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CASE REPORT

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Increased transcranial magnetic motor threshold after ECT

A case report

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Abstract Electroconvulsive therapy (ECT) is a powerful antidepressive treatment, but its mechanism of action remains poorly understood. To clarify the influence of ECT on corticospinal tract excitability we tested the motor threshold, the motor evoked potential (MEP) input/output curve, and the intracortical excitability using transcranial magnetic stimulation in a depressed patient before and after successful treatment with ECT. Resting motor thresholds were increased bilaterally after treatment, and the input/output curve less steep. These results point to a decreased excitability of the corticospinal motor tract after successful ECT.

Key words major depression · electroconvulsive therapy · transcranial magnetic stimulation

Introduction

A 66-year old woman was admitted to the Department of Psychiatry of the University of Göttingen for a severe episode of a recurrent major depressive disorder (DSM IV 296.33) (American Psychiatric Association 1994). She had a history of unipolar depression with previous hospitalizations for severe depressive episodes in 1985 and 1995. These episodes had been resistant to a variety of antidepressive drugs, but responsive to a series of ECTs. Upon the present admission, treatment consisted of Glibenclamid 1 tablet BID for diabetes, L-Thyroxin 100 µg QD for thyroid dysfunction, Nifedipine 5 mg QD as well as Furosemid 20 mg QD for arterial hypertension. Lithium had been stopped 6 month prior to admission. Symptoms worsened rapidly despite treatment with mirtazapine 60 mg per day for depression, trimipramine 25 mg at night for sleep induction, and pimozid 2 mg per day for intense ruminations of hopelessness. Therefore, we opted for 13 right unilateral ECTs carried out three times a week from day 10 to day 38 of hospitalization, and obtained informed consent from the patient and her daughter. The Montgomery-Asberg Depression Rating Scale (MADRS) (Montgomery and Asberg 1979) score was 53/60 before ECT. We used the Thymatron DG device (Somatics Inc. IL, USA) and placed electrodes over the right temple and on the right side lateral to the vertex (Swartz and Abrams 1994). To maintain a minimum cumulative seizure duration of 20 s the stimulus intensity needed to be increased from 60 % at the first to 100 % at the last ECT. There was a marked clinical improvement starting after the eighth ECT, resulting in an incomplete remission with a MADRS score of 26 after the last ECT. Medication was kept stable during the entire ECT treatment period. Four months later, the patient was again hospitalized for another major depressive episode, with a MADRS score of 46.

Transcranial magnetic stimulation

One day before the first, 2 days and four months after the last ECT treatment we studied conventional transcranial magnetic stimulation (TMS) measures (Rothwell et al. 1999; Sommer et al. 2001). Two Magstim 200 stimulators were connected via a bistimulation module to a figure-eight coil (The Magstim Company, Dyfed, UK) with an outer diameter of 7 cm in each wing, placed over the optimal cortical representation of the abductor digiti minimi muscle. This had been determined in preliminary trials by moving the coil in the sagittal and, subsequently, in the frontal axis in approximately 0.3 cm steps.

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The coil was held tangentially to the skull with the handle pointing backwards at about 45° laterally. To keep the inherent variability of TMS measures (Sommer et al. 2002) as low as possible, the same experienced investigator (M. S.) performed the investigations using an identical stimulator and coil at all testing times. In all measurements the inter-trial interval was at least 4 s, to rule out cumulative effects on cortical excitability observed with faster frequencies (Chen et al. 1997; Wu et al. 2000; Sommer et al. 2001).

We studied active and resting motor threshold bilaterally by reducing the stimulus intensity of single TMS in steps of 1 % stimulator output; at least 10 trials were used at each level of intensity. The resting motor threshold (RMT) was defined as the lowest intensity at which 5 out of 10 consecutive MEPs were larger than 50 μV while the ADM was at rest. Muscle relaxation was monitored by visual and auditory feedback. The lowest intensity at which 5 out of 10 consecutive MEPs were ≥200–300 μV in amplitude during voluntary abduction of the small finger was set as the active motor threshold (AMT) (Rothwell et al. 1999).

The MEP input/output curve was tested on the dominant, right hand by applying stimuli of 100 %, 110 %, 120 %, and 130 % RMT (Valls-Sole et al. 1994) to the optimal ADM representation; each level of intensity was tested 10 times.

We assessed the intracortical excitability of the dominant, left hemisphere 1 day before the first and 2 days after the last ECT using conditioning-test paired-pulse TMS with a subthreshold conditioning stimulus (90 % AMT) followed by a suprathreshold pulse yielding an MEP amplitude of ~1 mV after an interstimulus interval (ISIs) of 1, 2, 3, 4, 5, 6, 7, 8, 10, 15, 20 or 30 ms. Each ISI was tested 12 times and compared to unconditioned suprathreshold pulses. Conditioned peak-to-peak MEP amplitudes were normalized to unconditioned pulses.

We recorded MEPs using silver-silver chloride electrodes in a belly-tendon arrangement, sampled at 5 kHz and filtered data at 10 Hz and 2.5 kHz (Synamps, Neuroscan Inc., Herndon, VA, USA).

