# Distinctive neurocognitive effects of repetitive transcranial magnetic stimulation and electroconvulsive therapy in major depression

SVENJA C. SCHULZE-RAUSCHENBACH, UTA HARMS, THOMAS E. SCHLAEPFER, WOLFGANG MAIER, PETER FALKAI and MICHAEL WAGNER

**Background** Studies have compared electroconvulsive therapy (ECT) and repetitive transcranial magnetic stimulation (rTMS) with regard to clinical efficacy in the treatment of depression, but no study has yet addressed the differential impact on cognition.

**Aims** To compare the neurocognitive effects of unilateral ECT and rTMS.

**Method** Thirty patients with treatment-refractory non-psychotic major depression received an average of ten treatments with either unilateral ECT or left prefrontal rTMS and were assessed for objective and subjective cognitive impairments before and about a week after treatment.

**Results** Treatment response was comparable (46% of the ECT group and 44% of the rTMS group showed a reduction of 50% or more in Hamilton Rating Scale for Depression scores). In patients treated with rTMS, cognitive performance remained constant or improved and memory complaints alleviated, whereas in the ECT group memory recall deficits emerged and memory complaints remained.

**Conclusions** In contrast to unilateral ECT, rTMS has no adverse memory effects.

**Declaration of interest** None.

Electroconvulsive therapy (ECT) is highly effective in the treatment of severe depression (UK ECT Review Group, 2003). During the past decade, transcranial magnetic stimulation has emerged as a new antidepressant treatment (e.g. Berman et al, 2000). Some randomised trials suggest that repetitive transcranial magnetic stimulation (rTMS) might be as effective as ECT in the treatment of non-psychotic depression (Grunhaus et al, 2000, 2003; Janicak et al, 2002). However, recent reviews and metaanalyses show temperate enthusiasm for transcranial magnetic stimulation as an alternative to ECT (e.g. Martin et al, 2003; Schlaepfer et al, 2003) and emphasise the need for further studies.

In weighing the benefits and risks of different treatment methods, cognitive sideeffects are an important issue. Electroconvulsive therapy has been shown to induce anterograde amnesia, retrograde amnesia and subjective memory complaints (e.g. Squire & Slater, 1983; Lisanby et al, 2000). Although such deficits tend to cease within weeks to months, a review of patients' perspectives on ECT (Rose et al, 2003) indicates that persistent memory impairment following this therapy may be more frequent than is evident from testing with standard neuropsychological batteries. In contrast, rTMS seems not to have any substantial cognitive side-effects (e.g. Triggs et al, 1999). However, a comprehensive comparison of cognitive side-effects is lacking so far.

#### **METHOD**

#### **Participants**

Thirty patients referred to the Psychiatric University Hospital of Bonn with treatment-resistant, non-psychotic major depressive disorder participated in the study. All patients met the following inclusion criteria:

- (a) a DSM-IV diagnosis of major depressive disorder (American Psychiatric Association, 1994), as assessed by an experienced clinical psychiatrist;
- (b) no additional Axis I diagnosis;
- (c) unsuccessful treatment response to at least two different types of antidepressants, each given in a sufficient dosage range for at least 4 weeks;
- (d) age over 18 years;
- (e) no previous treatment with ECT or rTMS.

The patient sample consisted of 16 men and 14 women; the average age was 47 years (range 25–69) (Table 1).

All patients were referred for ECT or rTMS at the University Hospital of Bonn after prior treatments with antidepressant drugs had failed. The department offers both of these therapies, and is one of only a few specialised treatment centres in Germany to do so. All participants approached our clinic with the speciwish - or a referring doctor's recommendation - to receive either rTMS or ECT, and received the treatment of their choice if no clinical exclusion criterion was present. The study consisted of consecutively admitted cases within a specified period, going into either the rTMS or the ECT group with comparable likelihood. Fourteen patients were treated with ECT and 16 received rTMS. The two groups did not show significant differences on any of the variables measured; most importantly, they were comparable with regard to age, gender, level of depression, level of education and verbal IQ (Table 1). Furthermore, the cognitive status levels of the two groups at baseline were almost identical, allowing us to study the changes induced by ECT or rTMS. All participants gave informed consent to repeated neurocognitive assessment.

In order to disentangle treatment-related changes in performance from test repetition effects, a control group of 15 healthy volunteers, matched by age, gender, level of education and verbal IQ to the patient groups (see Table 1), was also assessed twice, with the same interval between testings as the patients.

# Clinical ratings and neuropsychological tasks

Patients and controls were assessed with an extensive test battery before and about a week after completion of the treatment.

