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**Is bitemporal ECT more effective than bifrontal ECT in reducing  
the symptoms of depression in adults?**

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A SELECTIVE EVIDENCE BASED MEDICINE REVIEW

In Partial Fulfillment of the Requirements For

The Degree of Master of Science

In

Health Sciences – Physician Assistant

Department of Physician Assistant Studies  
Philadelphia College of Osteopathic Medicine  
Philadelphia, Pennsylvania

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## ABSTRACT

**OBJECTIVE:** The objective of this selective EBM review is to determine whether or not bitemporal ECT is more effective than bifrontal ECT in the treatment of adults with major depressive disorder.

**STUDY DESIGN:** Review of three published randomized controlled trials, all English language. All RCTs were published after 1999 and studied patients older than 17 years old.

**DATA SOURCES:** Three randomized control trials were found using PubMed, OVID, and Medline. Articles were selected based on relevance and that the outcomes of the studies mattered to patients.

**OUTCOME(S) MEASURED:** Hamilton Rating Scale for Depression- 24 item completed by practitioner.

**RESULTS:** The results of the Kellner<sup>6</sup> study was that bitemporal ECT placement had an average change in HRSD-24 score of 22.4 points, from 33.7 to 11.3 ( $P < 0.0001$ ), and a remission rate of 64% (95% CI 53-75%). Bitemporal ECT was 3% more effective than bifrontal ECT for treating depression.<sup>6</sup> The Bailine<sup>2</sup> study concluded that bitemporal ECT placement had an average change in HRSD-24 score of 22.7 points, from 27.7 to 5.0 and a remission rate of 95.8%. Bifrontal ECT was 4.2% more effective than bitemporal ECT for treating depression.<sup>2</sup> The Ranjkesh<sup>8</sup> study reported that bitemporal ECT placement had an average change in HRSD-24 score of 24.3 points, from 32.1 to 7.8, and a remission rate of 100%. There was no difference in effectiveness when comparing bitemporal ECT to bifrontal ECT.<sup>8</sup>

**CONCLUSIONS:** The results of the three randomized controlled trials found that bitemporal ECT and bifrontal ECT are effective in the treatment of adults with major depressive disorder. The analysis of the three randomized controlled trials is inconclusive to whether bitemporal is more effective than bifrontal ECT in treating adults with major depressive disorder.

**KEY WORDS:** ECT, depression, bitemporal

## INTRODUCTION

Electroconvulsive therapy (ECT) is predominately used to treat severe depression. After the administration of general anesthesia, a small electric current is given via electrodes to the patient to produce a generalized cerebral seizure.<sup>1</sup> This paper evaluates three randomized controlled trials (RCTs) comparing the effectiveness of bitemporal electrode ECT placement for the treatment of severe depression with other electrode ECT placements.

This topic/question is relevant to practicing PA and patients because of the high prevalence and significant number of health care visits each year for major depressive disorder. Major depression affects 16.6% of the US population and is the leading cause of disability in Western countries between ages 15-44 years old.<sup>2</sup> ECT costs vary but range from \$300-\$800 per treatment. After eight sessions (average number to completion), the total cost is \$2400-\$6400 per patient.<sup>3</sup> 8.0 million people visited a physician office or ER with major depressive disorder as the primary diagnosis in 2009-2010.<sup>4</sup>

The exact cause of depression is unknown but is thought to be a combination of genetics, dysregulation of neurotransmitters (specifically serotonin, norepinephrine, and dopamine), immunologic abnormalities, and social/psychological factors.<sup>5</sup> Symptoms of depression include depressed mood, anhedonia, physical symptoms (fatigue, appetite problem, psychomotor changes, sleep disorder), and psychological symptoms (difficulty concentrating, guilt, thoughts of death).<sup>5</sup>

The usual methods of treatment for major depression include a combination of psychotherapy and pharmacology. The first line pharmacological agents are selective serotonin reuptake inhibitors (SSRI) that include fluoxetine, paroxetine, sertraline, citalopram, escitalopram. Alternative antidepressant agents are serotonin norepinephrine reuptake inhibitors

(SNRIs) :venlafaxine, duloxetine; noradrenergic and specific serotonergic antidepressant (NaSSa): mirtazapine; norepinephrine dopamine reuptake inhibitors (NDRI): bupropion; and tricyclic antidepressants (TCA); amitriptyline, and nortriptyline <sup>5</sup>.

