Neurocognitive function and symptom remission 2 years after ECT in major depressive disorders

Full-length research paper

Christine Mohn [1] and Bjørn Rishovd Rund [1,2]

[1] Research Department, Vestre Viken Hospital Trust, Drammen, Norway

[2] Department of Psychology, University of Oslo, Oslo, Norway

Corresponding author:

Christine Mohn

Research Department, Vestre Viken

Wergelands gate 10

3004 Drammen, Norway

Phone: + 47 22 84 51 15

Fax: + 47 22 84 50 01

e-mail: h.c.mohn@psykologi.uio.no

Word count: 5 414 words (text only)

Running head: Cognition after ECT

Abstract

Background: There is a lack of knowledge of possible cognitive side effects of electroconvulsive therapy (ECT) beyond the first few months after treatment. We aim to describe cognitive effects and symptom remission 2 years after ECT in major depressive disorders.

Method: Twenty-seven depression patients were assessed with the MATRICS Consensus Cognitive Battery (MCCB) and the Everyday Memory Questionnaire (EMQ) before and 2 years after ECT. Their scores were compared with those of healthy matches. Depression and remission status were assessed with the Montgomery-Åsberg Depression Rating Scale (MADRS). Main statistical analyses were ANOVAs and linear mixed model tests.

Results: At baseline, the patient group was significantly impaired on 7 of 10 cognitive tests compared to the control group. Two years later, this gap was reduced to impairment on 5 of 10 tests. Within the patient group, neurocognitive function either increased significantly from baseline to follow-up, or there was no change. Two years after ECT, 62.9% of the patients were in remission. Those in remission reported better subjective memory function, but displayed no different neuropsychological test results, compared to the non-remitters.

Limitations: Major limitations were low sample size and lack of uniform ECT procedure.

Conclusions: We found improved neurocognitive function 2 years after ECT. This effect occurred regardless of remission status, suggesting that ECT induces unique cognitive boosting processes.

Key words: Cognition, Depression, ECT, MCCB, Memory, Neuropsychology,

1. Introduction

Electroconvulsive therapy (ECT) is highly effective in reducing symptoms of severe depression, however, fear of cognitive side effects prevents many eligible patients from agreeing to this type of treatment (Prudic, 2008). Although not life-threatening in the same way that severe depression is, cognitive impairment may have negative psychological consequences through its effects on the ability to function at work or in an educational setting, or through the loss of personal memories important for one's identity and history. This applies in particular if the cognitive changes are long lasting.

In a prospective, naturalistic project, we have followed a group of depressive disorder patients with comprehensive neurocognitive testing before the onset of ECT and then 6 weeks and 6 months after treatment. We found cognitive function improvement after ECT compared to baseline, both at 6 weeks (Mohn and Rund, 2016a) and 6 months (Mohn and Rund, 2016b). At no point was there any deterioration of cognitive function compared to baseline. These findings correspond to those from other groups using different cognitive test batteries or with shorter follow-up intervals (Bodnar et al., 2016; Maric et al., 2016; Obbels et al., 2018; Semkowska and McLoughlin, 2010; Verwijk et al., 2012; Ziegelmayer et al., 2017).

A limitation of previous research is the lack of longitudinal studies beyond the first few months after ECT and using comprehensive neurocognitive assessment. In this paper, we present the results of our 2-year follow-up assessment of the same participants as previously studied (Mohn and Rund, 2016a,2016b). Although there are some reports of general cognitive measurement (e.g., the Mini-Mental State Exam) across 1 and 2 years (Kumar et al., 2016), we are aware of no other prospective study of the detailed neurocognitive effects of ECT in depressive disorder patients with such a long follow-up period.

The remission rates immediately after termination of ECT are high (60-80%, UK ECT Review group, 2003). However, relapses tend to occur, particularly during the first 2-6 months after treatment (van Beusekom et al., 2007; Jelovac et al., 2013). We are aware of only one remission/relapse study that has followed depression patients for more than 6 months after ECT. Martinez-Amaroso et al. (2012) reported a relapse rate of 50 % after 2 years. Considering the intensive debate of the benefits and risks of ECT in depression disorders, there is an astonishing lack of information on long-term illness progression beyond the first months after treatment.

