Efficacy and Cognitive Side Effects of Electroconvulsive Therapy (ECT) in Depressed Elderly Inpatients With Coexisting Mild Cognitive Impairment or Dementia

Lucrezia Hausner, Dr Med; Marinella Damian, PhD; Alexander Sartorius, MD, PhD; and Lutz Frölich, MD, PhD

Objective: To study cognitive performance in depressed geriatric inpatients with or without preexisting cognitive impairment who received a first course of electroconvulsive therapy (ECT).

Method: Forty-four elderly inpatients with major depressive disorder (*ICD-10* criteria) were included in a prospective consecutive case series of a university hospital. The patients were divided into 3 groups (no cognitive impairment [NCI], mild cognitive impairment [MCI], dementia) and rated for cognitive performance with the MMSE before first ECT, after sixth ECT, and 6 weeks and 6 months after ECT termination. Affective symptoms were rated by 21-item Hamilton Depression Rating Scale (HDRS-21) before and 6 weeks after ECT. Analysis of variance or Kruskal-Wallis tests on ECT-induced MMSE and HDRS-21 score changes were compared to baseline. Binary logistic regression was used for predictor analysis. The study was conducted from April 2004 to April 2008.

Results: After initial nonsignificant cognitive deterioration in all 3 groups, the NCI group improved cognitively 6 weeks ($P = .018$) and 6 months ($P = .027$) after ECT. The MCI group improved in cognition 6 months ($P = .036$) after ECT. In the dementia group, mean MMSE scores also improved numerically over the course of ECT without significance. Dementia patients with antidementia treatment improved in cognition to a clinically relevant extent after the sixth ECT. Dementia subjects without antidementia treatment deteriorated. After the sixth ECT, 70.0% of dementia patients ($P = .004$) presented a cognitive decline, and 68.8% of MCI patients ($P < .001$) presented a decline 6 weeks after ECT. Six months after ECT, one-third of the dementia patients ($P < .036$) still had a cognitive decline. Affective symptoms remitted after ECT in all 3 groups ($P < .001$). Pre-ECT cognitive deficits were the best predictor of MMSE decline (6 weeks after ECT, $P = .007$; 6 months after ECT, $P = .055$).

Conclusions: ECT is effective and well tolerated in geriatric depressed inpatients regardless of preexisting cognitive impairment. Cognitive deficits were transient.

J Clin Psychiatry 2011;72(1):91–97

Submitted: *January 11, 2010; accepted April 12, 2010.*
Online ahead of print: *November 30, 2010 (doi:10.4088/JCP.10m05973gry).*
Corresponding author: *Lucrezia Hausner, Dr Med, Central Institute of Mental Health, Sq J5, D-68159 Mannheim, Germany (Lucrezia.hausner@gmx.de).*

The prevalence of major depressive disorder in subjects older than 60 years is estimated to be around 2%.[1] The prevalence of subsyndromal depressive syndromes in elderly subjects is about 12.5%, including major and minor depressive disorders and dysthymia.[1] In patients with dementia, Parkinson's disease, and cerebrovascular accidents, depression is even more common and more pronounced and creates a high burden of disease, both to the individual and to society. Electroconvulsive therapy (ECT) is a safe and effective treatment for affective disorders like severe or delusional depression, especially in frail elderly subjects with multiple comorbidities.[2,3]

Although there are only few controlled studies about this important treatment option, it may be concluded that ECT could be more efficacious for treating severe affective disorders in elderly than in young adults.[4] In geriatric patients, 50%–60% are thought to improve clinically after an antidepressant medication,[5] but the immediate efficacy of ECT is higher.[6] Continuation or maintenance ECT may also successfully be applied to prevent a relapse of depression after a first effective course of ECT.[7–9]

One of the most frequently observed side effects of ECT are cognitive disturbances, which are debated especially before treating elderly subjects. Studies examining cognitive side effects in adult nongeriatric patients showed reversible effects like reduced concentration, sustained disorientation, impaired attention, retrograde memory loss, and problems with the reproduction of autobiographic facts immediately after ECT treatment.[10–12] However, Hihn et al[13] showed an improvement of memory encoding after ECT, even when delayed recall remained impaired. There also was a significant short-term anterograde memory impairment directly after an ECT session but no influence on non-mnestic cognitive functions.[14] Bilateral electrode placement tends to exert more memory dysfunction than right unilateral electrode placement.[11,15,16] There are few studies on long-term ECT effects on cognitive functioning and the results vary: some studies observed an improvement of cognitive deficits occurring directly after an ECT session,[17] some reported vulnerability for persisting deficits of autobiographical amnesia, especially in subjects with preexisting global cognitive impairment before ECT or postictal confusion.[12] In contrast, the few existing long-term maintenance ECT studies have even demonstrated cognitive improvement after 12–24 months of maintenance ECT.[9]

In geriatric patients, depression may frequently occur with comorbid cerebral conditions like cerebrovascular or neurodegenerative diseases, and symptoms of depression in elderly subjects may also include cognitive impairments. Such patients may be even more vulnerable to ECT-induced cognitive side effects than otherwise healthy elderly people. Recent studies on this topic are scarce: there is a reluctance of treating elderly depressed patients with preexisting cognitive impairments or even dementia with ECT, mainly because of detrimental effects of a short-term narcosis[18] but also because of the idea that ECT could irreversibly worsen preexisting cognitive dysfunction. Furthermore, it is difficult to get a long-term follow-up because of high mortality in this age range or the discontinuation of contact to a specialist physician after moving into a nursing home. Further investigations are necessary because therapy-refractory affective disorders are often found in the elderly population because of cerebral changes[19] and drug-treatment resistance or the high sensitivity for pharmacologic side effects[20,21] and polypharmacy.