Select patients have refractory cases of depression that cannot be managed by the treatment options mentioned above. The method of treatment is being proposed because the use of ECT has been shown to be effective in the treatment of major depressive disorder in adults who have not benefited or been treated adequately with traditional psychotherapy and pharmacology.

#### OBJECTIVE

The objective of this selective EBM review is to determine whether or not bitemporal ECT is more effective than bifrontal ECT in the treatment of adults with major depressive disorder

#### METHODS

The population studied was men and women with severe depression older than 17 years of age. The intervention studied was bitemporal ECT. All three randomized control studies being used compared bitemporal ECT to bifrontal ECT therapy. Outcomes were measured on the severity of depression as rated on the Hamilton Depression Score that was completed by a practitioner.

Keywords used in the search to find these studies were ECT, bitemporal, and depression. All articles were published in peer-reviewed journals and in English. The author researched the articles via Medline, PubMed, and OVID search engines. Articles were selected based on relevance and that the outcomes of the studies mattered to patients (POEMs). The inclusion criteria included studies that were RCTs published after 1999. The exclusion criteria included pts

under the age of 17 years old. Summary statistics were reported or used RBI, ABI, NNT, and p-values.

Table 1 - Demographics & Characteristics of included studies

Study	Type	#Pts	Age	Inclusion Criteria	Exclusion Criteria	W/D	Interventions
Ranjesh <sup>6</sup> (2005)	RCT	45	>18	Score greater than 16 on the HDRS score greater, more than 2 days' antidepressant discontinuation for a wash-out period	history of ECT during the preceding 3-month period, taking nonbenzodiazepine anticonvulsants, lidocaine, theophylline, or lithium, a history of psychiatric disorders not related to a mood disorder	6	Bitemporal, Right unilateral, bifrontal ECT placement
Bailine <sup>7</sup> (2000)	RCT	58	>17	score higher than 17 on the HRDS, score higher than 2 on the first item (sad mood), score higher than 24 on the standardized Mini-Mental State	history of any other psychiatric disorder not related to a mood disorder, ECT within the past 6 months, use of psychotropic medication, except up to 3 mg/day of lorazepam as needed for agitation or anxiety	10	Bitemporal, bifrontal ECT placement
Kellner <sup>8</sup> (2010)	RCT	230	20-87	Score higher than 21 on the HRDS, ability to cooperate in detailed neuropsychological testing, referred for ECR for primary major depressive disorder or bipolar disorder, w or w/o psychosis	History of any psychiatric disorder not related to a mood disorder, a mood disorder that was not depression before this episode of depression, any disease affecting cognition, substance abuse in the last 6 months, medical conditions contraindicating ECT, ECT in the last 6 months, MMSE >21	63	Bitemporal, Right unilateral, bifrontal ECT placement

## OUTCOMES MEASURED

Study outcomes measured were the severity of depression. Outcomes were measured by using the Hamilton Rating Scale for Depression- 24 (HRSD-24) item completed by practitioner. Practitioner assigns a number to the severity of symptoms. Symptoms assessed include: depressed mood, feelings of guilt, suicide, insomnia early, insomnia middle, insomnia late, work and activities, psychomotor retardation, agitation, anxiety (psychological), anxiety somatic, somatic symptoms (gastrointestinal), somatic symptoms general, genital symptoms, hypochondriasis, loss of weight, insight, diurnal variation, depersonalization and derealization, paranoid symptoms, obsessional and compulsive symptoms.

Kellner et al measured outcome was the severity of depression using continuous HRSD-24 scores approximately three times a week and a single end of treatment HRSD-24 score within 24-36 hours of the final ECT.<sup>8</sup>

Bailine et al measured outcomes were the severity of depression using the HRSD-24 score, severity of symptoms in depression using the Clinical Global Impression scale, and cognitive impairment using the standardized Mini Mental scores at baseline and 24 hours after each treatment.<sup>7</sup>

Ranjesh et al measured outcomes were the severity of depression using the HRSD-24 score, and cognitive impairment using the standardized Mini Mental scores. These were assessed before receiving the initial ECT session, before the fourth ECT session, and on day after the eighth ECT session. A clinical psychologist unaware of the ECT electrode placement performed the tests at approximately 8 am.<sup>6</sup>

## RESULTS

The three studies compared bitemporal ECT to bifrontal ECT placement. All trials were done on adults > 17 yo.

