief or ultrabrief, bidirectional stimulus delivered by a constant current device (spECTrum 5000 Q MECTA Inc; Tualatin, Oregon) and a maximum stimulus level of 1,152 mC using RUL d'Elia electrode placement.[18]

During the first session, the seizure threshold was determined by applying an electrical stimulus at the lowest charge possible. In the absence of a seizure, the charge was doubled by increasing stimulus duration (Table 1). This procedure was continued for a maximum of 4 times within the same session until an adequate seizure was induced, defined by clonic movements in the ipsilateral cuffed arm or leg or an EEG seizure recording of at least 20 seconds' duration. The first and successive treatment sessions were then continued with a stimulus 8 times the seizure threshold. At the seventh session, the seizure threshold was reassessed and the dose adjusted accordingly to continue stimulation with 8 times the seizure threshold. The ECT course was terminated when the patient reached remission.

Assessments

Clinical assessment and demographic features. At baseline, sociodemographic and clinical data were collected: age, gender, level of education, marital status, inpatient/outpatient status, age at onset, duration of the index major depressive episode, psychosis, polarity, number of previous admissions, history of ECT treatment, medication resistance score according to a modified Antidepressant Treatment History Form (ATHF),[20] and medication. The scoring system of Verhage[19] (range, 1–7; 1 = less than 6 years of education, 2 = 6 years, 3 = 7–8 years, 4 = 9 years, 5 = 10–14 years, 6 = more than 14 years, 7 = university) was used to define a subject's level of education.

Depression severity and response criteria. For blinded assessment of efficacy, trained nurses rated the severity of depression using the Montgomery-Asberg Depression Rating Scale (MADRS).[21] Severity was rated at baseline and weekly until the end of the study period, after 48 hours but within 7 days after the ECT sessions. The nurses of the clinical psychiatric wards were trained by experienced researchers.

We defined all patients who were randomized for treatment as the intention-to-treat (ITT) group. The completers group consisted of all patients who completed the study protocol. The IRB-approved primary efficacy outcome criteria were 60% response, defined as a decrease in the MADRS score of at least 60% from baseline, and remission, defined as a MADRS score < 10 at 2 consecutive weekly assessments. Secondary efficacy outcome criteria were the number of ECT sessions needed to achieve remission, decrease in MADRS score of at least 50% from baseline, and effect size of the change in MADRS score from baseline until the end of the study.

Cognitive assessment. Cognitive assessment was performed by a neuropsychologist or supervised trainee neuropsychologist, blinded for treatment condition, within a week prior to the first ECT (T0) and 48 hours after but within 1 week after finishing the treatment course (T1).

The Autobiographical Memory Interview (AMI)[22,23] is a reliable and standardized test to assess personal remote memory. The AMI measures personal semantic memories and autobiographical incidents from different time periods: childhood (ages 0–18 years), early adulthood (ages 19–30 years), and recent (within the past 5 years). In relation to the autobiographical incident questions, subjects are asked to relate incidents that occurred during each of the 3 time periods. The Amsterdam Media Questionnaire (AMQ)[23] is a public events questionnaire consisting of 40 open-ended questions about news events that occurred during the 1970s, 1980s, 1990s, and 2000s.

For the retrograde amnesic evaluation, the total AMI and AMQ scores were used as the IRB-approved primary outcome measures. Next to these scores, the percentage of recall was calculated. At successive test sessions, questions were specifically asked following the responses provided at baseline. This so-called recall index was the percentage of baseline items (T0) recalled at the post-ECT session (T1).

Other cognitive domains included semantic memory (category fluency—animals and professions)[24] and lexical memory (letter fluency—"D," "A," "T").[24] In both tests, subjects generate as many words as possible from a category (semantic and phonemic) in 60 seconds.