Table I Demographic and clinical variables

	ECT group (n=14)	rTMS group (n=16)	Control group (n=15)	ECT v. rTMS P <sup>i</sup>	Patients v. controls
Age, years: mean (s.d.)	46.7 (11.0)	47.7 (13.1)	48.9 (13.8)	0.828 <sup>2</sup>	0.6722
Gender, n					
Male	7	9	8	0.7323	1.0003
Female	7	7	7		
HRSD score: mean (s.d.)	22.3 (3.0)	21.3 (3.5)		0.3932	
Level of education, n					
No graduation	0	0	1	0.8493	0.280 <sup>3</sup>
Elementary school	6	9	4		
Secondary school	3	3	3		
A-levels	3	3	3		
A-levels and course of studies	2	1	4		
Verbal IQ (WST score): mean (s.d.)	101.9 (17.0)	99.9 (16.6)	108.2 (17.5)	0.7792	0.1872

ECT, electroconvulsive therapy; HRSD, Hamilton Rating Scale for Depression; rTMS, repetitive transcranial magnetic stimulation; WST, Wortschatztest (Schmidt & Metzler, 1992).

Pre-treatment testing took place 1-3 days before the first treatment session, and the post-treatment testing was done 8.8 days on average after the last ECT or rTMS session with equal intervals between the last treatment and post-treatment testing for both groups (P=0.68, NS). The clinical effects of ECT and rTMS were assessed using the 17-item Hamilton Rating Scale for Depression (HRSD; Hamilton, 1967; German version by the Collegium Internationale Psychiatriae Scalarum, 1978) and the Beck Depression Inventory (BDI; Beck et al, 1961; German version by Hautzinger et al, 1994). The ratings were made by the treating clinical psychiatrist. Cognitive effects of ECT and rTMS were assessed with a comprehensive neuropsychological battery (see Appendix) with special emphasis on memory functions. Cognitive testing was done by psychologist masked to the treatment assignments.

### **Treatments**

## Electroconvulsive therapy

Electroconvulsive therapy was given in accordance with current clinical guidelines (American Psychiatric Association, 1990; Folkerts, 1997), using a Thymatron III DG stimulator (Somatics Inc., Illinois, USA), which delivers a brief-pulse bi-directional current. All treatments were given under anaesthesia with propofol (2 mg/kg), muscle relaxation with

suxamethonium (1 mg/kg) and 100% oxygenation. Medication was not changed during treatment. Antidepressants, low-potency neuroleptics and benzodiazepine hypnotics were allowed. Stimulation was always unilateral on the right hemisphere (all patients were reported to be right-handed for several manual activities). Seizure threshold was determined by a titration method and was age-based. Stimulation intensity was 2-2.5 times the seizure threshold. Therapy was given twice-weekly with a minimum interval of 48 h between treatments. Decisions concerning the number of treatments were made by the psychiatrist in attendance; participants received a mean of 9.9 (s.d.=2.7) treatments.

# Transcranial magnetic stimulation

Transcranial magnetic stimulation was given with a Magstim Rapid machine (Magstim Co. Ltd, Whitland, UK). To make the frequencies of ECT and rTMS comparable, patients were treated two or three times per week; they received a mean of 10.8 (s.d.=1.4) treatments. Medication was kept constant as well. Stimulation was applied over the left dorsolateral prefrontal cortex with an intensity of 100% and a frequency of 10 Hz (20-30 trains of 2 s duration per treatment session, 5 s intertrain interval). Stimulation frequency was identical to that in previous studies comparing rTMS and ECT (Grunhaus et al, 2000, 2003; Janicak et al, 2002).

#### Data analysis

Data analysis was done using the Statistical Package for the Social Sciences, for Windows version 10.0. To compare the two treatment methods, analyses of variance (ANOVAs) with repeated-measures, between-group t-tests (Welch-corrected for unequal variances) and within-group t-tests were performed. In addition, the numbers of responders in both groups were compared using a chi-squared test. Patients were considered to be responders to treatment if their HRSD scores had decreased by at least 50% from baseline levels. One person in the ECT group withdrew from the study because of severe orientation and memory problems after two ECT treatments; these data were not included in the analysis.

#### **RESULTS**

#### **Clinical effectiveness**

Both treatment methods resulted in a marked reduction of depression, as assessed by HRSD score, BDI score and response rates. In the ECT group the mean HRSD scores decreased by 35% from 22.4 (s.d.=3.1) to 14.5 (s.d.=5.7), P<0.001. In the rTMS group the mean HRSD score decreased by 39%, from 21.3 (s.d.=3.5) to 13.0 (s.d.=4.9), P < 0.001 (Fig. 1). The ANOVA showed a significant time effect  $(F_{(1,27)}=65.25, P<0.001)$ , but no group effect and no interaction. Similar results were found for self-ratings of depression on the BDI. In the ECT group the mean BDI scores decreased by 7.6 points (24%) and in the rTMS group the decrease was 6.4 points (27%). The ANOVA revealed a significant time effect  $(F_{(1,24)}=8.40,$ P < 0.008), but no significant group effect and no interaction.