Results

Immediately after ECT, the RMT was increased, and the MEP input/output curve less steep, with both measures returning to values within baseline range with time. AMT was unchanged, while the change in intracortical excitability is likely an artifact (see discussion). Fig. 1 illustrates these findings.

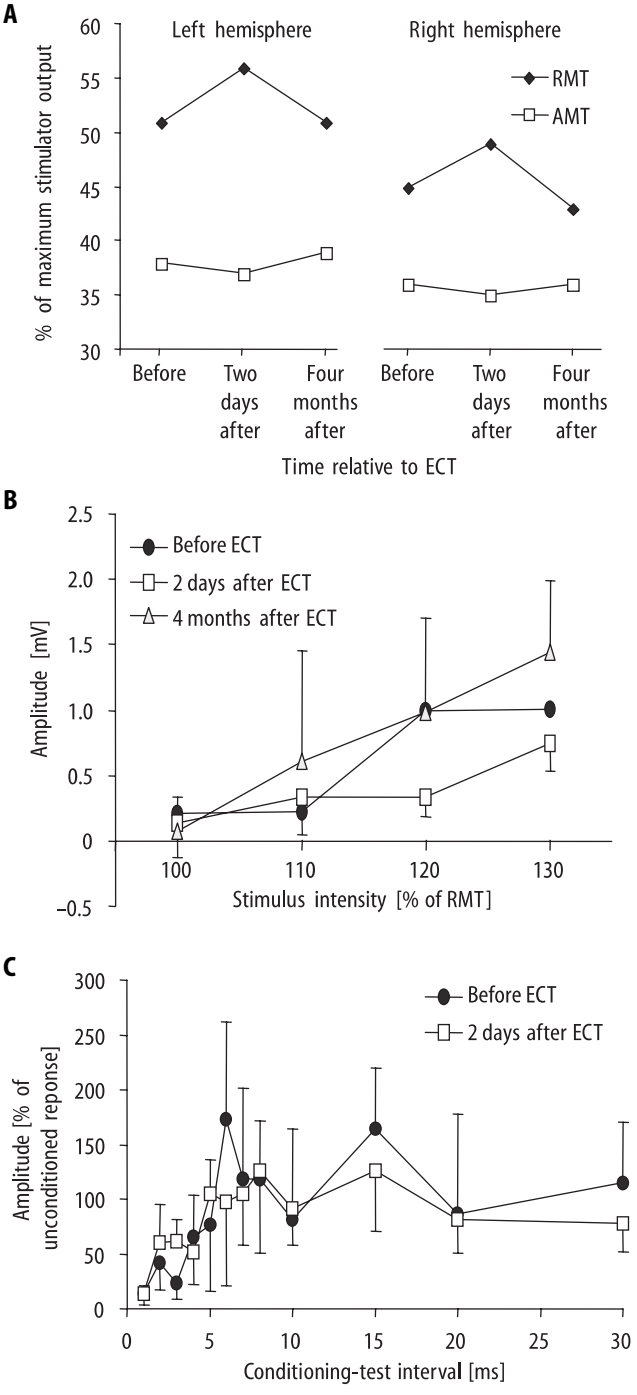

Fig. 1 **A** Resting (RMT) and active (AMT) motor threshold in the optimal motor cortical representation of the abductor digiti minimi. Note the bilateral RMT increase days after ECT. **B** MEP input/output curve of the dominant abductor digiti minimi, mean ± SD. Note the reduced slope days after rTMS. **C** Intracortical excitability of the dominant hemisphere, mean ± SD

Discussion

Here we demonstrate alterations of TMS measures during the course of ECT treatment. The motor threshold reflects the excitability of the corticospinal motor tract and is increased by antiepileptic drugs altering membrane potentials (Ziemann and Hallett 2000). Hence, our findings suggest a reduced corticospinal motor tract excitability after successful ECT, possibly mediated by a hyperpolarization of cortical or spinal motor neurons or related interneurons. Our findings are consistent with an increased seizure threshold observed over the course of ECT treatments (Sackheim et al. 1987).

The slope of the MEP input/output also reflects corticospinal tract excitability and is reduced both by GABAergic as well as sodium and calcium channel blocking drugs (Boroojerdi et al. 2001). Its reduced slope, consistent with the RMT, points to a reduced corticospinal tract excitability immediately after ECT.

The alteration of intracortical excitability cannot be interpreted with certainty, since the absence of AMT change resulted in a weaker relative intensity of the conditioning pulse after ECT than before ECT. This can explain the reduced intracortical inhibition and reduced intracortical facilitation, since they depend on the conditioning pulse intensity (Ziemann et al. 1996). Future studies should choose a conditioning pulse proportional to the RMT.

We acknowledge that antidepressive medication may have an effect on motor cortex excitability per se (Manganotti et al. 2001). Here we tried to overcome this influence by keeping medication constant throughout the time of investigation.

In summary, this case report suggests that ECT reduces human motor corticospinal tract excitability. Future work using the simple procedure of TMS in conjunction with therapeutic ECT should clarify whether 1) our results can be confirmed in a larger group of subjects, 2) TMS is suitable to predict the optimal ECT intensity, and 3) the change in corticospinal excitability is related to the changes in mood-regulating circuits.

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