In the present study, we investigated the course of cognitive performance and affective symptoms in a consecutive series of psychiatric inpatients with geriatric depression undergoing a first course of ECT. The indication for ECT in the elderly subjects was given according to routine procedures at our institution. Subjects with and without preexisting cognitive impairments (ie, mild cognitive impairment [MCI] and dementia) were included and their cognitive follow-up monitored.

We hypothesized that in elderly patients with therapy-resistant depression, a preexisting cognitive impairment, ie, MCI or dementia, predisposes to more severe cognitive side effects of ECT than in no cognitive impairment (NCI) patients. Further, we hypothesized that the emergence of cognitive side effects is modulated by a number of biologic variables, eg, age, cerebral pathologies on magnetic resonance imaging (MRI), and medication.

METHOD

Design and Study Population

From April 2004 to April 2008, a consecutive series of 44 elderly (age > 65 years) depressed inpatients were treated with ECT for the first time at the Central Institute of Mental Health, according to the standard indication of ECT in Germany. All subjects had an affective disorder and fulfilled the *ICD-10* criteria for a current major depressive disorder. They showed a clinical phenotype of delusional depression or *treatment-resistant severe depression*, defined as at least 2 sufficient trials (adequate in dose, duration, and compliance) with antidepressants from different pharmacologic classes that failed to produce a significant clinical improvement. Since this was an open-label and noncontrolled study, the clinical decision to use ECT was strictly independent from study participation. All patients provided written informed consent, and the study was approved by the local ethics committee.

Thirteen subjects were cognitively intact (NCI), according to clinical investigation and neuropsychological findings. Twelve subjects with dementia had preexisting Alzheimer's disease with or without vascular contribution, according to *ICD-10* criteria and the National Institute of Neurologic and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders criteria[22] for probable or possible Alzheimer's disease of mild to moderate severity. Nineteen subjects had MCI and fulfilled the criteria according to Winblad et al.[23] The distinction between dementia and MCI relies on a clinical decision and relates to the lack of impairment in general intellectual functioning and lack of impairment in (instrumental) activities of daily living in MCI. Subjects with major cerebrovascular changes or non–Alzheimer's disease dementia etiology were excluded from this study.

The present clinical investigation had a prospective observational design with a 6-month follow-up. Mini-Mental State Examination (MMSE)[24] ratings were performed prior to the first ECT session, after the sixth ECT session, and 6 weeks and 6 months after the termination of the ECT course. The 21-item Hamilton Depression Rating Scale (HDRS-21)[25] was administered prior to the index ECT and 6 weeks after the last ECT. The enrollment of the subjects in this study did not influence their pharmacologic treatment. The dropout rate after 6 months was 45% in the total sample.

Assessment Methods

Affective symptoms were assessed by rating the HDRS-21[25] (*complete remission* defined as HDRS-21 ≤ 7), and cognitive performance was measured with the MMSE. All ratings were done by a trained psychiatrist administering the questionnaire. All subjects underwent an MRI < 12 months before the first ECT session, which was examined by an experienced neuroradiologist in our center. The cranial MRI was specifically examined for signs of cerebral pathology as neurodegeneration or cerebrovascular disease.

Electroconvulsive Therapy (ECT) Methods

Five days prior to the first application of ECT, any psychotropic medication except benzodiazepine was stopped to lower the risk of adverse side effects. Benzodiazepines were usually kept (maximum 2 mg at the day of application) because of the suicidal risk or the severity of affective symptoms bothering the patient. Electroconvulsive therapy was started right unilaterally at minimal 2.5 times over seizure threshold or bilaterally at minimal 1.5 times over seizure threshold, respectively. Switching was considered according to clinical necessity. Seizure threshold was titrated during the first treatment, and the energy was subsequently increased if a patient did not clinically respond or showed insufficient seizures during the ECT course (usually motor response time < 20 seconds and electroencephalogram seizure activity < 30 seconds; total seizure coherence and concordance, seizure energy index, postictal suppression, midictal amplitude, and maximal poststimulation heart rate were

© COPYRIGHT 2010 PHYSICIANS POSTGRADUATE PRESS, INC.