The Kellner<sup>8</sup> study was a randomized control, double blind, comparison trial that randomized 230 subjects into groups receiving right unilateral ECT (77 patients), bifrontal ECT (81 patients), and bitemporal ECT (72 patients). Each patient was treated with their assigned ECT electrode placement until they reached pre-specified remission criteria, then patients were followed naturalistically for 2 months. Of the 230 participants who entered the trial, 63 (27.4%) exited the study early due to confusion/cognitive impairment, ECT not working, non cognitive-side effect, and improvement in condition. “Worst-case” analysis was not done on the participants that did not complete the trial. There was no statistically significant difference between the participants in all three trial groups as determined by the general linear model. ( $P < 0.0001$ ). The mean age of the participants was 53 years old, 63.5% female, and 95.5 % of participants were white. In regards to the severity of their depression, the participants initially had a mean HRSD-24 baseline of 34.6, the average length of their current depressive episode was 2.4 years, and they had an average of 4.6 psychiatric admissions. Patients were treated with ECT until pre-specified remission criteria and were assessed with the HRSD-24 at baseline, the fourth ECT, and the last ECT, 1 week after the last ECT, and 2 months after the last ECT. After completion of the study, all three electrode placements had statistically significantly decrease in symptoms of depression. Right unilateral ECT placement had an average change in HRSD-24 score of 21.0 points, from 34.9 to 13.9 ( $P < 0.0001$ ), and a remission rate of 55% (95% CI 43-66%). Bifrontal ECT placement had an average change in HRSD-24 score of 23.4 points, from 35.1 to 11.7 ( $P < 0.0001$ ), and a remission rate of 61% (95% CI 50-71%). Bitemporal ECT placement had an average change in HRSD-24 score of 22.4 points, from 33.7 to 11.3

( $P < 0.0001$ ), and a remission rate of 64% (95% CI 53-75%). Table 2 shows the treatment effects of bitemporal ECT on the symptoms of depression, when compared to bifrontal ECT as control. Relative benefit increase (RBI) was calculated to be 0.05. Absolute benefit increase (ABI) was calculated to be 3%. Numbers needed to treat (NNT) was calculated as 33, indicating that 33 patients need to be treated with bitemporal ECT rather than bifrontal ECT to see one more patient have remission of depressive symptoms 8 weeks after their last ECT treatment.<sup>8</sup>

Table 2: Treatment effect of bitemporal ECT on depression

CER	EER	RBI	ABI	NNT	P
61%	64%	0.05	3%	33	0.0001

The Bailine<sup>7</sup> study was a randomized control, double blind, comparison trial that randomized 58 subjects into groups receiving bifrontal ECT (24 patients), and bitemporal ECT (24 patients), 10 patients did not complete the study due to medical problems unrelated to ECT, two require antipsychotic medication, two discharged before completing the study. ‘Worst-case’ analysis was not done on the participants that did not complete the trial by the 12<sup>th</sup> treatment, 24/24 patients in the bifrontal ECT group and 23/24 patients in the bitemporal ECT group met remission criteria for depression. There was no statistically significant difference between the participants of each group as analyzed with chi-square tests for categorical variables and t test for continuous variables. ( $P = 0.90$ ). The mean age of the participants was 52.86 years old and 53.3% female. In regards to the severity of their depression, the participants initially had a mean HRSD-24 baseline of 28.3. Patients received ECT three times a week until they met remission criteria. If a patient did not meet the criteria by their 12<sup>th</sup> treatment they were considered a failure. After completion of the study, both electrode placements had statistically significantly decrease in

symptoms of depression. Bifrontal ECT placement had an average change in HRSD-24 score of 22.2 points, from 28.1 to 6.7 (P- 0.09), and a remission rate of 100%. Bitemporal ECT placement had an average change in HRSD-24 score of 22.7 points, from 27.7 to 5.0 and a remission rate of 95.8%. Table 3 shows the treatment effects of bitemporal ECT on the symptoms of depression, when compared to bifrontal ECT as control. Relative benefit increase (RBI) was calculated to be -0.04. Absolute benefit increase (ABI) was calculated to be -4.2%. Numbers needed to treat (NNT) was calculated as -24, indicating that for every 24 patients treated with bitemporal ECT one fewer would have remission of depressive symptoms by their 12<sup>th</sup> ECT treatment compared to bifrontal ECT treatment.<sup>7</sup>