Patients were considered to be responders to treatment if their final HRSD score had decreased by 50% or more from baseline. According to this criterion, 46% of the ECT group and 44% of the rTMS group were treatment responders ( $\chi^2_{(1)}$ =0.02, P=0.90, NS).

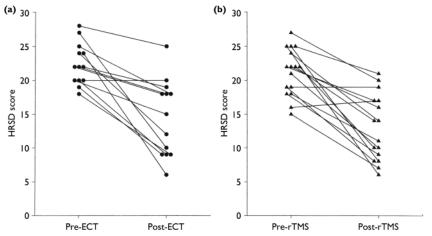
# **Neuropsychological effects**

Before treatment, the two groups with depressive disorder did not differ from each other on any of the neuropsychological measures (Table 2). After treatment, significant differences between the ECT and rTMS treatment groups emerged for specific memory functions; these differences

I. All P values not significant.

<sup>2.</sup> t-test.

<sup>3.</sup>  $\chi^2$  test.



**Fig. 1** Clinical improvement shown by reductions in Hamilton Rating Scale for Depression (HRSD) scores following (a) electroconvulsive therapy (ECT) and (b) transcranial magnetic stimulation (rTMS).

Table 2 Cognitive measures in the three study groups

were consistently in favour of rTMS. Significant differences between patient groups after treatment were found in five measures of long-term memory recall or recognition, but not for any non-memory measure (Table 2).

#### Anterograde memory function

Significant differences to the disadvantage of ECT were found in two variables of the Auditory Verbal Learning Test (AVLT; Rey, 1964): loss after interference (trial 5 minus trial 6) and loss after delay (trial 5 minus trial 7). In the ANOVA, the group × time interaction was significant for both measures ( $F_{(1,23)}$ =7.81, P=0.010

Measure <sup>1</sup> -	Test scores: mean (s.d.)								
	Control group		ECT g	ECT group		rTMS group		t-test: ECT v. rTMS <sup>2</sup>	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	
Learning and anterograde memory  AVLT									
Immediate recall (trials I-5)	59.4 (10.0)	62.0 (11.0)	42.1 (8.5)	46.7 (8.5)	39.6 (10.0)	44.2 (14.4)	NS	NS	
Recall after interference (trial 5 minus trial 6)	1.2 (1.2)	0.8 (1.3)	2.8 (2.2)	3.9 (1.9)	3.2 (1.9)	1.8 (2.0)	NS	**	
Recall after delay (trial 5 minus trial 7)	1.1 (1.6)	0.1 (0.6)	2.4 (1.8)	4.2 (1.6)	3.2 (1.6)	2.4 (2.0)	NS	*	
Recognition hits	14.4 (1.4)	14.1 (2.0)	12.8 (2.1)	12.7 (1.8)	13.2 (1.9)	12.6 (2.6)	NS	NS	
Recognition false alarms	0.3 (1.3)	0.1 (0.4)	4.4 (5.8)	4.9 (6.1)	6.1 (5.9)	5.5 (6.2)	NS	NS	
MPT	0.5 (1.5)	0.1 (0.1)	1.1 (3.0)	1.7 (0.1)	0.1 (3.7)	3.3 (0.2)			
Recall trial 3	20.3 (4.9)	20.3 (4.5)	11.4 (5.9)	10.7 (5.9)	13.2 (6.9)	12.2 (7.2)	NS	NS	
Delayed recall	18.9 (5.3)	19.2 (4.1)	9.5 (4.7)	8.2 (4.5)	11.9 (6.7)	10.9 (6.8)	NS	NS	
Retrograde memory	,		, ,		,	()			
Retrograde AVLT									
Recall		4.3 (3.7)		2.5 (2.6)		1.7 (2.2)	NA	NS	
Recognition hits		12.5 (2.1)		10.8 (2.5)		9.3 (3.5)	NA	NS	
Recognition false alarms		1.8 (1.6)		5.0 (3.0)		1.1 (1.1)	NA	*	
Four-card task									
Free recall		2.0 (1.4)		0.4 (0.5)		1.4 (1.2)	NA	*	
Recognition		3.1 (0.7)		2.3 (0.7)		2.6 (0.5)	NA	NS	
AMI									
Recall score	27.3 (2.2)	27.9 (2.3)	26.9 (1.8)	26.6 (2.4)	26.3 (2.6)	27.0 (2.6)	NS	NS	
Subjective memory									
SSMQ	2.7 (10.2)	2.3 (8.0)	<b>– 20.7 (19.0)</b>	— I5.2 (25.2)	- 16.8 (16.9)	3.8 (11.8)	NS	*	
Other cognitive functions									
MMSE	29.1 (1.0)	29.2 (1.1)	27.9 (1.7)	28.3 (1.3)	26.9 (3.4)	27.9 (3.0)	NS	NS	
Trail Making Test A	37 (19)	36 (18)	56 (24)	53 (22)	51 (32)	51 (32)	NS	NS	
Trail Making Test B	82 (39)	76 (34)	162 (134)	144 (96)	164 (149)	161 (149)	NS	NS	
Digit span (WAIS-R)	17.1 (4.8)	18.1 (4.6)	12.6 (3.0)	13.7 (4.1)	11.3 (3.0)	12.8 (4.5)	NS	NS	
Letter-number span	18.2 (2.7)	18.9 (3.4)	14.1 (3.4)	13.9 (3.6)	13.0 (3.9)	13.0 (5.1)	NS	NS	
Word fluency (LPS)	40.0 (15.1)	39.9 (14.7)	29.6 (11.2)	27.9 (10.1)	29.3 (11.2)	28.5 (9.9)	NS	NS	

