

# Changes in Everyday and Semantic Memory Function After Electroconvulsive Therapy for Unipolar Depression

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**Objectives:** This long-term prospective study focuses on the effects of electroconvulsive therapy (ECT) on everyday memory function and on semantic memory function.

**Methods:** Results of memory test from 96 consecutive inpatients treated for unipolar depression were analyzed prospectively before ECT, after ECT treatment, and at 3- and 12-month follow-up. Everyday memory function was assessed by means of the Rivermead Behavioural Memory Test (RBMT) and semantic memory by 2 forms of the word fluency test.

**Results:** In our study, age had a constant and significant negative effect on everyday memory (RBMT score) over time. Bilateral electrode placement mainly influenced everyday memory, which was significantly improved at 3-month follow-up. One year after discharge, the RBMT scores were not significantly different from pretreatment levels, indicating that ECT does not affect everyday memory on the longer term.

Scores on both word fluency tests for semantic memory were significantly influenced by age over time. The effect of age changed from a negative influence directly after ECT to a positive effect at follow-up. This advantage of higher age indicates that the semantic memory of older patients receiving ECT for severe mood disorder shows greater improvement at follow-up compared with younger patients. Over time, the scores on only 1 of the word fluency tests were significantly influenced by mainly bilateral electrode placement.

**Conclusions:** A small but reversible decrease in everyday memory occurs after ECT in depressed patients, which is influenced by age and electrode placement. Semantic memory shows a fluctuating but recovering course, which is also influenced by age and electrode placement. During follow-up, the improvement in semantic memory was greater in the older patients.

**Key Words:** ECT, everyday memory, semantic memory, depression, electrode placement, age, follow-up

(*J ECT* 2007;23:153–157)

**M**emory impairment is a serious side effect of electroconvulsive therapy (ECT). Although there is usually

some cognitive improvement from pretreatment to posttreatment, resulting from termination of the negative influence depression exerts on cognitive function,<sup>1,2</sup> an exception to this rule exists for memory function. The anterograde amnesia usually subsides within weeks; the retrograde amnesia, however, does improve but is reported to have a lasting component.<sup>3</sup>

We were interested in the effect of ECT on memory skills related to everyday situations and on the effects of ECT on semantic memory. The Rivermead Behavioural Memory Test (RBMT) was designed to assess memory function related to everyday situations. This test is useful to predict everyday life task memory problems in patients. The RBMT includes the following subtests: remembering an appointment, remembering a short route (immediate and delayed), remembering a belonging, remembering to deliver a message, picture recognition, orientation, story recall (immediate and delayed), remembering a name, and face recognition. Administration time is 20 to 30 minutes.

Semantic memory is a structured record of acquired facts, concepts, and skills. The word fluency tests used are the naming of animals and professions during 1 minute. The information in semantic memory is derived from that in our own episodic memory, such that we can learn new facts or concepts from our experiences. Episodic memory represents our memory of events and experiences in a serial form from which we can reconstruct events that took place at a given point in our lives. Episodic memory and semantic memory are 2 types of long-term memory.<sup>4–6</sup>

Several studies have identified variables that correspond to memory impairment after ECT. Some authors suggested that older patients are more likely to have cognitive impairment after ECT,<sup>7,8</sup> whereas others found no effect of age.<sup>9</sup> Bilateral electrode placement has been associated with more severe cognitive impairment than unilateral electrode placement.<sup>3,10</sup> In addition to these diverse findings, studies on the effects of ECT typically involve small patient groups, focus exclusively on short-term effects, and often combine findings from patients who have different psychiatric disorders.

In the present study, the memory function of patients with a depressive disorder, all treated with ECT, was monitored before and during the 12-month period after discharge from the hospital.

In addition, we tested whether any changes found had interacted with age, electrode placement, or pretreatment score on the Hamilton Rating Scale for Depression (HRSD) 17-item version, a severity scale for depressive disorder.

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Received for publication January 4, 2007; accepted March 21, 2007.