Moreover, there is a need for investigations of the relationship between remission status and neurocognitive function after ECT. The elucidation of this association is necessary in order to evaluate a patient's functional capacity. The concept of remission is usually defined as clinically significant improvement in mood. However, the neurocognitive impairment that may be a core feature of affective disorders and unlikely to disappear completely despite full symptomatic remission (Bora et al., 2013) may still influence functional outcome in a negative manner. A significant proportion of the large economic burden caused by depression disorders in the Western world is likely to be mediated by neurocognitive dysfunction manifesting itself in loss of work productivity, absenteeism, or inability to finish schooling. Moreover, neurocognitive dysfunction in spite of mood improvement is likely to influence interaction with family and friends and adequate performance of daily life activities (Gonda et al., 2015; Lam et al., 2014). In consequence, cognitive remission has been suggested as an additional aim for treatment of affective disorders (Bortolato et al., 2016). The topic of the relationship between remission status and neurocognitive function after ECT has hardly been investigated, however. We are aware of only one such study: For bipolar type II patients in

their depressive phase, Kessler et al. (2014) reported that the overall cognitive function score of the MCCB was significantly higher in the remitted group as compared to the non-remitters.

In order to fill a large knowledge gap in the literature on neurocognitive function after ECT, we aim to answer the following research questions: (1) Are there neurocognitive changes from baseline 2 years after ECT in major depressive disorders? (2) What is the remission rate 2 years after ECT, and is remission status related to neurocognitive function?

2. Methods

2.1 Participants

The current patient sample consists of the 27 individuals (Table 1) with a major depressive episode included in our baseline study (Mohn and Rund, 2016c) who were available for testing 2 year later. The project participants were recruited from the ECT clinical sections at Vestre Viken Hospital Trust and Vestfold Hospital Trust in South-Eastern Norway from March 2011 to November 2014. Of all eligible patients who were scheduled to receive ECT in this time period, five refused participation in this project due to fatigue. A further three eligible patients could not be included for practical reasons, i.e., no time for neurocognitive assessment before start of ECT. The original sample included at baseline consisted of 35 individuals, of which 31 were available for re-tests at 6 weeks and 6 months after ECT (Mohn and Rund, 2016a,2016b). Four of the 31 patients who had performed the previous assessments had dropped out by the current 2-year follow-up test, for the following reasons: Two declined further project participation due to fatigue and/or refusal of further contact with the mental health care system, one had moved overseas, and one had committed suicide. A drop-out

number of 4 patients out of a total of 35 in addition to the 8 eligible patients could not or would not participat at baseline results in a non-participation rate of 38% at 2 years follow-up.

Inclusion criteria were age above 18 and below 70 years (in order to reduce the risk of possible dementia-related cognitive impairment) , capacity for giving informed consent to both ECT and participation in this project, ability to understand spoken and written Norwegian, and a diagnosis of a treatment resistant major depressive episode. The diagnosis of "treatment resistant depression" was made by the clinicians based on previous lack of response to antidepressant medication in combination with psychotherapy. Exclusion criteria were ongoing alcohol or drug abuse, ongoing neurological illness, and ECT within the last two years before baseline.

A healthy control sample was drawn from the control group of our baseline study (Mohn and Rund, 2016c). No follow-up testing 2 years after baseline was made, and the current controls were 27 age, gender, and education level matches from the baseline study. The recruitment and assessment procedure of the controls has been extensively described elsewhere (Mohn and Rund, 2016c; Mohn et al., 2012). The controls were tested only at baseline, and their neurocognitive scores from that time point were used as comparisons for the patient scores both at baseline and at 2-year follow-up (Tables 2 and 4).