AMI, Autobiographical Memory Interview; AVLT, Auditory Verbal Learning Test; ECT, electroconvulsive therapy; LPS, Leistungs-Prüf-System; MMSE, Mini-Mental State Examination; MPT, Memory for Persons Test; NA, not applicable; NS, not significant; rTMS, repetitive transcranial magnetic stimulation; SSMQ, Squire Subjective Memory Questionnaire; WAIS-R, Wechsler Adult Intelligence Scale — Revised.

<sup>\*</sup>P < 0.05, \*\*P < 0.01.

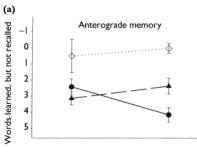
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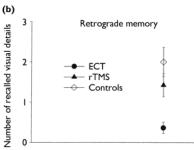
<sup>2.</sup> Contrasts at baseline and about I week after treatment.

and  $F_{(1,23)}$ =15.56, P=0.001), whereas the effects of time and group were not significant (Fig. 2(a)).

#### Retrograde memory function

After treatment, participants in the ECT group made significantly more errors than those in the rTMS group in recognising words learned before treatment (P=0.025). After treatment, they also recalled significantly fewer items from the visual card task administered before treatment, compared with the rTMS group (P=0.012) (Fig. 2(b)).





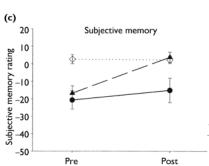


Fig. 2 Memory functions and memory complaints before (Pre) and about I week after (Post) treatment with electroconvulsive therapy (ECT) or repetitive transcranial magnetic stimulation (rTMS). Control group participants were tested twice at comparable intervals. (a) Anterograde memory: Auditory Verbal Learning Test, delayed recall, trial 5 minus trial 7. (b) Retrograde memory (four-card task): recall of visual material seen before treatment. (c) Subjective memory, relative to premorbid state (patients) or relative to I year earlier (controls): Squire Subjective Memory Questionnaire score (0, normal memory). Means and standard errors are shown.

#### Subjective memory complaints

After treatment, participants given ECT reported no change in memory problems compared with before treatment (P=0.38, NS), whereas the rTMS patients judged their own memory much more positively after treatment (P=0.002). The ANOVA of the subjective memory measure showed a significant time effect (F<sub>(1,23)</sub>=11.04, P=0.003) and a group×time interaction approaching significance (F<sub>(1,23)</sub>=3.68, P=0.067) in the absence of any group effect (Fig. 2(c)).

In summary, significant between-group differences were found in anterograde verbal memory, in two retrograde memory parameters and in participants' subjective estimation of their own memory abilities. In contrast to memory, other cognitive functions measured remained constant in both treatment groups; we found no significant group, time or interaction effect in these variables (Table 2).