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## MATERIALS AND METHODS

### Subjects

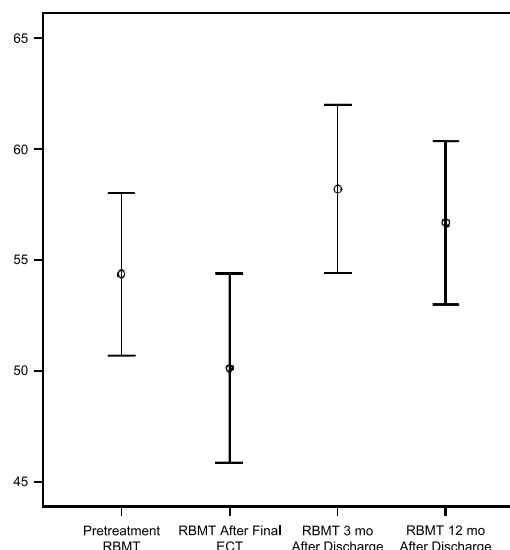
The study was performed at the depression unit of the Department of Psychiatry (Erasmus Medical Centre, Rotterdam). The local ethics committee approved the study, and written informed consent was obtained from all depressed inpatients included in the study. Patients were included if they met the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* criteria for depressive disorder, excluding patients with a bipolar disorder, schizoaffective disorder, dementia, drug or alcohol abuse, or inadequate command of the Dutch language. Diagnosis was based on clinical observations during a routinely drug-free period.

### ECT Method

All patients received treatment with ECT according to the Dutch guidelines for ECT.<sup>11</sup> Patients were withdrawn from medication before ECT and were maintained medication-free during the course of ECT; in case of severe agitation, incidental use of haloperidol was allowed.

Electroconvulsive therapy was administered with a brief-pulse, constant-current apparatus (Thymatron DGx, Somatics, Lake Bluff, Ill). Seizure threshold was determined during the first session with stimulus titration. If the starting stimulus dose failed to elicit a seizure of at least 25 seconds' duration measured with the cuff method, stimulus charge was increased according to the titration schedule (for patients younger than 50 years: 5%, 10%, 20%, 40%, and 80%; for patients aged 50 years and older: 10%, 20%, 40%, and 80%), and the patient was restimulated after 30 seconds. At the second session, dosage was set at 1.5-times seizure threshold for bilateral treatment and 2.5-times seizure threshold for unilateral treatment. Dosage was adjusted during the course of the ECT to maintain seizure duration of at least 25 seconds as measured with the cuff method. Patients were treated twice weekly.

Patients were initially treated with right unilateral ECT; patients were crossed over to bilateral ECT if response was inadequate after 6 treatments. Patients in a critical condition started with bilateral ECT. Anesthesia was achieved with intravenous administration of 10 mg metoprolol, 0.25 mg methylatropine during the titration session, 0.002 to 0.003 mg/kg glycopyrrolate during the subsequent sessions, a bolus injection of 0.010 to 0.015



**FIGURE 1.** Data on RBMT scores from pretreatment to 12 months after discharge. The data are mean scores and standard errors.

mg/kg alfentanil, and 0.2 to 0.3 mg/kg etomidate followed by 0.5 to 1.0 mg/kg succinylcholine.

### Data Collection

Patients were diagnosed and screened for exclusion criteria before the start of ECT. A trained clinical evaluation team assessed the patient's depression severity using the HRSD.<sup>12</sup> Everyday memory function was assessed by means of the RBMT,<sup>13</sup> which is especially suited for the detection of problems in everyday memory function and is sensitive to prospective memory complaints. In addition, semantic memory was assessed with 2 categorical word fluency tests taken from the Groninger Intelligence Test (word fluency tests 1 and 2 [WF-1 and WF-2])<sup>14</sup>; these tests explore semantic memory function and provide information on possible damage to existent memory stores. This clinical evaluation took place during formal testing sessions at 4 points in time: 3 days before ECT treatment, within 7 days after final ECT treatment, and at 3 and 12 months after discharge from the hospital. The neuropsychologists performed the neuropsychological assessments; they were blind to the treatment status.

### Statistical Analyses

Independent-sample *t* tests were used to analyze baseline differences in RBMT and WF-1 and WF-2 levels regarding the

**TABLE 1.** Baseline Characteristics of the Study Patients (n = 96)

Male, n (%)	28 (29.2)
Female, n (%)	68 (71.8)
Age, yrs, mean (SD) (range)	55.7 (13.5) (14–86)
HRSD-17, mean (SD), n = 96	28.1 (7.9)
RBMT, mean (SD), n = 80	52.2 (13.1)
WF-1, mean (SD), n = 83	3.9 (2.4)
WF-2, mean (SD), n = 83	3.5 (2.3)
Unilateral, n (%)	17 (17.7)
Bilateral, n (%)	79 (82.3)

HRSD-17 indicates Hamilton Depression Rating Scale 17-item version.