Table 3: Treatment effect of bitemporal ECT on depression

CER	EER	RBI	ABI	NNT	P
100%	95.8%	-0.04	-4.2%	-24	0.77

The Ranjkesh<sup>6</sup> study was a randomized control, double blind, comparison trial that randomized 45 subjects into groups receiving bifrontal ECT (15 patients), right unilateral ECT (15 patients) and bitemporal ECT (15 patients), 6 patients did not complete the study, 2 from the bifrontal group, 1 from the bitemporal group, and 3 from the right unilateral group. “Worst-case” analysis was not done on the participants that did not complete the trial. There was no statistically significant difference between the participants of each group as analyzed with chi-square tests and one way analysis of variance (P> 0.05). The mean age of the participants was 34.7 years old and 61.5% female. In regards to the severity of their depression, the participants initially had a mean HRSD-24 baseline of 34.7. Patients received at least 8 ECT treatments, with the final HRSD-24 score recorded for the study completed after that treatment. After completion of the

study, all electrode placements had statistically significantly decreased the symptoms of depression according to the HRSD-24 score. Bifrontal ECT placement had an average change in HRSD-24 score of 25.7 points, from 35.0 to 9.3 (P= 0.09). Right unilateral ECT placement had an average change in HRSD-24 score of 24.8 points, from 32.2 to 7.4, 100% remission. Bitemporal ECT placement had an average change in HRSD-24 score of 24.3 points, from 32.1 to 7.8, 100% remission. All three methods demonstrated effectiveness in reducing HRSD-24 scores over time and treating depression, with no significant difference in one method over another (P > 0.05). Table 3 shows the treatment effects of bitemporal ECT on the symptoms of depression, when compared to bifrontal ECT as control. Relative benefit increase (RBI) was calculated to be 0. Absolute benefit increase (ABI) was calculated to be 0%. Numbers needed to treat (NNT) was calculated as 0, indicating that neither ECT electrode placement will cause more negative or positive outcomes to a patient.<sup>6</sup>

Table 4: Treatment effect of bitemporal ECT on depression

CER	EER	RBI	ABI	NNT	P
100%	100%	0	0%	0	> 0.05

## DISCUSSION

This selective evidence based medicine review investigated three randomized controlled trials to determine whether or not bitemporal ECT is an effective treatment for depression. All three studies were analyzed by comparing bitemporal ECT to bifrontal ECT.

All three trials concluded that when analyzed individually bitemporal ECT, and bifrontal ECT were effective in treating depression. When the analysis was done comparing bitemporal ECT to bifrontal ECT the results were inconclusive. There was a lack of studies comparing

bitemporal ECT to placebo in the initial search for studies, which made it necessary to compare bitemporal ECT to bifrontal ECT.

The results of the Kellner<sup>8</sup> study are generalizable to adult patients with major depression and suggests that bitemporal ECT is very effective at treating depression. However the RBI of 0.05 is small and suggests that it is not much more effective than bifrontal ECT. The ABI suggests that 3% of patients receiving bitemporal ECT will have improvement of their depression when compared to patients receiving bifrontal ECT. Some limitations of this study include a high drop out rate (27.4%), and the frequency of data collection (5 collections). This study did conclude that bitemporal ECT has more rapid symptom reduction when compared to bifrontal, and right unilateral ECT.<sup>8</sup>

The results of the Bailine<sup>7</sup> study are generalizable to adult patients with major depression. The study concluded that both bitemporal and bifrontal ECT were efficacious in treating depression. In this review, comparing bitemporal and bifrontal ECT an ABI of -4.2% suggests that bifrontal ECT will have more improvement on depression when compared to bitemporal ECT. The p-value in this study was 0.77, suggesting the results are not statistically significant. Some limitations of this study include a small sample size (58), and a high drop out rate (17.2%).<sup>7</sup>

The results of the Ranjkesh<sup>6</sup> study are generalizable to adult patients with depression. The study concluded that bitemporal and bifrontal ECT are effective at treating depression in adults, both with 100% effectiveness. When comparing bitemporal to bifrontal ECT the RBI, and ABI were both 0. This is stating that there is no difference in efficacy when choosing bifrontal to bitemporal ECT. The p-value in this study was  $>0.05$  making the results not statistically

significant. Some limitations of this study include small sample size 45, and high drop out rate (13.3%).<sup>6</sup>

#### CONCLUSION

When analyzed without comparison, bitemporal ECT is effective at treating major depression.

When bitemporal ECT is compared to bifrontal ECT the results are conflicting. Future studies are warranted comparing bitemporal ECT to placebo. A study of this design would be limited by not being able to be double blinded because it is very obvious to both the patient and clinician if a patient received ECT or not.

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