Randomization

After the baseline clinical assessments were finished, a computer random number generator was used to select random permuted blocks with a block size of 4 and an equal allocation ratio. Stratification was done on the basis

Table 1. Titration Procedure for Brief Pulse and Ultrabrief Pulse Electroconvulsive Therapy

	Threshold					Treatment Level (8 × seizure threshold)				
Treatment Condition and Step	Pulse Width (ms)	Pulse Frequency (Hz)	Stimulus Duration (s)	Current (mA)	Charge (mC)	Pulse Width (ms)	Pulse Frequency (Hz)	Stimulus Duration (s)	Current (mA)	Charge (mC)
Ultrabrief pulse										
1	0.3	20	1	800	9.6	0.3	80	2	800	76.8
2	0.3	20	2	800	19.2	0.3	80	4	800	153.6
3	0.3	20	3	800	28.8	0.3	80	6	800	230.4
4	0.3	20	4	800	38.4	0.3	110	6	800	316.8
5	0.3	20	8	800	76.8	0.4	120	8	800	614.4
Brief pulse										
1	1.0	20	1	800	32	1.0	80	2	800	256
2	1.0	20	2	800	64	1.0	80	4	800	512
3	1.0	20	3	800	96	1.0	80	6	800	768
4	1.0	20	4	800	128	1.0	110	6	800	1,056

of duration of the index episode (more or less than 2 years) and presence/absence of psychosis or melancholic features according to the MINI.

Statistical Analysis

In the power analysis, for an assumed effect size of 0.25, we calculated a sample size of 65 patients in each group to achieve a power of 0.80 with an α of .05. In the comparison of baseline variables between the ITT groups, we used χ^2 tests for categorical variables and Student *t* tests or Mann-Whitney test for continuous variables.

To quantify clinical relevance, we calculated the effect sizes (Cohen *d*) of the change in MADRS outcome. Effect sizes were interpreted as suggested by Cohen.[25] Changes in MADRS were calculated with paired *t* tests.

Response and remission status was analyzed in the ITT and the completers samples using multivariate logistic regression with age, current depressive episode duration, psychosis, polarity, treatment center, treatment condition, ATHF score, earlier ECT, and baseline MADRS score as covariates. The speed of remission was analyzed using multivariate linear regression, adjusted for age, current depressive episode duration, baseline MADRS score, and treatment condition because of smaller sample size. In the ITT analysis for total ECT sessions, dropouts were corrected for receiving fewer sessions by imputing the maximum number of 12 sessions. Statistical significance for efficacy was defined as $P < .05$. For the analyses of the cognitive measures, all patients who completed a pre- and post-ECT cognitive assessment were included (n = 76). For the comparison of cognitive performances between the brief pulse and the ultrabrief pulse groups, the mean scores of each test were calculated together with the standard deviation and range of performance. We used *t* tests to analyze differences between the groups at baseline (T0), at the end of the ECT course (T1), and in the change in cognitive performance (T1 – T0).

Multivariate linear regression analyses, adjusted for baseline, endpoint, and change in MADRS score and number of ECT sessions received, were done to explore the relation between the severity of depression, change in depression severity, total amount of ECT received, and neurocognitive outcome. Results of cognitive assessments were considered statistically significant at $P < .01$ to correct for multiple testing. All tests were 2-sided.

IBM SPSS version 20.0[26] was used for all statistical analyses.

RESULTS

Clinical and Demographic Characteristics

No statistical differences in the demographic and clinical parameters were found between the brief pulse and ultrabrief pulse groups in the ITT sample except for treatment group–dependent seizure threshold differences (Table 2). Concomitant psychotropics were used in 98% of the cases. Use of hypnotics, anxiolytics, antipsychotics, lithium, antiepileptics, and antidepressants showed no differences between brief pulse and ultrabrief pulse samples in the ITT, completers, or completers of the cognitive assessment (χ^2 or Fisher exact $P > .05$; data not shown).

Of the 116 patients who entered the study, 87 (75%) completed the study until remission was achieved or for the maximum of 12 sessions (Figure 1). There were no significant clinical or demographic baseline differences between completers and dropouts (n = 29) apart from polarity (percentage bipolar subjects in completers vs dropouts, 14.9% [13/87] vs 44.8% [13/29]; $P = .001$) and treatment condition (percentage brief pulse in completers vs dropouts, 43.7% [38/87] vs 69.0% [20/29]; $P = .018$). In the brief pulse sample, the rate of dropout due to transient confusion was higher, but not significantly, than in the ultrabrief pulse sample .

Of 87 completers, 76 patients (brief pulse n = 34, ultrabrief pulse n = 42) received both pre- and post-ECT cognitive assessments. Due to refusal or inability to comply with the testing procedures, some patients were lost to follow-up. The demographic and clinical parameters were comparable between the brief pulse and ultrabrief pulse groups for participants who completed both cognitive assessments, except for the baseline MADRS scores (mean [SD]: brief pulse = 27.4 [9.3] vs ultrabrief pulse = 32.1 [8.2]; $P = .023$).