# Association of memory and depression

Weiner et al (1986) found no relationship between subjective and objective memory measures in patients given ECT, and concluded that self-rated memory changes may be more a function of clinical symptoms than of objectively demonstrable changes in memory function. We explored this issue, correlating the subjective memory complaints, rated with the Squire Subjective Memory Questionnaire (Squire et al, 1979), with the level of depression (BDI and HRSD scores) and with the assessed neuropsychological variables. The patients' memory complaints correlated with depression as well as with several cognitive measures. The patients' self-ratings of memory functions correlated significantly with their self-ratings of depression (BDI: r = -0.67, P < 0.01), but less so with the clinician ratings of depression (HRSD: r=-0.31, P=0.13). Self-rating of memory also correlated with the ability to learn and recall new verbal and visual material (AVLT sum of trials 1-5: r=0.42, P < 0.05; AVLT trial 7 after delay: r=0.46, P<0.05; Memory for Persons Test, delayed recall, r=0.48, P<0.05), and with the ability to correctly recognise words learned before treatment (retrograde AVLT, false alarms: r = -0.61, P < 0.05), but not with their autobiographical memory (r=0.07, P=0.75, NS). Importantly, the correlations between subjective and objective memory did not change markedly when controlling for self-rated (BDI) depression by partial correlations.

#### Comparison with healthy controls

The group of healthy controls was included to control for test repetition effects and to see whether (and which) impaired cognitive functions would return to normal levels after treatment in both groups. A comparison of the cognitive functions of the participants with depression and the healthy controls at baseline showed highly significant deficits on the part of the patients in almost all measures. Repeated-measures ANOVAs comparing each treatment group separately with the healthy control group revealed that the performance gap between the ECT and control groups with regard to anterograde memory increased (group × time interaction, P < 0.05 for recall after interference and P < 0.001 for recall after delay). In contrast, the difference between the rTMS and control groups remained unchanged (the group × time interactions were not significant).

After treatment, the ECT and control groups differed considerably in their ability to remember words or cards from pretreatment testing (retrograde AVLT: P=0.049; four-card task: P=0.001), whereas the rTMS group showed retrograde memory functions identical to those of the control group (retrograde AVLT: P=0.33, NS; four-card task: P=0.26, NS). Similarly, the self-rating of memory functions by the rTMS group differed significantly from that in the control group only before treatment (P=0.001); after treatment the rTMS group rated their memory functions to be as good as those of the healthy group (P=0.69, NS). In contrast, the ECT group rated their memory abilities more negatively than the control group both before (P=0.001) and after treatment (P=0.039). The group×time interaction in the ANOVA comparing control and rTMS groups was significant (P < 0.001), but this interaction was not significant in the ANOVA comparing the control and ECT groups (P=0.30, NS).

#### **DISCUSSION**

The major conclusion to be drawn from this study pertains to the cognitive effects of unilateral ECT and left prefrontal rTMS in patients with severe depression, since this study was designed to assess these effects with sensitive neuropsychological measures. Because the antidepressant effect of both treatments was identical, and the groups did not differ prior to treatment, the cognitive changes over time and the post-treatment group differences can be attributed to the different treatments. In the ECT group, not a single cognitive variable improved after treatment, and the recall of newly learned material even became worse. In the rTMS group, some objective memory measures and the subjective memory rating improved in parallel with the improvement in mood, and reached normal performance levels.

# Clinical effectiveness of ECT and rTMS

The two treatments appeared to be clinically equivalent in this group of patients with treatment-resistant, non-psychotic depression. Although the study was not randomised, its finding of comparable antidepressant efficacy of ECT and rTMS is in line with the results of all three randomised comparison studies published so far (Grunhaus et al, 2000, 2003; Janicak et al, 2002). The rates of those responding to unilateral ECT are in the expected range for medication-resistant non-psychotic depression (McCall, 2001), but might have been higher if a higher ECT dosage had been used (Sackeim et al, 2000). However, a higher dosage would probably increase the risk of cognitive adverse effects. A definitive answer to the question of clinical equipotency of ECT and rTMS will have to await further studies.

#### **Anterograde memory**

Patients treated with ECT showed more anterograde memory problems at the posttreatment assessment than did either patients treated with rTMS or healthy controls. In particular, they remembered fewer words only after learning the interference word list of the Auditory Verbal Learning Test (between Trials 5 and 6 of the AVLT), indicating a recall deficit rather than a working memory or learning deficit. This extends findings by Hasse-Sander et al (1998), who reported impaired verbal delayed recall 1-2 days after unilateral ECT (no longer follow-up was made), and of Cronholm & Ottosson (1961), who described specific deficits in the delayed recall of newly learned words, figures and persons 1 week after bilateral ECT. For the rTMS group, the lack of anterograde memory effects is in line with previous studies (e.g. Triggs et al, 1999).