Table 1. Sociodemographic and Clinical Characteristics of the Patient Sample and the Created Subgroups: NCI, MCI, and Dementia

Characteristic	Total Patient Cohort (N = 44)	NCI (n = 13)	MCI (n = 19)	Dementia (n = 12)	*P*
Age, mean ± SD (range), y	73.0 ± 6.0 (65–89)	70.4 ± 5.3 (65–82)	73.5 ± 5.0 (66–84)	75.0 ± 7.4 (66–89)	.148
Women, n (%)	33 (75.0)	8 (61.5)	16 (84.2)	9 (75.0)	.364
Bilateral ECT stimulation, n (%)	12 (27.3)	3 (23.1)	5 (26.3)	4 (33.3)	.850
Trapanal anesthesia, n (%)	40 (90.0)	12 (92.3)	17 (10.5)	11 (91.7)	.899
MRI pathology (WML or atrophy), n (%)[a]	24 (54.5)	2 (15.4)	12 (63.2)	10 (83.3)	.001
Affective disorder, n (%)					
Recurrent depressive disorder (F33)	29 (65.9)	9 (69.2)	14 (73.7)	6 (50.0)	
Depressive episode (F32)	11 (25.0)	3 (23.1)	4 (21.1)	4 (33.3)	
Bipolar affective disorder (F31)	1 (2.3)			1 (8.3)	
Schizoaffective disorder (F25)	3 (6.8)	1 (7.7)	1 (5.3)	1 (8.3)	
Dementia disorder, n (%)					
Alzheimer's dementia, early onset				1 (8.3)	
Alzheimer's dementia, late onset				7 (58.3)	
Mixed Alzheimer's dementia				4 (33.3)	
Antidementia drug therapy	5 (11.4)			5 (41.6)	
Rivastigmine	3 (6.8)			3 (25.0)	
Memantine	2 (4.5)			2 (16.7)	

[a]Post hoc test (Scheffé): NCI versus MCI, $P = .015$; NCI versus dementia, $P = .002$; MCI versus dementia, $P = .406$.
Abbreviations: ECT = electroconvulsive therapy, MCI = mild cognitive impairment, MRI = magnetic resonance imaging, NCI = no cognitive impairment, WML = white matter lesions.

also used to some extend to clinically identify nonadequate seizures). Electroencephalogram was recorded electronically by the ECT device (Thymatron IV; Somatics, LLC, Lake Bluff, Illinois) with bilateral frontomastoid leads. The frequency of ECT treatment was 2–3 times per week, according to clinical judgment, and anesthesia was achieved by administering thiopental (90%) or etomidate (10%).

Statistical Analysis

The statistical analyses were performed by an independent investigator who was not involved in the data collection or data management. All statistical analyses were performed with the software SPSS, Version 15 (SPSS Inc, Chicago, Illinois). For normally distributed quantitative variables, statistical significance was tested with paired or unpaired Student *t* tests, as applicable, and analysis of variance with post hoc Scheffé tests. For not normally distributed variables, we performed nonparametric Kruskal-Wallis tests with post hoc Mann-Whitney *U* tests. Differences between qualitative variables were tested using χ^2 or Fisher exact tests. Stepwise binary logistic regression analyses were computed to analyze the extent and factors of ECT-induced MMSE score decline. In these analyses, the factors preexisting MRI pathology, preexisting cognitive deficits, prior antidementia drug treatment, and age were entered as independent variables to predict the binary dependent variable MMSE score decline versus no MMSE score decline. As there were 3 different follow-up times (after the sixth ECT, 6 weeks after the last ECT, and 6 months after the last ECT), 3 binary logistic regression analyses were computed, each of which comparing the initial MMSE score to 1 of the 3 follow-up scores. Two different sets of samples were analyzed: To avoid too many missing values in the outcome parameters, missing values were replaced by the last observed value of the respective variable (last observation carried forward [LOCF]). We also analyzed the sample without replacing missing values (observed cases) to be able to compare these analyses with the LOCF analyses. Statistical significance was set at the $P < .05$ level. Because of the exploratory nature of the study, no adjustment for multiple comparisons was performed.

RESULTS

Patient Characteristics and Disposition

Table 1 reports in detail the baseline characteristics of all patients and of the subgroups NCI, MCI, and dementia as well as the variables' type of ECT stimulation, type of anesthesia, preexisting pathology in MRI, type of affective disorder and dementia, and use of antidementia drugs. All patients were 65+ years of age, with a mean age of 73 ± 6 years. Twenty-four subjects had cerebral pathologies on MRI with relevance for a dementia disorder, eg, subcortical white matter lesions or cerebral atrophy. Only 2 of 13 subjects without cognitive deficits had pathologies on MRI, and 10 of 12 subjects with dementia had MRI pathologies ($P = .001$), which is consistent with diagnoses of dementia.

Cognitive Performance Under ECT

Intergroup differences in cognitive functioning (given as MMSE score), depressive symptoms (given as HDRS score), and the rate of MMSE score decline from baseline at each point of the assessment are presented in Table 2. The 3 groups did not differ in the initial severity of the affective symptoms (initial HDRS-21 scores) and in the severity of the symptoms 6 weeks after ECT termination. As expected, NCI subjects had the best cognitive scores at baseline, whereas subjects with dementia had the lowest ($P = .031$). At each assessment time point, the MMSE scores differed significantly between the subgroups ($P = .003$ after the sixth ECT, $P < .001$ six weeks after the last ECT, and $P = .001$ six months after the last ECT), with NCI subjects always having the highest cognitive scores and the demented subjects having the lowest. After the sixth ECT, subjects with dementia most frequently showed a decline in cognitive functioning (70.0%), and those who

© Copyright 2010 Physicians Postgraduate Press, Inc.