Efficacy

In the ITT group and the completers group, there was a significant difference in the 60% response rate (Table 3) between the brief pulse and ultrabrief pulse groups and no

Table 2. Demographic and Clinical Characteristics for the Intention-To-Treat Sample (N = 116)

	Brief Pulse (n = 58)		Ultrabrief Pulse (n = 58)		
Variable	n	%	n	%	*P* Value
Female (n = 116)	41	70.7	41	70.7	1.00
Bipolar (n = 116)	15	25.9	11	19.0	.37
Psychotic (n = 116)	30	51.7	21	36.2	.09
History of depression (n = 115)	44	75.9	40	70.2	.49
History of ECT (n = 115)	18	31.0	12	21.1	.22
Early onset (< 55 y) (n = 114)	42	73.7	39	68.4	.54
	Mean (range)	SD	Mean (range)	SD	
Age, y (n = 116)	60.8 (24–90)	14.6	60.4 (26–92)	16.3	.88
Duration of current episode, mo (n = 112)	24.0 (1–324)	53.4	16.3 (1–120)	20.1	.96[a]
MADRS score (n = 116)	29.1 (5–52)	9.7	32.0 (11–51)	7.5	.08
Total admissions (n = 110)	3.9 (0–10)	2.6	4.3 (1–50)	6.8	.46[a]
Initial seizure threshold, mC (n = 112)	61.5	20.5	23.2	10.0	< .001
	Median (range)		Median (range)		
Level of education[b] (n = 109)	4 (1–7)		5 (2–7)		.05[a]
ATHF[c] (n = 91)	3 (1–5)		3 (1–5)		.72[a]

[a]Mann-Whitney test.
[b]The scoring system of Verhage[19] (range, 1–7; 1 = less than 6 years of education, 2 = 6 years, 3 = 7–8 years, 4 = 9 years, 5 = 10–14 years, 6 = more than 14 years, 7 = university).
[c]Each medication trial was rated on a scale from 0 to 5; a threshold score of 3 indicated an adequate trial and was judged to represent treatment resistance.
Abbreviations: ATHF = Antidepressant Treatment History Form, ECT = electroconvulsive therapy, MADRS = Montgomery-Asberg Depression Rating Scale.

significant difference in the 50% response rate. The remission rate for brief pulse ECT was significantly higher than for ultrabrief pulse ECT (Figure 2). The effect sizes[25] in the ITT and completers groups were large for the brief pulse sample as well as the ultrabrief pulse sample. The number of treatment sessions needed to achieve remission was significantly lower in the brief pulse sample than in the ultrabrief pulse sample in the ITT group as well as in the completers group. The number of treatment sessions was significantly associated only with the current depressive episode duration in both the ITT (B = 0.01, *P* = .008) and completers (B = 0.09, *P* = .015) groups.

There were significant associations for age with 60% response (OR = 1.06; 95% CI, 1.01–1.10; *P* = .013) and remission (OR = 1.06; 95% CI, 1.01–1.11; *P* = .11) in the ITT group and with 60% response (OR = 1.05; 95% CI, 1.01–1.10; *P* = .029) in the completers group. The duration of the current depressive episode was significantly associated with 60% response (OR = 0.94; 95% CI, 0.89–0.98; *P* = .007) and remission (OR = 0.93; 95% CI, 0.89–0.98; *P* = .006) in ITT and 60% response (OR = 0.94; 95% CI, 0.90–0.99; *P* = .015) and remission (OR = 0.94; 95% CI, 0.89–0.98; *P* = .009) in the completers group. Thus, higher age and shorter duration of the current depressive episode were associated with higher response and remission rates. For all other covariates, we found no association with response or remission.

Cognitive Side Effects

Concerning retrograde amnesia, no significant group differences between the brief pulse and ultrabrief pulse groups were found (Table 4). The change in performance and the percentage of recall between the baseline and post-ECT assessments was also similar for both treatment groups. There were no significant differences between the brief pulse and ultrabrief pulse groups either post ECT or in terms of performance change on both fluency tests. We found no significant association for the covariates severity of depression, depression change, or total number of ECT sessions received.