### **Retrograde memory**

The ECT patients, in contrast to the patients treated with rTMS or the control group, also showed retrograde memory problems after treatment. They remembered fewer of the pictures and made more errors in recalling words learned before treatment. No difference emerged for autobiographical memory, which is in line with previous studies demonstrating deficits in recall of past events only after bilateral ECT, not after unilateral therapy (Squire et al, 1981; Weiner et al, 1986; Lisanby et al, 2000). The verbal and visual retrograde memory tasks used here might be more sensitive to ECT-induced impairments than the Autobiographical Memory Interview, possibly because recent memory traces formed during the days before treatment are more vulnerable to ECT effects than are more remote memories (Squire et al, 1981; Lisanby et al, 2000).

#### **Subjective memory**

After treatment, the ECT patients complained more about memory problems than the rTMS patients and the controls. Squire et al (1979), Freeman et al (1980) and Squire & Slater (1983) also found subjective cognitive side-effects after ECT. After rTMS the patients' subjective memory ratings equalled those of the healthy controls, whereas after ECT the patients' ratings were very negative. This group difference cannot be explained by different clinical effects of the two treatment methods. At least in part, this group difference in subjective memory appears to be related to objectively measurable memory impairments after ECT, because the subjective memory functions not only correlated with the level of depression, which is a common finding (e.g. Weiner et al, 1986), but also with several objective memory measures (even when statistically controlling for the level of depression). Associations between subjective and objective memory measures after ECT have often found to be lacking (e.g. Prudic et al 2000), but some studies suggest that such a relationship may exist, at least for certain forms of memory and for specific periods after ECT (e.g. Freeman et al, 1980). Thus, complaints of patients about memory deficits (metamemory) may partly result from the experience of objective memory

failures after ECT, and should not be dismissed as being simply a sign of depressive complaints.

#### **Clinical implications**

With regard to objective and subjective memory function, patients with severe depression appear to be cognitively better off 1 week after a course of rTMS than 1 week after a course of unilateral ECT. despite (in this study) an indistinguishable antidepressive effect of the two treatments. Adverse memory effects after ECT may fully resolve after a longer interval, usually after several months (Weeks et al, 1980); nevertheless, if rTMS evolves into an alternative treatment for some forms of medication-resistant depression, clinicians and patients should be aware of its reduced risk for adverse memory effects, compared with unilateral ECT. Future comparison studies of ECT, rTMS and magnetic seizure therapy (Kosel et al, 2003) should include sensitive memory assessments and longer follow-up intervals to evaluate fully the ratio of benefits and risks of these treatment methods.

### Limitations

Because our study lacked a sham-treated patient control group and patients were not randomly assigned to treatments, no conclusion should be drawn regarding the absolute or relative antidepressant effectiveness of rTMS or ECT. Although the pattern of cognitive findings, in line with previous work, suggests that unilateral ECT, in contrast to rTMS, specifically impairs several aspects of memory for at least a week after a treatment series, the small number of participants in our study renders this a preliminary finding requiring confirmation in other samples.

#### **APPENDIX**

# **Neurocognitive test battery**

Learning and anterograde memory function

- (a) Auditory Verbal Learning Test (AVLT; Rey, 1964); German version by Helmstaedter et al (2001).
- (b) Memory for Persons Test (Bulla-Hellwig & Spanhofer, 1996); a German visual memory test in which each of 12 different faces has to be associated with a name and an occupation.

## Retrograde memory function

(a) Autobiographical Memory Interview (Kopelman et al, 1990); shortened German version.

- (b) Retrograde AVLT: at the post-treatment assessment participants were asked to recall the I5 AVLT words they had learned before treatment. The task involved a free recall and a recognition task. This measure was introduced after the study began, therefore only data from I3 patients (6 receiving electroconvulsive therapy, 7 repetitive transcranial magnetic stimulation) and I5 controls were available.
- (c) Four-card task: before treatment, participants were asked to reproduce a demonstrated arrangement of four picture cards from the Rivermead Behavioural Memory Test (Wilson et al, 1991); after treatment they were asked details about the 'test with cards' (number of cards, kind of task, recall and recognition of depicted objects), and the number of correct details was scored.

# Subjective memory function

Squire Subjective Memory Questionnaire (Squire et al, 1979): this 18-item self-rated scale of memory functions comprises items such as 'My ability to hold in my memory things that I have learned is...'. Respondents were asked to compare their present memory with their memory before they became ill (patients) or with their memory I year ago (controls), on a nine-point scale from -4 (worse than before) to +4 (better than before).