**TABLE 2.** Scores on Baseline Memory Function Before ECT

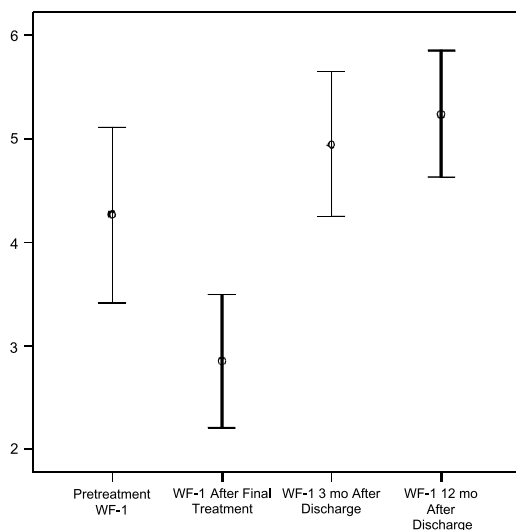
	RBMT, mean (SD) n = 80	WF-1, mean (SD) n = 83	WF-2, mean (SD) n = 83
Unilateral	56.41 (9.7), n = 16	5.06* (1.6), n = 16	4.25 (2.4), n = 16
Bilateral	51.20 (13.7), n = 64	3.61* (2.5), n = 67	3.34 (2.3), n = 67

\*Significant (*P* = 0.031).

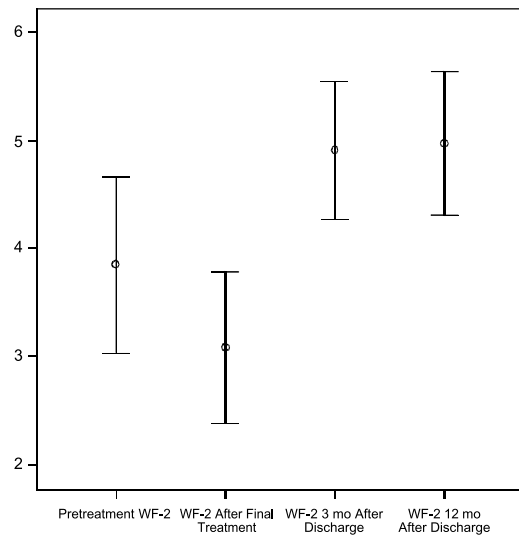
**TABLE 3.** Effect of Electrode Placement on RBMT Score at the 3 Follow-Up Assessments Compared With Baseline

	Bilateral (P)	Unilateral (P)	Bilateral-Unilateral (P)
Difference between pretreatment score and score after ECT	-3.77 (0.020)	1.79 (0.549)	-5.56 (0.086)
Difference between pretreatment score and 3 mo after discharge	5.68 (0.004)	-3.39 (0.341)	9.06 (0.018)
Difference between pretreatment score and 12 mo after discharge	2.57 (0.197)	-1.18 (0.780)	3.75 (0.40)

dichotomous independent variables unilateral/bilateral electrode placement. The levels of RBMT, WF-1, and WF-2 scores at the 4 assessment times were analyzed using repeated-measures analysis of variance with an unstructured covariance matrix for the residuals. The following independent variables were entered in the model: age, electrode placement, HRSD score, and time. Age and HRSD were introduced as continuous fixed variables, electrode placement as a categorical fixed variable that was considered to be effective only after baseline, and time as a time-dependent categorical variable. We also analyzed the interaction between time and the other independent variables. If a significant interaction was present, this interaction was added to the model of repeated-measures analysis of variance to estimate how the time course of the memory test was modified. Based on the model estimates, results were expressed as changes compared with pretreatment levels. If a significant interaction was present between time and



**FIGURE 2.** Data on WF-1 scores from pretreatment to 12 months after discharge. The data are mean scores and standard errors.