DISCUSSION

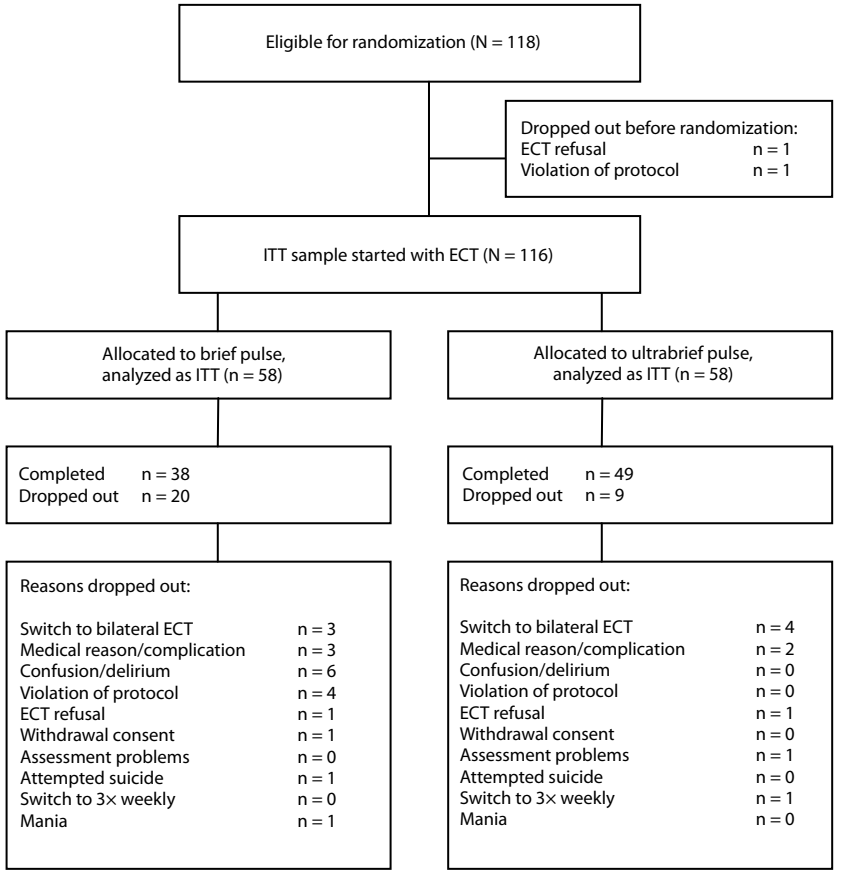
Efficacy

In contrast to our hypothesis, the principal finding of this study is that, although brief pulse RUL ECT and ultrabrief pulse RUL ECT are both highly effective treatments for depression, brief pulse RUL ECT is significantly more efficacious, with higher rates of 60% response and remission. This effect was demonstrated in the ITT group as well as in the completers group. The difference in efficacy is clinically relevant, as remission in the completers was achieved 2 sessions (1 week) earlier using brief pulse RUL ECT.

We can compare our results with only 2 studies on RUL brief pulse versus RUL ultrabrief pulse ECT.[10] Sackeim et al[7] found no significant differences in remission rate and number of treatment sessions between the 2 treatments. Our study contained more than twice as many patients, and differences in response and remission outcome between brief pulse and ultrabrief pulse samples were in the same range, which may be the reason we did not confirm the results of Sackeim et al.[7] The 2 studies differ in more aspects, like concomitant medication, anesthesia, twice- versus thrice-weekly ECT sessions, and 8 times versus 6 times seizure threshold stimulation. All of these variables may influence outcome.[27–33] Still, there is no reason why this would specifically influence 1 treatment condition above the other in our study.

Loo et al[9] found no significant differences for the 50% response and remission between brief pulse and ultrabrief pulse RUL ECT. However, although the ultrabrief pulse sample in the study was large (n = 76), the brief pulse sample

Figure 1. Participant Flow



Abbreviations: ECT = electroconvulsive therapy, ITT = intention-to-treat.