2.2 Clinical assessment

The diagnosis of a major depressive episode (F 32.1, F 32.2, F 32.3) was established by clinical interviews using the M.I.N.I International Neuropsychiatric Interview by hospital staff according to the ICD-10 criteria (WHO, 1993). Several different clinicians were involved in the diagnostic process, and the clinicians, although experiences specialists in

psychiatry, were not subject to inter-rater reliability tests. The patients were severely ill, and the decision to commence ECT was sometimes made so rapidly that the diagnostic process could not be undertaken by one and the same clinician. We did, however, rely on comprehensive information from the patients' case files to support the diagnosis made according to the ICD-10 system.

Twenty of the patients were diagnosed with recurrent unipolar depression (F 33) and 7 with bipolar disorder type II (F 31) (WHO, 1993). Six had experienced psychotic symptoms during the present depressive episode, 8 had moderate anxiety symptoms, and 3 partially fulfilled the criteria for a personality disorder (emotionally unstable personality disorder, F 60.3, and anxious personality disorder, F 60.6). Severity of depression was assessed with the Montgomery-Åsberg Depression Rating Scale (Montgomery and Åsberg, 1979), at the start of the neuropsychological assessment session. Remission of depression was defined as a MADRS score ≤ 12, in accordance with the cut off used in another Norwegian study of neurocognitive function after ECT (Kessler et al., 2014).

Four of the patients had been treated with 1-2 series of ECT more than 2 years previously. All patients had discontinued their psychotropic medication 1-7 days before baseline testing. Medication for anxiety (diazepam or oxazepam) and/or insomnia (zopiclone or zolpidem) had been permitted the evening before baseline testing if needed. One patient did not use any regular medication at baseline, and 5 were medication free 2 years after ECT. Calculated daily doses (CDD) of medication were based on the international defined daily dose (DDD) of medication technical measurement system (WHO, 2010) before baseline and at 2 years follow-up (Table 1). A CDD is the outcome of the prescribed daily dose divided by the defined daily dose of medication. At 2 years follow-up, 10 patients used a medication dose

higher than the average DDD: 7 of those were on antidepressants, 2 on antipsychotics, and 1 on lithium.

(Insert Table 1 here)

2.3 Electroconvulsive therapy

No uniform ECT procedure was followed, and each treatment procedure was tailored to the individual patient. All patients received square wave, brief pulse (0.5 ms) stimulation from a Thymatron system machine 2 (n=1) or 3 (n=26) times a week. The stimulation dose was age based, i.e. the electrical current delivered was based on the patient's age as percentage of 504 mC. Mean number of applications per ECT index series was 11.2 (SD 3.4, range 6-20). Right unilateral electrode placement was used in 22 cases, bifrontal placement in 1 case, and mixed placement (switching from right unilateral to bifrontal in mid-series) in 4 cases. Anesthetic agents were alfentanil, propofol, or thiopental. Succinylcholine was used as a muscle relaxant. These pharmacological agents were administered in dosages according to the physical characteristics of each participant.

After this index series and between the 6-week follow-up assessment, 5 patients received a new ECT series with a mean 9.8 of applications (SD 6.7, range 5-18). Among these, 3 had right unilateral, 1 bifrontal, and 1 mixed electrode placement. Between the 6-month and the 2-year follow-up assessment, 2 patients received a new ECT series with a mean of 8.0 applications (SD 0.0). One of these had right unilateral and 1 had mixed electrode placement.

The participants were cognitively assessed 1-3 days before the start of ECT, 6 weeks, 6 months, and 2 years after completion of ECT. For the patients who received a new series, the

follow-up cognitive assessments were performed 6 weeks or 2 years after the final application of ECT.

All participants signed an informed consent form before both testing sessions. These consents were given in addition to their consenting to ECT treatment, which was obtained by the clinical wards. The study was conducted according to the Helsinki Declaration and was approved by the Regional Committee for Research Ethics for Health Region South-East (REK Sør-Øst).