**FIGURE 3.** Data on WF-2 scores from pretreatment to 12 months after discharge. The data are mean scores and standard errors.

another covariable, changes from baseline were expressed as either a linear function of the continuous covariable or per category of the categorical covariable. Results were considered statistically significant at a P value lower than 0.05. All calculations were performed using SPSS version 11.

## RESULTS

### Subjects

Between October 1996 and June 2002, 124 consecutive patients received ECT in our clinic. Finally, 104 patients met the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* criteria for depressive disorder; of these, 4 patients refused participation, and 4 other patients needed acute treatment because of illness severity and could not be included in the baseline assessment. For all 96 participating patients, an HRSD score could be obtained at baseline; however, because of their illness, not all patients could perform all 3 memory tests (n = 80 for RBMT; n = 83 for the WF-1 and WF-2). Table 1 presents the baseline characteristics of the 96 patients included in the study.

### Baseline Memory Function

Table 2 presents mean baseline scores on RBMT, WF-1, and WF-2 per independent variable (electrode placement). Age and HRSD score as continuous variables had no significant influence. The mean pretreatment WF-1 scores of unilaterally treated patients were significantly higher than those of patients who received bilateral treatment.

### RBMT Change

Figure 1 shows the mean RBMT scores at the 4 assessment times. Age had a constant significant negative effect on RBMT scores over time: -0.4 points per year of age (95% confidence interval [CI], -0.56 to -0.25; P < 0.0005). The effect of electrode placement on RBMT scores varied

**TABLE 4.** Effect of Age on WF-1 Score at the 4 Assessment Times

Sessions	Effect of Age (per yr)	95% CI	P
Before ECT	-0.043	-0.083 to -0.003	0.037
After ECT	-0.006	-0.040 to 0.029	0.742
3 mo After discharge	0.050	0.005 to 0.095	0.031
12 mo After discharge	0.024	-0.020 to 0.067	0.282

significantly over time ( $P < 0.0005$ ; Table 3). The HRSD score at baseline had no significant effect on the RBMT score over time ( $P = 0.604$ ).

**Word Fluency-1 Change**

Figure 2 shows the mean WF-1 scores at the 4 assessments times. The effect of age on the WF-1 score varied significantly over time ( $P = 0.001$ ; Table 4).

Electrode placement ( $P = 0.534$ ) and HDRS ( $P = 0.521$ ) score at baseline had no significant effect on the WF-1 score over time.

**Word Fluency-2 Change**

Figure 3 shows the mean WF-2 scores at the 4 assessment times. The effect of age on WF-2 score varied significantly over time ( $P = 0.001$ ; Table 5). The effect of electrode placement on WF-2 score also varied significantly over time ( $P < 0.005$ ; Table 6). The HDRS score at baseline had no significant effect on the WF-2 score over time.

**DISCUSSION**

This study investigated whether changes in 2 aspects of memory (everyday memory and semantic memory) occurred after treatment with ECT and during the 12-month follow-up. We also aimed to identify effects of age, electrode placement, or HDRS score on these memory functions after ECT treatment.

At pretreatment assessment, scores on the WF-1 test were significantly lower for patients treated with bilateral ECT compared with those treated unilaterally. This could be due to illness severity because patients in a critical condition started with bilateral ECT.

During follow-up, the RBMT scores were influenced by age and electrode placement. The influence of age on everyday memory was constant, and older patients scored consistently less than younger patients. The influence of electrode placement was significantly present in case of bilateral electrode placement (Table 3). Unilateral electrode placement had no significant effect on RBMT scores at follow-up compared with baseline. The effect of bilateral electrode placement was significantly improved at 3-month follow-up. One year after discharge, the RBMT scores were not significantly different

**TABLE 5.** Effect of Age on WF-2 Score at the 4 Assessment Times

Session	Effect of age (per yr)	95% CI	P
Before ECT	-0.048	-0.086 to -0.010	0.014
After ECT	-0.004	-0.039 to 0.031	0.828
3 mo After discharge	0.026	-0.018 to 0.069	0.242
12 mo After discharge	0.041	-0.001 to 0.083	0.053

from those at pretreatment, indicating that ECT does not affect everyday memory on the longer term.

Scores on both WF tests for semantic memory were significantly influenced by age over time. The effect of age changed from a negative influence directly after ECT to a positive effect at follow-up. This advantage of higher age indicates that the semantic memory of older patients receiving ECT for severe mood disorder shows greater improvement at follow-up compared with younger patients.