Table 3. Response and Remission Rates, Number of Treatments, and Treatment Parameters

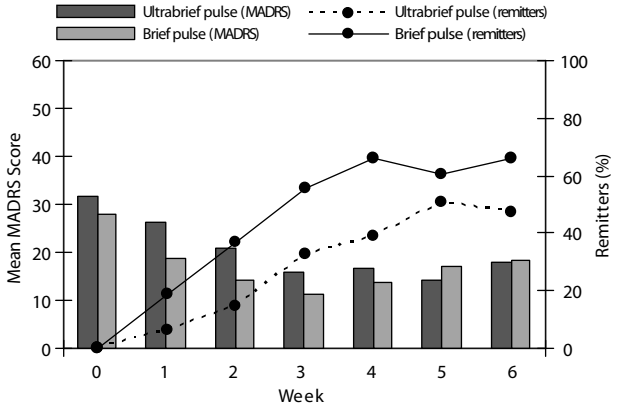
	Intention to Treat (N = 116)				Completers (n = 87)			
	Brief Pulse (n = 58), n (%)	Ultrabrief Pulse (n = 58), n (%)	OR (95% CI)	*P* Value	Brief Pulse (n = 38), n (%)	Ultrabrief Pulse (n = 49), n (%)	OR (95% CI)	*P* Value
50% Response rate[a]	30 (51.7)	31 (53.4)	2.31 (0.77–6.90)	.135	28 (73.7)	30 (61.2)	3.60 (0.98–13.26)	.054
60% Response rate[a]	27 (46.6)	26 (44.8)	3.56 (1.04–12.12)	.043	24 (63.2)	26 (53.1)	4.37 (1.16–16.51)	.030
Remission rate[a]	29 (50.0)	24 (41.4)	3.86 (1.07–13.96)	.039	26 (68.4)	24 (49.0)	5.58 (1.33–23.48)	.019
	Mean (SD)	Mean (SD)			Mean (SD)	Mean (SD)		
Initial seizure threshold, mC	61.5 (20.5)	23.2 (10.0)		< .001	61.7 (19.5)	23.9 (10.2)		< .001
Total charge, mC	3,730 (1,795)	1,988 (788)			3,930 (1,628)	2,030 (769)		< .001
Pre-ECT MADRS score	29.1 (9.7)	32.0 (7.5)		.079	28.0 (9.4)	31.8 (8.0)		.045
Post-ECT MADRS score	12.2 (12.7)	15.0 (11.8)		.240	8.0 (9.1)	12.9 (10.9)		.028
Change in MADRS score	17.0 (11.9)[b]	17.0 (11.9)[b]		.33[a]	20.0 (10.4)[c]	18.9 (11.1)[c]		.059[a]
Total ECT sessions[d]	9.4 (3.1)	10.6 (2.1)		.017	8.4 (3.1)	10.4 (2.1)		.001
Total ECT sessions among remitters[d]					7.1 (2.6)	9.2 (2.3)		.008

[a]Response and remission analyses are adjusted for age, current depressive episode duration, psychosis, polarity, treatment center, treatment condition, Antidepressant Treatment History Form, earlier ECT, and baseline MADRS as covariates.
[b]Brief pulse effect size $d = 1.50$; 95% CI, 1.08–1.91 and ultrabrief pulse effect size $d = 1.72$; 95% CI, 1.32–2.18.
[c]Brief pulse effect size $d = 2.16$; 95% CI, 1.60–2.73 and ultrabrief pulse effect size $d = 1.98$; 95% CI, 1.49–2.46.
[d]Number of ECT sessions adjusted for age, current depressive episode duration, treatment condition, and baseline MADRS score as covariates.
Abbreviations: ECT = electroconvulsive therapy, MADRS = Montgomery-Asberg Depression Rating Scale, OR = odds ratio.

was less than half the size (n = 22) of ours. On the other hand, the final treatment dose of the brief pulse sample (469 mC) was not much higher than the final treatment dose of the ultrabrief pulse sample (419 mC), which may have reduced the actual differences. Our higher speed of remission in the brief pulse sample is supported by their findings of a lower number of treatments in the brief pulse sample than in the ultrabrief pulse sample (mean [SD] = 7.6 [2.8] vs 10.3 [3.2]).

We included patients with major depression regardless of baseline MADRS score, and therefore 2 remitted participants could not reach the 60% response criterion, which explains

Figure 2. MADRS Scores and Percentages of Remitters in the Brief Pulse (n = 38) and Ultrabrief Pulse (n = 49) Electroconvulsive Therapy Groups



Abbreviation: MADRS = Montgomery-Asberg Depression Rating Scale.

why the number of brief pulse remitters is higher than the number of responders (Table 3). This may also explain why our baseline depression ratings were lower than in comparable ECT trials,[7,9,34,35] but they were still in the severe depressive range (Table 2).