#### Other neurocognitive functions

- (a) Mini-Mental State Examination (Folstein et al, 1975); German version by Kessler et al (1990).
- (b) Trail MakingTest A and B (Reitan, 1979).
- (c) Digit span: Wechsler Adult Intelligence Scale Revised (Wechsler, 1981).
- (d) Letter-number span (Gold et al, 1997).
- (e) Word fluency: Leistungs-Prüf-System (Horn, 1983).

# **REFERENCES**

American Psychiatric Association (1990) The Practice of Electroconvulsive Therapy: Recommendations for Treatment, Training and Privileging. A Task Force Report. Washington, DC: APA.

American Psychiatric Association (1994) Diagnostic and Statistical Manual of Mental Disorders (4th edn) (DSM-IV). Washington, DC: APA.

**Beck, A.T., Ward, C. H., Mendelson, M., et al (1961)** An inventory for measuring depression. *Archives of General Psychiatry*, **4**, 561–571.

**Berman, R. M., Narasimhan, M., Sanacora, G., et al** (2000) A randomized clinical trial of repetitive transcranial magnetic stimulation in the treatment of major depression. *Biological Psychiatry*, **57**, 332–337.

**Bulla-Hellwig, M. & Spanhofer, D. (1996)** Der Gedächtnis für Personen Test. Theoretischer Hintergrund und Materialentwicklung zweier Parallelformen zur alltagsnahen Gedächtnisprüfung. Zeitschrift für Neuropsychologie, **7**, 16–24.

**Collegium Internationale Psychiatriae Scalarum (eds) (1978)** *Internationale Skalen für Psychiatrie.* Weinheim: Beltz Test Gesellschaft.

#### **CLINICAL IMPLICATIONS**

- In people with treatment-resistant depression, even unilateral electroconvulsive therapy (ECT) is associated with memory deficits I week after the last treatment.
- Repetitive transcranial magnetic stimulation is not accompanied by such memory impairments.
- Self-reported memory impairments after ECT can be related to objective memory deficits and must not be dismissed as being depressive complaints only.

#### LIMITATIONS

- Patient groups were not randomised and no patient control group was assessed, limiting conclusions about clinical efficacy.
- Sample sizes were small.
- There was no long-term follow-up.

SVENJA C. SCHULZE-RAUSCHENBACH, Dipl-Psych, MD, UTA HARMS, MD, THOMAS E. SCHLAEPFER, MD, WOLFGANG MAIER, MD, PETER FALKAI, MD, MICHAEL WAGNER, PhD, Department of Pschiatry, University of Bonn, Germany

Correspondence: Dr Michael Wagner, Department of Psychiatry, University of Bonn, Sigmund-Freud-Str. 25, D 53105 Bonn, Germany. Tel: +49 228 287 6377; fax: +49 228 287 6371; e-mail: michael.wagner@ukb.uni-bonn.de

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Cronholm, B. & Ottosson, J.-O. (1961) Memory functions in endogenous depression: before and after electroconvulsive therapy. *Archives of General Psychiatry*, **5**, 193–199.

Folkerts, H. (1997) Elektrokrampftherapie. Ein praktischer Leitfaden für die Klinik. Stuttgart: Enke.

Folstein, M. F., Folstein, S. E. & McHugh, P. R. (1975) 'Mini-Mental State'. A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research*, 12, 189–198.

Freeman, C. P., Weeks, D. & Kendell, R. E. (1980) ECT. II: Patients who complain. *British Journal of Psychiatry*, 137, 17–25.

Gold, J. M., Carpenter, C., Randolph, C., et al (1997) Auditory working memory and Wisconsin card sorting test performance in schizophrenia. Archives of General Psychiatry, 54, 159–165.

Grunhaus, L., Dannon, P. N., Schreiber, S., et al (2000) Repetitive transcranial magnetic stimulation is as effective as electroconvulsive therapy in the treatment of nondelusional major depressive disorder: an open study. Biological Psychiatry, 47, 314–324.

**Grunhaus, L., Schreiber, S., Dolberg, O.T., et al** (2003) A randomized controlled comparison of electroconvulsive therapy and repetitive transcranial magnetic stimulation in severe and resistant nonpsychotic major depression. *Biological Psychiatry*, **53**, 324–331.

**Hamilton, M. (1967)** Development of a rating scale for primary depressive illness. *British Journal of Clinical Psychiatry*, **6**, 278–296.

Hasse-Sander, I., Müller, H., Schurig, W., et al (1998) Auswirkungen der Elektrokrampftherapie auf die

kognitiven Funktionen bei therapieresistenten Depressionen. Nervenarzt, **69**, 609–616.

Hautzinger, M., Bailer, M., Worall, H., et al (1994) Beck-Depressions-Inventar. Testhandbuch. Bern: Huber.