A recent Dutch study also showed that after ECT, cognitive functioning may improve in nondemented elderly at follow-up.<sup>15</sup> These positive age-related effects belong to a component of memory.

Possible explanations for this age-related effect are tentative. Semantic memory is a structured record of acquired facts, concepts, and skills. The information in semantic memory is derived from that in our own episodic memory, such that we can learn new facts or concepts from our experiences. Therefore, this positive age effect could be due to the degree of cognitive reserve whereby innate intelligence or aspects of life experiences (eg, education or occupational attainments) may supply a mental reserve against brain dysfunction<sup>16</sup>; this could benefit the elderly compared with younger patients. Another possible explanation is that stimulation of the neural system results in restorative plasticity, especially in the elderly.<sup>15,17</sup> Because with ECT the elderly are at a disadvantage for disturbance of other kinds of memory (such as short-term memory), restorative plasticity may adhere to specific brain regions.<sup>7,18</sup>

Only the scores on WF-2 were significantly affected by electrode placement over time. Again, mainly bilateral electrode placement had a negative influence on the scores (Table 6) up to 1 year after discharge. The difference between the influence of bilateral and unilateral ECT was significant only directly after ECT.

This differential effect related to electrode placement requires some discussion. This effect might result from the design of the present study, in which assignment to treatment conditions regarding dosage, electrode placement, and treatment duration was based on the initial clinical response of the individual patient and not on an experimental

**TABLE 6.** Effect of Electrode Placement on WF-2 Score at the 3 Follow-Up Assessments Compared With Baseline

	Bilateral (P)	Unilateral (P)	Bilateral-Unilateral (P)
Difference between pretreatment score and score after ECT	-3.02 (0.008)	-1.82 (0.115)	-1.20 (0.028)
Difference between pretreatment score and 3 mo after discharge	-3.02 (0.012)	-2.73 (0.025)	-0.30 (0.620)
Difference between pretreatment score and 12 mo after discharge	-3.42 (0.008)	-3.86 (0.004)	0.44 (0.496)

paradigm, in contrast to other studies.<sup>3,10</sup> This constitutes a limitation when viewed from an experimental point of view, as no objective comparison of effects of unilateral and bilateral treatment can be made.

The observed pattern of fluctuation in memory function should also be interpreted with caution, because several influences might be present. Memory function is reported to be impaired during severe depression, and after recovery, cognition usually improves.<sup>2,19</sup> In our study, the pretreatment HRSD score proved to have no effect on the differences in the scores on the memory assessment tests at follow-up. The temporary cognitive deterioration is most likely attributable to the ECT. The improvement observed at 3 and 12 months after treatment indicates that the negative effect of ECT on everyday and semantic memory function is temporary. However, it is important to note that, because no data on premonitory levels of memory function or a control group were available, our study design does not allow to draw conclusions about possible permanent memory impairment. The current data only support the conclusion that a small reversible decrease in memory function occurs after ECT, followed by an improvement of everyday and semantic memory function to at least pretreatment levels.

The approach taken in this study reflects existing treatment protocols, in which individual seizure threshold is used as a point of reference for determining dosage, and response to unilateral electrode placement determines whether it is necessary to switch to bilateral treatment; therefore, the present findings provide information emerging from actual psychiatric practice. The present data suggest that, when decisions regarding electrode placement and dosage are made based on patients' individual responses, no significant differences in the effect of ECT on memory function between unilateral and bilateral electrode placement occur.

## CONCLUSION

Everyday memory is constant and negatively influenced by age over time. Bilateral electrode placement only briefly influences everyday memory compared with baseline scores; restoration of memory already occurs at the 3-month follow-up assessment, and at 12 months, no significant difference exists compared with baseline. Unilateral electrode placement has no effect on everyday memory.

Scores on both WF tests for semantic memory were significantly influenced by age over time. The effect of age changed from a negative influence directly after ECT to a positive effect during follow-up. This advantage of higher age

indicates that the semantic memory of older patients receiving ECT for severe mood disorder shows greater improvement at follow-up compared with younger patients. Of the word fluency tests, only WF-2 was significantly influenced by mainly bilateral electrode placement over time.

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