2.4 Neuropsychological assessment

The cognitive assessment was carried out by a clinical psychologist with extensive neuropsychological training (CM). The participants were tested at their respective clinical wards at baseline and at their respective outpatient clinic or at home at follow-up.

The MCCB covers 7 cognitive domains using 10 subtests (Nuechterlein and Green, 2006,2009): Speed of Processing [Trail Making Test A (TMT-A; US War Department, 1994), Symbol Coding (Brief Assessment of Cognition in Schizophrenia, BACS; Keefe, 1999), and Fluency (Category Fluency; Blair and Spreen, 1989)], Attention/Vigilance [Continuous Performance Test-Identical Pairs (CPT-IP; Cornblatt et al., 1988)], Working Memory [Spatial Span (The Wechsler Memory Scale, SS-WMS; Wechsler, 1997) and Letter Number Span (The University of Maryland Letter Number Span test, LNS; Gold et al., 1997)], Verbal Learning [the revised Hopkins Verbal Learning Test (HVLT-R, immediate recall; Brandt and Benedict, 2001)], Visual Learning [the revised Brief Visuospatial Memory Test (BVMT-R; Benedict, 1997)], Reasoning/Problem Solving [the Mazes test (Neuropsychological Assessment Battery, NAB; White and Stern, 2003)], and Social Cognition [the Managing

Emotions part of the Mayer-Salovey-Caruso Emotional Intelligence Test (MSCEIT; Mayer et al., 2002)].

The average time of completion of the MCCB is approximately 60 min. Due to excessive fatigue, 4 patients did not perform the MSCEIT and 9 did not perform the CPT-IP test (the 2 final tests) at baseline. Two years later, 4 and 6 patients did not perform the MSCEIT and CPT-IP test, respectively. The individuals not performing these tests were not the same at baseline as at 2 years, therefore, we do not expect any systematic bias to arise.

Norwegian T scores have been published for the 20-59 years age group (Mohn et al., 2012). As the current study includes participants above 60 years, the MCCB results are presented in raw scores.

After the completion of the MCCB, the patients filled in the Everyday Memory Questionnaire (EMQ; Sunderland et al., 1984), assessing practical attention and memory functions in 28 items.

2.5 Statistics

All statistical calculations were carried out using the IBM SPSS Statistics version 25. Tests of normality revealed that the TMT-A score of the patient group (1.19) and the control group (1.26) was slightly skewed at baseline. Moreover, there was kurtosis in the patient group MSCEIT score (1.99) and control group CPT-IP score (2.53) at baseline. The non-parametric results are reported where appropriate. An alpha-level of .05 was chosen for this study.

Categorical repeated measures remission data were analyzed with the Chi square test (Table 1). Independent samples neurocognitive data were analyzed with one-way ANOVA with partial eta square as an indication of effect size (Tables 2 and 4). Continuous repeated measures variables were analyzed with the linear mixed model approach, as we had random missing data from the MSCEIT and CPT-IP tests (Table 3). As two patients had received a new series of ECT between the 6-month and 2-year assessments, we performed all statistical analyses again omitting these two cases. This procedure did not alter the numbers or figures described in the Results section in any statistically significant manner, and we therefore present data from the entire patient sample throughout this paper.

3. Results

3.1 Remission rates

At baseline, no patients were in remission from their depressive disorder. The remission rates increased significantly across the 2 years measurement span from *n*=7 of 26 individuals (26.9%) at 6 weeks, to *n*=11 of 24 individuals (45.8%) at 6 months, and *n*=17 of 27 individuals (62.9%) at 2 years (X^2 = 29.36, $p < .001$).

3.2 Group differences in neurocognition

At baseline, the healthy controls showed statistically significant higher function compared to the depression patients on 8 of the 10 cognitive tests (Table 2). As there was no follow-up assessment performed in the healthy controls, their baseline scores were used as basis for comparison with the post-ECT depression group scores. Two years after ECT, the performance gap had been reduced, as the depression group scored significantly lower than the control group at baseline on 5 of the 10 cognitive tests (Table 4).