Table 2. Intergroup Differences of Cognitive Function (given as MMSE score) and Depressive Symptoms (given as HDRS-21 score) at Each Time Point of Assessment: NCI, MCI, and Dementia

Measure	n	%	NCI, Mean ± SD (range)	MCI, Mean ± SD (range)	Dementia, Mean ± SD (range)	*P*	Post Hoc Test (Scheffé), *P*		
							NCI vs MCI	NCI vs Dementia	Dementia vs MCI
Initial HDRS-21 score	44		30.1 ± 5.2 (23–37)	27.8 ± 7.1 (14–39)	27.6 ± 6.7 (17–36)	.554	.620	.651	.999
HDRS-21 score 6 wk after last ECT	44		8.3 ± 3.5 (5–15)	9.2 ± 4.7 (1–18)	8.3 ± 4.0 (4–15)	.782	.835	1.000	.850
Initial MMSE score	42	95.5	27.6 ± 1.9 (24–30)	23.6 ± 6.3 (5–29)	22.7 ± 4.4 (15–29)	.031	.082	.058	.905
MMSE score after sixth ECT	41	93.2	27.4 ± 2.0 (23–30)	22.3 ± 5.5 (12–28)	22.3 ± 3.3 (17–28)	.003	.007	.022	.994
MMSE score 6 wk after last ECT	41	93.2	29.2 ± 0.8 (28–30)	23.6 ± 4.2 (14–29)	24.1 ± 3.8 (17–29)	< .001	< .001	.002	.948
MMSE score 6 mo after last ECT	30	68.2	29.4 ± 0.7 (28–30)	26.5 ± 3.3 (20–30)	26.0 ± 2.6 (22–29)	.001	.002	.016	.945
			n/n (%)[a]	n/n (%)[a]	n/n (%)[a]				
MMSE score decline after sixth ECT			6/13 (46.2)	12/18 (66.7)	7/10 (70.0)	.004	.007	.023	1.000
MMSE score decline 6 wk after last ECT			2/13 (15.4)	11/16 (68.8)	4/11 (36.4)	< .001	< .001	.003	.944
MMSE score decline 6 mo after last ECT			1/8 (12.5)	2/10 (20.0)	2/6 (33.3)	.036	.075	.077	.943

[a]Denominator equals sample size available at each measurement point for each subgroup.
Abbreviations: ECT = electroconvulsive therapy, HDRS-21 = 21-item Hamilton Depression Rating Scale, MCI = mild cognitive impairment, MMSE = Mini-Mental State Examination, NCI = no cognitive impairment.

were cognitively unimpaired least frequently showed a decline in cognitive functioning ($P = .004$). Six weeks after ECT, MCI subjects more frequently showed (68.8%) a cognitive decline versus baseline ($P < .001$) than the other patient groups. Six months after ECT, one-third of subjects with dementia had a cognitive decline compared to baseline more frequently than the other 2 groups ($P = .036$).

The detailed development of the affective and cognitive symptoms in the 3 patient groups (NCI, MCI, and dementia) over the course of ECT is reported in Table 3 and Figure 1. After an initial (nonsignificant) cognitive deterioration in all 3 patient groups, the NCI group improved significantly 6 weeks ($P = .018$) and 6 months ($P = .027$) after the last ECT (compared to baseline). In the MCI group, cognitive symptoms improved significantly ($P = .036$) from baseline 6 months after the ECT course. In the group of patients with dementia, the mean MMSE scores also improved continuously over the course of ECT, but this improvement in score was not significant. Furthermore, demented patients with antidementia treatment improved in cognition to a numerically relevant extent (+4.2 points on MMSE) 6 weeks after ECT termination as compared to their baseline scores, whereas cognition in demented subjects without antidementia treatment deteriorated (−1 point); however, both changes in cognition were not significant (dementia without antidementia treatment $P = .264$, dementia with antidementia treatment $P = .639$).

Affective symptoms remitted almost completely 6 weeks after termination of ECT, with highly significant reductions in the HDRS-21 scores ($P < .0001$), regardless of the patient's initial cognitive status.

Prediction of Cognitive Decline Under ECT

According to logistic regression analysis, pre-ECT cognitive deficits were the best predictor of MMSE score decline from baseline at the follow-up time point 6 weeks after the last ECT treatment ($P = .007$) and with a trend to statistical significance from baseline to 6 months after the last ECT ($P = .055$). The predictive accuracy could not be further enhanced by adding another predictor.

DISCUSSION

Our data show that ECT does not induce cognitive deficits in geriatric patients, irrespective of preexisting cognitive impairment (MCI or Alzheimer's disease). In agreement with recent literature, all cognitive side effects after the sixth ECT were reversible and transient, even in dementia subjects. Second, geriatric depression was treated effectively, as has been shown before.[4,26–28] Third, the cognitive performance of NCI depressed elderly patients improved. Preexisting cognitive deficits were the best clinical predictor of a reversible cognitive decline. An additional observation was that demented subjects numerically improved cognitively in the short term, if treated with antidementia drugs, while untreated demented subjects declined.