Cognitive Side Effects

Our results concerning cognitive side effects can be compared with the same 2 studies described above.[7,9] In line with these studies, our results also showed no difference in impairment on both the fluency tasks (letter and category) between the brief pulse and ultrabrief pulse samples. In contrast with our hypothesis and also in contrast with both of the other studies, our results demonstrated no difference in impairment of retrograde memory, either in autobiographical memory or in public events.

For the assessment of autobiographical memory, we used the AMI of Kopelman et al,[22] whereas the previous 2 studies used the Columbia Autobiographical Memory Interview—Short Form (AMI-SF).[36] The AMI-SF focuses on the recent events (approximately the past year) of someone's personal life, whereas the AMI of Kopelman et al[22] focuses on events from different time periods: childhood (ages 0–18 years), early adulthood (ages 19–30 years), and recent years (within the past 5 years). Comparing this specifically recent part of the autobiographic memory, we still demonstrated no significant difference between the brief pulse and ultrabrief pulse samples.

In our study, the number of treatment sessions for achieving remission was significantly less in the brief pulse group than in the ultrabrief pulse group. Since a higher number of treatment sessions is generally associated with more pronounced cognitive side effects,[37,38] the cognitive impact of ECT could have been reduced in the brief pulse group, resulting in similar cognitive effects of both treatments.

Methodological differences such as selection bias and small sample sizes between the studies may also account for the inconsistencies in results found for retrograde memory. Patients in the study by Loo et al[9] were not randomly allocated to the 2 ECT groups. This selection bias could have favored a lesser response of brief pulse ECT and harmed the cognitive outcome of ultrabrief pulse ECT, because the treating psychiatrists may have assigned more severely ill patients to brief pulse ECT and patients who had an increased risk of cognitive impairment to ultrabrief pulse ECT. Nevertheless, in the study by Loo et al,[9] outcome of depression was comparable between brief pulse and ultrabrief pulse ECT, but cognitive functioning assessed with the AMI-SF was better for the ultrabrief pulse ECT group (n = 27) compared to the small brief pulse ECT sample (n = 3).

The first treatment doses used by Loo et al,[9] 219 mC in the ultrabrief pulse group and 494 mC in the brief pulse group, were comparable with the average charges per ECT session with cognitive assessments in our study, 206 mC in the ultrabrief pulse group and 495 mC in the brief pulse group (data not shown). Therefore, the treatment with a stimulus 8 times seizure threshold in our ultrabrief pulse sample did not obscure finding any cognitive differences between the ultrabrief pulse and brief pulse groups.

In the present study, we treated the patients twice weekly versus thrice weekly in the studies by Loo et al[9] and Sackeim et al,[7] resulting in a longer interval between sessions in our study, which can be regarded as recuperation time. If the impact of brief pulse RUL ECT on cognition is indeed larger than that of ultrabrief pulse RUL ECT and we hypothesize that it takes more time to regain the pre-ictal level of cognition, a twice-weekly schedule would provide patients with more time to recuperate.[39]

Strengths, Limitations, and Future Research

A major strength of this study is that it was a prospective, double-blind, randomized controlled design in a relatively large group. With only a few exclusion criteria and continuation of most psychotropic medication, the efficacy results can be generalized to daily clinical practice. Comparison of unilateral with bilateral brief pulse ECT twice weekly was not included but should be considered for future research.

Recruitment rates in cognitive testing are discussed as a major limitation in ECT studies because patients with the highest risk for cognitive side effects are not able to participate, limiting the capacity to generalize findings.[40] In our study, the recruitment rate of 91% was high, but may still limit the generalizability of our cognitive findings to the group of patients (9%) who were unable to perform cognitive assessments before or after ECT treatment.

To conclude, here, we report the comparison of efficacy and cognitive side effects directly after the end of an ECT course. An interesting focus for future research would be to evaluate the long-term efficacy of brief pulse and ultrabrief pulse RUL ECT and cognitive outcome.