Helmstaedter, C., Lendt, M. & Lux, S. (2001) Verbaler Lern- und Merkfähigkeitstest. Manual. Göttingen: Beltz.

**Horn, W. (1983)** *Leistungs-Prüf-System* (2nd edn). Göttingen: Hogrefe.

Janicak, P. G., Dowd, S. M., Martis, B., et al (2002) Repetitive transcranial magnetic stimulation versus electroconvulsive therapy for major depression: preliminary results of a randomized trial. Biological Psychiatry, 51, 659–667.

Kessler, J., Markowitsch, H. J. & Denzler, P. (1990) Mini-Mental-Status Test. Weinheim: Beltz.

Kopelman, M. D., Wilson, B. A. & Baddeley, A. D. (1990) The Autobiographical Memory Interview. Bury St Edmunds: Thames Valley Test.

Kosel, M., Frick, C., Lisanby, S. H., et al (2003) Magnetic seizure therapy improves mood in refractory major depression. *Neuropsychopharmacology*, II, 2045–2048.

**Lisanby, S. H., Maddox, J. H., Prudic, J., et al (2000)** The effects of electroconvulsive therapy on memory of autobiographical and public events. *Archives of General Psychiatry*, **57**, 581–590.

Martin, J. L. R., Barbanoj, M. J., Schlaepfer, T. E., et al (2003) Repetitive transcranial magnetic stimulation

for the treatment of depression: systematic review and meta-analysis. *British Journal of Psychiatry*, **182**, 480–491.

**McCall, W. V. (2001)** Electroconvulsive therapy in the era of modern psychopharmacology. *International Journal of Neuropsychopharmacology*, **4**, 315–324.

#### **Prudic, J., Peyser, S. & Sackeim, H. A. (2000)** Subjective memory complaints: a review of patient self-

Subjective memory complaints: a review of patient self-assessment of memory after electroconvulsive therapy. Journal of ECT, 16, 121–132.

Reitan, R. M. (1979) Trail Making Test. Weinheim: Beltz.

**Rey, A.** (1964) L'Examen de Clinique en Psychologie. Paris: Presses Universitaires.

Rose, D., Wykes, T., Leese, M., et al (2003) Patients' perspectives on electroconvulsive therapy: systematic review. *BMJ*, **326**, 1363–1367.

Sackeim, H. A., Prudic, J., Devanand, D. P., et al (2000) A prospective, randomized, double-blind comparison of bilateral and right unilateral electroconvulsive therapy at different stimulus intensities. Archives of General Psychiatry, 57, 425–434.

#### Schlaepfer, T. E., Kosel, M. & Nemeroff, C. B. (2003)

Efficacy of repetitive transcranial magnetic stimulation (rTMS) in the treatment of affective disorders. Neuropsychopharmacology, **28**, 201–205.

**Schmidt, K.-H. & Metzler, P. (1992)** *Wortschatztest Handbuch.* Weinheim: Beltz.

**Squire, L. R. & Slater, P. C. (1983)** Electroconvulsive therapy and complaints of memory dysfunction: a prospective three-year follow-up study. *British Journal of Psychiatry*, **142**, 1–8.

#### Squire, L. R., Wetzel, C. D., Slater, P. C. (1979)

Memory complaint after electroconvulsive therapy: assessment with a new self-rating instrument. *Biological Psychiatry*, **14**, 791–801.

#### Squire, L. R., Slater, P. C. & Miller, P. L. (1981)

Retrograde amnesia and bilateral electroconvulsive therapy. Long-term follow-up. Archives of General Psychiatry, **38**, 89–95.

Triggs, W. J., McCoy, K. J. M., Greer, R., et al (1999) Effects of left frontal transcranial magnetic stimulation

on depressed mood, cognition and corticomotor threshold. *Biological Psychiatry*, **45**, 1440–1446.

**UK ECT Review Group (2003)** Efficacy and safety of electroconvulsive therapy in depressive disorders: a systematic review and meta-analysis. *Lancet*, **361**, 799–808.

**Wechsler, D. (1981)** Wechsler Adult Intelligence Scale — Revised. New York: Psychological Corporation.

Weeks, D., Freeman, C. P. & Kendell, R. E. (1980) ECT. III: Enduring cognitive deficits? *British Journal of Psychiatry*, **137**, 26–37.

Weiner, R. D., Rogers, H. J., Davidson, J. R. T., et al (1986) Effects of stimulus parameters on cognitive side effects. *Annals of the New York Academy of Science*, 462, 315–325.

**Wilson, B., Cockburn, J. & Baddeley, A. (1991)** The Rivermead Behavioural Memory Test. Suffolk: Thames Valley Test.