We investigated a large and fairly homogeneous clinical case series with comparable severity of depression between the groups and with long-term follow-up. They were all elderly depressed patients with or without a preexisting cognitive impairment or dementia. The sample included old (age > 65 years) and old-old (age > 85 years) patients. All patients underwent ECT for the first time in their life. During treatment, they were inpatients in a tertiary specialized referral center, receiving state-of-the-art gerontopsychiatric care. Such studies are rare and of strong clinical relevance[29] because (1) ECT represents an effective treatment option for this patient population, although (2) it could confer high risks of cognitive side effects due to the increased vulnerability of the brain, mainly because of coexisting cerebrovascular

Table 3. Development of Affective and Cognitive Symptoms in 3 Groups of Patients Over the Course of ECT: NCI, MCI, and Dementia

	Dementia Without Antidementia Drug Treatment		Dementia With Antidementia Drug Treatment		Dementia		NCI		MCI	
	Observed Cases	LOCF	Observed Cases	LOCF	Observed Cases	LOCF	Observed Cases	LOCF	Observed Cases	LOCF
Initial MMSE vs MMSE after sixth ECT										
n	6	6	4	5	10	11	13	13	18	18
Initial MMSE score, mean ± SD	22.5 ± 3.2	22.5 ± 3.2	22.8 ± 6.9	23.0 ± 6.0	22.6 ± 4.6	22.7 ± 4.4	27.6 ± 1.9	27.6 ± 1.9	23.6 ± 6.3	23.6 ± 6.3
MMSE score after sixth ECT, mean ± SD	20.2 ± 1.8	20.2 ± 1.8	25.5 ± 2.1	25.2 ± 2.1	22.3 ± 3.3	22.5 ± 3.2	27.4 ± 2.0	27.4 ± 2.0	22.3 ± 5.5	22.3 ± 5.5
t	2.150	2.150	−1.000	−1.000	0.208	0.209	0.524	0.524	0.648	0.648
df	5	5	3	4	9	10	12	12	17	17
P (2-sided)	.084	.084	.391	.374	.840	.839	.610	.610	.526	.526
Initial MMSE vs MMSE 6 wk after ECT										
n	6	6	5	5	11	11	13	13	16	18
Initial MMSE score, mean ± SD	22.5 ± 3.2	22.5 ± 3.2	23.0 ± 6.0	23.0 ± 6.0	22.7 ± 4.4	22.7 ± 4.4	27.6 ± 1.9	27.6 ± 1.9	23.1 ± 6.5	23.6 ± 6.3
MMSE score 6 wk after ECT, mean ± SD	21.5 ± 2.7	21.5 ± 2.7	27.2 ± 2.2	27.2 ± 2.2	24.1 ± 3.8	24.1 ± 3.8	29.2 ± 0.8	29.2 ± 0.8	23.9 ± 4.2	23.9 ± 4.0
t	0.605	0.605	−1.510	−1.510	−0.812	−0.812	−2.739	−2.739	−0.365	−0.180
df	5	5	4	4	10	10	12	12	15	17
P (2-sided)	.572	.572	.206	.206	.436	.436	.018	.018	.720	.859
Initial MMSE vs MMSE 6 mo after ECT										
n	4	6	2	5	6	11	8	13	10	18
Initial MMSE score, mean ± SD	22.5 ± 3.3	22.5 ± 3.3	22.0 ± 9.9	23.0 ± 6.0	22.1 ± 5.1	22.7 ± 4.4	27.3 ± 2.1	27.6 ± 1.9	23.5 ± 5.3	23.6 ± 6.3
MMSE score 6 mo after ECT, mean ± SD	26.3 ± 3.1	24.8 ± 3.5	25.5 ± 2.1	26.4 ± 2.3	26.0 ± 2.6	25.6 ± 3.0	29.4 ± 0.7	29.3 ± 0.8	26.8 ± 3.3	25.3 ± 4.0
t	−1.372	−1.091	−0.636	−1.245	−1.645	−1.737	−2.229	−2.513	−2.459	−1.074
df	3	5	1	4	5	10	7	12	9	17
P (2-sided)	.264	.325	.639	.281	.161	.113	.061	.027	.036	.298
Initial HDRS-21 vs HDRS-21 6 wk after ECT										
n	7	7	5	5	12	12	13	13	19	19
Initial HDRS-21 score, mean ± SD	28.4 ± 7.8	28.4 ± 7.8	26.6 ± 5.4	26.6 ± 5.4	27.7 ± 6.7	27.7 ± 6.7	30.1 ± 5.2	30.1 ± 5.2	27.8 ± 7.1	27.8 ± 7.1
HDRS-21 score 6 wk after ECT, mean ± SD	8.1 ± 4.4	8.1 ± 4.4	8.6 ± 3.9	8.6 ± 3.9	8.3 ± 4.0	8.3 ± 4.0	8.3 ± 3.5	8.3 ± 3.5	9.2 ± 4.7	9.2 ± 4.7
t	6.731	6.731	5.400	5.400	8.916	8.916	14.206	14.206	10.651	10.651
df	6	6	4	4	11	11	12	12	18	18
P (2-sided)	.001	.001	.006	.006	< .001	< .001	< .001	< .001	< .001	< .001

Abbreviations: ECT = electroconvulsive therapy, HDRS-21 = 21-item Hamilton Depression Rating Scale, LOCF = last observation carried forward, MCI = mild cognitive impairment, MMSE = Mini-Mental State Examination, NCI = no cognitive impairment.

and/or neurodegenerative disorder. So far, no controlled empirical data exist.