CONCLUSION

The efficacy and speed of remission of right unilateral high-dose brief pulse ECT twice weekly were superior

Table 4. Pre-ECT (T0) and Post-ECT (T1)[a] Cognitive Assessments

	Pre-ECT (T0)				Post-ECT (T1)				(T1 – T0)			
Assessment	n	Brief Pulse[b]	Ultrabrief Pulse[b]	*P* Value	n	Brief Pulse[b]	Ultrabrief Pulse[b]	*P* Value	n	Brief Pulse[b]	Ultrabrief Pulse[b]	*P* Value
AMI												
Youth	74				74				74			
Mean (SD)		14.7 (5.4)	15.7 (4.4)	.38		15.7 (4.1)	16.2 (4.6)	.63		1.0 (4.2)	0.5 (3.3)	.55
Range		3 to 21	4 to 21			6 to 21	1.5 to 21			−13 to 12.5	−10.5 to 6.5	
Adulthood	74				74				74			
Mean (SD)		17.4 (4.5)	16.4 (3.3)	.25		18.1 (3.3)	17.0 (3.9)	.18		0.7 (3.8)	0.6 (3.8)	.91
Range		4.5 to 22	7.5 to 21			8 to 21	4.5 to 21			−9 to 12.5	−7.5 to 11	
Recently	74				74				74			
Mean (SD)		16.7 (3.8)	16.8 (3.5)	.97		16.2 (4.4)	16.4 (3.8)	.82		−0.5 (3.0)	−0.4 (3.8)	.81
Range		7 to 21	7 to 23			4.5 to 21	5 to 21.0			−8 to 10	−9.5 to 6.5	
Total (YAR)	74				74				74			
Mean (SD)		49.1 (12.4)	48.7 (8.5)	.87		50.0 (10.2)	49.5 (10.6)	.85		0.8 (8.1)	0.8 (8.4)	.98
Range		21 to 67	18.5 to 62			21 to 61.5	15 to 61.5			−18.5 to 19.5	−22 to 15.5	
Incidents	74				74				74			
Mean (SD)		11.1 (7.6)	10.7 (7.8)	.80		11.3 (7.1)	9.7 (6.6)	.31		0.2 (5.2)	−1.0 (6.4)	.40
Range		0 to 27	0 to 25			2 to 24	0 to 24			−11 to 11.5	−19 to 15	
AMQ	71				73				69			
Mean (SD)		20.7 (9.8)	19.5 (10.0)	.61		21.2 (9.4)	22.3 (10.3)	.66		0.6 (5.1)	1.7 (4.3)	.31
Range		1 to 41	4 to 38			0 to 38	5 to 40			−15 to 12	−5 to 15	
Category fluency	73				73				70			
Mean (SD)		24.2 (11.8)	25.3 (9.5)	.65		24.0 (10.6)	23.5 (8.5)	.82		−0.1 (10.3)	−3.4 (9.0)	.17
Range		5 to 54	7 to 49			6 to 51	10 to 50			−26 to 20	−22 to 17	
Letter fluency	74				72				71			
Mean (SD)		26.3 (16.5)	26.2 (13.2)	.98		25.0 (14.9)	22.5 (12.6)	.44		−1.9 (9.2)	−4.6 (12.1)	.31
Range		2 to 65	3 to 60			2 to 65	4 to 65			−21 to 18	−37 to 22	
Percentage of recall						%	%					
AMI total	74											
Mean (SD)						10.8 (12.2)	12.0 (12.9)	.70				
Range						0 to 44	0 to 50					
AMI incidents	74											
Mean (SD)						13.5 (12.4)	15.3 (14.6)	.56				
Range						0 to 47	0 to 50					
AMQ	69											
Mean (SD)						17.6 (20.6)	14.0 (14.4)	.40				
Range						0 to 100	0 to 56					

[a]All multivariate analyses are adjusted for baseline, end, and change in Montgomery-Asberg Depression Rating Scale score and total ECT sessions as covariates.
[b]For all mean scores, higher scores mean better performance.
Abbreviations: AMI = Autobiographical Memory Interview, AMQ = Amsterdam Media Questionnaire, ECT = electroconvulsive therapy, YAR = Youth + Adulthood + Recently.

compared to right unilateral high-dose ultrabrief pulse ECT, with equal cognitive side effects as defined by retrograde amnesia, semantic memory, and lexical memory.

Drug names: diazepam (Diastat, Valium, and others), lithium (Lithobid and others).

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