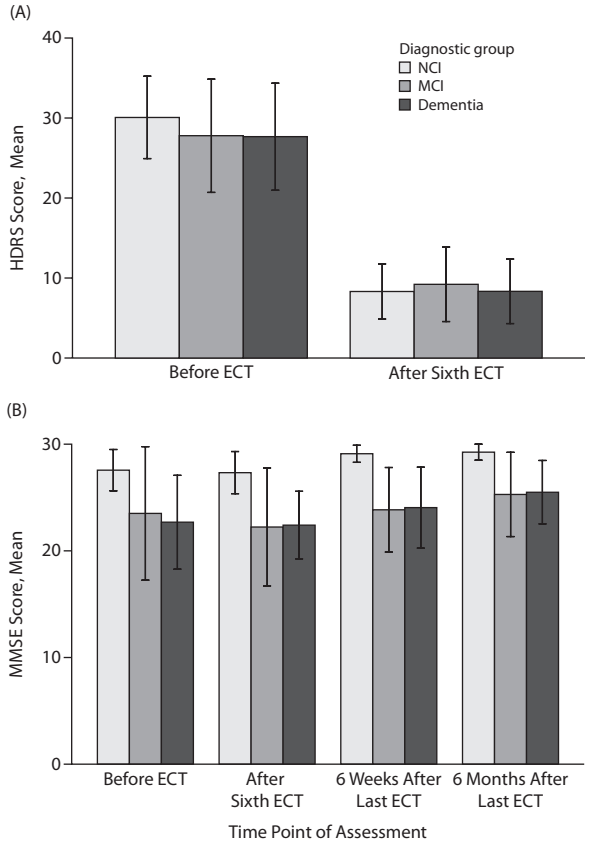
The effects of ECT on cognition in elderly depressed patients are still discussed controversially. Factors contributing to the variability of results include the inclusion or exclusion of patients with preexisting dementia, generally small sample sizes, and uncontrolled study designs; the lack of discrimination between electrode placements; and the use of tests insensitive to subtle cognitive changes.[30] However, our data prove that there is no long-term cognitive decline (time points 6 weeks and 6 months after ECT) induced by ECT in either group.

The significant improvement of cognitive functioning among the groups of nondemented elderly (cognitively healthy and MCI subjects) needs further comment: because of the larger variability of cognitive effects in cognitively impaired subjects (SD for MMSE mean score in the NCI group, 0.7–1.9; in the MCI group, 3.3–6.3; in the DEM group, 2.6–4.4), a larger sample size for the demented group would be required to demonstrate statistical significance. Generally, a larger sample size might detect further effects of ECT in subjects with cognitive impairment. The quantitative cognitive improvement in MCI and dementia was larger than in the NCI group (MMSE score difference in NCI, 1.8; in MCI, 2.9; in dementia, 3.3). Potential explanations may be the positive effects of ECT on the cognitive symptoms of depression in all groups (pseudodementia) and in particular in the groups with preexisting cognitive impairment.[27,31–35]

Because of the limitations of our study, these results have to be interpreted cautiously. The lack of a randomized controlled setting including a comparator group is a general limitation that restricts the interpretation of results to a comparison to the baseline condition. The small changes in the MMSE scores of the NCI depressed subjects may be partially due to ceiling effects of the MMSE in unimpaired subjects. With respect to the small group size, several practical difficulties limit the recruitment of depressed demented patients

© Copyright 2010 Physicians Postgraduate Press, Inc.

Figure 1. Time Course of HDRS-21 and MMSE Scores in NCI, MCI, and Dementia Patients



Abbreviations: ECT = electroconvulsive therapy, HDRS-21 = 21-item Hamilton Depression Rating Scale, MCI = mild cognitive impairment, MMSE = Mini-Mental State Examination, NCI = no cognitive impairment.

for a prospective study, making it difficult to demonstrate significant changes.[36] Furthermore, the degree of cognitive decline after the sixth ECT compared to baseline is smaller in NCI subjects than in the other groups (MMSE score difference in NCI, 0.2; in MCI, 1.3; in dementia, 0.4 points), but none of these can be regarded as clinically relevant. A larger proportion of patients with preexisting cognitive impairment experience a numerical cognitive drop during and after ECT compared to the patients without preexisting cognitive impairment, demonstrating a higher vulnerability of the patients to side effects of ECT, as had been reported before.[37] In summary, in this cohort including subjects aged 65 years and older with and without prediagnosed MCI or dementia, the cognitive side effects of ECT were transient and manageable.

Almost all patients in the sample achieved remission or at least response of the affective symptoms. Electroconvulsive therapy proved to be an effective antidepressant therapy in our cohort. In the literature, the remission rates under ECT for late-life depression amount to 70%–90% for depressive symptoms and, for depressive symptoms that had been treatment resistant to pharmacotherapy, 50%–70%.[38] In addition, some ECT studies report even higher response and remission rates for late-life depression than for depression in adulthood,[4,39] and ECT has been shown to be more efficacious than antidepressants in elderly people.[6]

In our study, the 5 of 12 depressed demented subjects receiving antidementia drugs during ECT improved in cognition, whereas the 7 of 12 subjects without antidementia drug therapy did not, or their cognition even deteriorated. Recent studies have shown that patients receiving an acetylcholinesterase inhibitor (ACHE-I) performed better on delayed memory and abstract reasoning following ECT and recovered more rapidly in personal memory,[40,41] potentially due to a functional reversal of reduced brain muscarinic cholinergic receptors under ECT.[40] The administration of physostigmine reversed the ECT-induced memory impairment,[43] and some case reports have suggested the usefulness of combining ACHE-I with ECT.[44,45] Antidementia drug treatment may protect against cognitive side effects in demented subjects treated with ECT against depression.

In our sample, the best predictor of a reversible cognitive decline after ECT was whether or not a patient had preexisting cognitive impairments. Age-associated comorbidities, but not age itself, increases the likelihood of ECT side effects in geriatric depressed subjects.[27] Most frequent among those age-related comorbidities are cerebrovascular brain lesions or cerebrovascular risk factors,[46] which are potentially involved in the etiology of depression in the elderly.[20,47]

In summary, the results of our investigation confirm that ECT is an effective treatment in geriatric depressed patients. In this group with treatment-resistant depression, depressive symptoms remitted partially or completely for the whole sample and all subgroups. Furthermore, ECT does not induce long-term cognitive deficits in subjects with and without preexisting cognitive impairment. So, ECT is safe and well tolerated in geriatric patients irrespective of preexisting cognitive impairment. This finding has implications for clinical practice.

Drug names: etomidate (Amidate and others), memantine (Namenda), rivastigmine (Exelon and others).

Author affiliations: Department of Geriatric Psychiatry (Drs Hausner, Damian, and Frölich) and Department of Psychiatry and Psychotherapy (Drs Hausner and Sartorius), Central Institute of Mental Health, Medical Faculty Mannheim, University of Heidelberg, Germany.

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

REFERENCES

1. Beekman AT, Copeland JR, Prince MJ. Review of community prevalence of depression in later life. *Br J Psychiatry*. 1999;174(4):307–311.
2. Van der Wurff FB, Stek ML, Hoogendijk WL, et al. Electroconvulsive therapy for the depressed elderly. *Cochrane Database Syst Rev*. 2003;(2):CD003593.
3. A. Sartorius, W. Hewer. Safe performance of ECT in severely ill patients: a retrospective study. *Eur J Psychiat*. 2007;21(4):237–247.
4. Tew JD Jr, Mulsant BH, Haskett RF, et al. Acute efficacy of ECT in the treatment of major depression in the old-old. *Am J Psychiatry*. 1999; 156(12):1865–1870.
5. Schneider LS, Olin JT. Efficacy of acute treatment for geriatric depression. *Int Psychogeriatr*. 1995;7(suppl):7–25.
6. Salzman C, Wong E, Wright BC. Drug and ECT treatment of

 © COPYRIGHT 2010 PHYSICIANS POSTGRADUATE PRESS, INC.

depression in the elderly, 1996–2001: a literature review. *Biol Psychiatry*. 2002;52(3):265–284.
7. Kellner CH, Knapp RG, Petrides G, et al. Continuation electroconvulsive therapy vs pharmacotherapy for relapse prevention in major depression: a multisite study from the Consortium for Research in Electroconvulsive Therapy (CORE). *Arch Gen Psychiatry*. 2006;63(12):1337–1344.
8. Vothknecht S, Kho KH, van Schaick HW, et al. Effects of maintenance electroconvulsive therapy on cognitive functions. *J ECT*. 2003;19(3): 151–157.
9. Sartorius A, Henn FA. [Treating depressive disorders with continuation electroconvulsive therapy] [(Article in German]. *Nervenarzt*. 2005; 76(11):1363–1369].
10. Agelink MW, Andrich J, Postert T, et al. Relation between electroconvulsive therapy, cognitive side effects, neuron specific enolase, and protein S-100. *J Neurol Neurosurg Psychiatry*. 2001;71(3):394–396.
11. Lisanby SH, Maddox JH, Prudic J, et al. The effects of electroconvulsive therapy on memory of autobiographical and public events. *Arch Gen Psychiatry*. 2000;57(6):581–590.
12. Sobin C, Sackeim HA, Prudic J, et al. Predictors of retrograde amnesia following ECT. *Am J Psychiatry*. 1995;152(7):995–1001.
13. Hihn H, Baune BT, Michael N, et al. Memory performance in severely depressed patients treated by electroconvulsive therapy. *J ECT*. 2006; 22(3):189–195.
14. Ng C, Schweitzer I, Alexopoulos P, et al. Efficacy and cognitive effects of right unilateral electroconvulsive therapy. *J ECT*. 2000;16(4):370–379.
15. Sackeim HA, Prudic J, Devanand DP, et al. Effects of stimulus intensity and electrode placement on the efficacy and cognitive effects of electroconvulsive therapy. *N Engl J Med*. 1993;328(12):839–846.
16. Fink M, Petrides G, Kellner C, et al; CORE Group. Change in seizure threshold during electroconvulsive therapy. *J ECT*. 2008;24(2):114–116.
17. Calev A, Nigal D, Shapira B, et al. Early and long-term effects of electroconvulsive therapy and depression on memory and other cognitive functions. *J Nerv Ment Dis*. 1991;179(9):526–533.
18. Philpot M, Treloar A, Gormley N, et al. Barriers to the use of electroconvulsive therapy in the elderly: a European survey. *Eur Psychiatry*. 2002; 17(1):41–45.
19. Alexopoulos GS, Meyers BS, Young RC, et al. 'Vascular depression' hypothesis. *Arch Gen Psychiatry*. 1997;54(10):915–922.
20. Katona CL. Psychotropics and drug interactions in the elderly patient. *Int J Geriatr Psychiatry*. 2001;16(suppl 1):S86–S90.
21. Woodhouse K, Wynne HA. Age-related changes in hepatic function. Implications for drug therapy. *Drugs Aging*. 1992;2(3):243–255.
22. McKhann G, Drachman D, Folstein M, et al. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. *Neurology.* 1984;34(7):939–944.
23. Winblad B, Palmer K, Kivipelto M, et al. Mild cognitive impairment—beyond controversies, towards a consensus: report of the International Working Group on Mild Cognitive Impairment. *J Intern Med*. 2004; 256(3):240–246.
24. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state." A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res.* 1975;12(3):189–198.
25. Hamilton M. A rating scale for depression. *J Neurol Neurosurg Psychiatry*. 1960;23(1):56–62.
26. Flint AJ, Gagnon N. Effective use of electroconvulsive therapy in late-life depression. *Can J Psychiatry*. 2002;47(8):734–741.
27. Wesson ML, Wilkinson AM, Anderson DN, et al. Does age predict the long-term outcome of depression treated with ECT? (a prospective study of the long-term outcome of ECT-treated depression with respect to age). *Int J Geriatr Psychiatry*. 1997;12(1):45–51.
28. Zervas IM, Calev A, Jandorf L, et al. Age-dependent effects of electroconvulsive therapy on memory. *Convuls Ther*. 1993;9(1):39–42.
29. Shanmugham B, Karp J, Drayer R, et al. Evidence-based pharmacologic interventions for geriatric depression. *Psychiatr Clin North Am*. 2005; 28(4):821–835, viii.
30. Gardner BK, O'Connor DW. A review of the cognitive effects of electroconvulsive therapy in older adults. *J ECT*. 2008;24(1):68–80.
31. American Psychiatric Association. Task Force on Electroconvulsive Therapy. The practice of ECT: recommendations for treatment, training and privileging. *Convuls Ther*. 1990;6(2):85–120.
32. Steffens DC, Otey E, Alexopoulos GS, et al. Perspectives on depression, mild cognitive impairment, and cognitive decline. *Arch Gen Psychiatry*. 2006;63(2):130–138.
33. Alexopoulos GS. Depression in the elderly. *Lancet*. 2005;365(9475): 1961–1970.
34. Kiosses DN, Alexopoulos GS. IADL functions, cognitive deficits, and severity of depression: a preliminary study. *Am J Geriatr Psychiatry*. 2005;13(3):244–249.
35. Alexopoulos GS. Clinical and biological interactions in affective and cognitive geriatric syndromes. *Am J Psychiatry*. 2003;160(5):811–814.
36. Amazon J, McNeely E, Lehr S, et al. The decision making process of older adults who elect to receive ECT. *J Psychosoc Nurs Ment Health Serv*. 2008;46(5):45–52.
37. Glass RM. Electroconvulsive therapy: time to bring it out of the shadows. *JAMA*. 2001;285(10):1346–1348.
38. Gormley N. ECT should be treatment option in all cases of refractory depression. *BMJ*. 1998;316(7126):233.
39. O'Connor MK, Knapp R, Husain M, et al. The influence of age on the response of major depression to electroconvulsive therapy: a CORE Report. *Am J Geriatr Psychiatry*. 2001;9(4):382–390.
40. Matthews JD, Blais M, Park L, et al. The impact of galantamine on cognition and mood during electroconvulsive therapy: a pilot study. *J Psychiatr Res*. 2008;42(7):526–531.
41. Prakash J, Kotwal A, Prabhu H. Therapeutic and prophylactic utility of the memory-enhancing drug donepezil hydrochloride on cognition of patients undergoing electroconvulsive therapy: a randomized controlled trial. *J ECT*. 2006;22(3):163–168.
42. Lerer B. Studies on the role of brain cholinergic systems in the therapeutic mechanisms and adverse effects of ECT and lithium. *Biol Psychiatry*. 1985;20(1):20–40.
43. Levin Y, Elizur A, Korczyn AD. Physostigmine improves ECT-induced memory disturbances. *Neurology*. 1987;37(5):871–875.
44. Zink M, Sartorius A, Lederbogen F, et al. Electroconvulsive therapy in a patient receiving rivastigmine. *J ECT*. 2002;18(3):162–164.
45. Boman B. Concurrent use of ECT and cholinesterase inhibitor medications. *Aust N Z J Psychiatry*. 2002;36(6):816.
46. Robinson RG. Poststroke depression: prevalence, diagnosis, treatment, and disease progression. *Biol Psychiatry*. 2003;54(3):376–387.
47. Krishnan KR, Hays JC, Blazer DG. MRI-defined vascular depression. *Am J Psychiatry*. 1997;154(4):497–501.

Editor's Note: We encourage authors to submit papers for consideration as a part of our Early Career Psychiatrists section. Please contact Marlene P. Freeman, MD, at mfreeman@psychiatrist.com.

© Copyright 2010 Physicians Postgraduate Press, Inc.