3.3 Neurocognitive function 2 years after ECT

Two years after ECT, the neurocognitive function of the depression patients was significantly increased from baseline for the following tests: TMT-A, Symbol coding, CPT-IP, and BVMT-R. Most of this improvement in test performance was seen early after cessation of treatment, i.e., at the 6 weeks assessment point, and this level of performance was sustained across the entire follow-up phase (Table 3). As there may be associations between the number of ECT applications in an index series and subsequent cognitive function (Prudic, 2008), we performed Pearson's correlation analyses of these variables. This procedure generated no statistically significant results or non-significant trends (data not shown).

In order to study the possible influence of psychotropic medication on the neurocognitive test scores, we performed Pearson's and Spearman's correlation analyses between doses of antidepressants and antipsychotics and the MCCB scores at baseline and 2-years follow-up. This generated one near-significant association between antidepressant dose and the BVMT-R score at baseline *(r* .47, p = .056). None of the other correlations were verging on statistical significance. The participants using lithium or anticonvulsants could not be subject to the same analyses, as these groups were too small.

Although the analyses of variance showed significant improvement or no change in neurocognitive function, there may be instances of deterioration that are not captured by these mean level calculations. Therefore, we present the numbers of participants whose MCCB test results were worsened, not changed, or improved from baseline to 2-years follow-up (Table 5). We used a small interval (+/- 1 or 0.1 raw score point) to calculate the changes. These numbers indicate that the Mazes test results deteriorated in 33% of the cases, while the most

frequently improved test scores were the TMT-A, Symbol Coding, CPT-IP, and BVMT-R, confirming the results of the analyses of variance.

(Insert Tables 2-5 here)

In our previous studies, we found a statistically significant association between current depression level and subjective memory complaints (Mohn and Rund 2016a,2016b). We performed similar correlation analyses on the current sample, revealing a statistical significance between the MADRS and EMQ scores at 2-years follow-up (r .62, p = .01). None of the correlation analyses between the MADRS score and the MCCB test scores (all rs between .00 and -.28, all ps > .14) or between EMQ or the MCCB test scores (all rs between .01 and -.25, all ps > .20) were statistically significant.

3.4 Remission and neurocognitive function

The MADRS score of the patient group was significantly reduced across the follow-up phase compared to baseline, and most of the reduction had occurred at the 6-weeks assessment (Table 3). Univariate ANOVAs of the relationship between remission status (yes/no) and MCCB test performance at each follow-up point generated no statistically significant group differences, nor were there any discernible non-significant trends in the data (all ps > .09, data not shown). However, the non-remitters (see Table 1 for numbers) showed significantly higher levels of subjective cognitive problems (the EMQ score) at 6 weeks (non-remitters mean 118.4, SD 38.1, remitters mean 64.7, SD 15.3, F = 12.87, p <.001, η^2 .35), 6 months (non-remitters mean 118.5, SD 41.9, remitters mean 68.0, SD 24.4, F = 12.87, p <.001, η^2 .36), and 2 years (non-remitters mean 128.9, SD 31.5, remitters mean 78.3, SD 30.0, F =

17.29, p <.001, η^2 .41). The higher EMQ score in the non-remitters was the only statistically significant difference between this group and the remitted group.

4. Discussion

4.1 Neurocognitive function 2 years after ECT

This is the post-ECT study with the longest follow-up period of comprehensive neurocognitive assessment to date. The results of the 2-year follow-up tests confirm our earlier reports of significantly improved cognitive function in several domains after ECT (Mohn and Rund, 2016a,2016b). Moreover, we have not found any cognitive deterioration in any of the domains assessed at any time point over the 2-year interval. Others have reported similar increases in neurocognitive function with shorter follow-up intervals (Bodnar et al., 2016; Maric et al., 2016; Semkowska and McLoughlin, 2010; Falconer et al., 2010). As in our previous studies, the improvement was seen in 4 tests of processing speed, attention/vigilance, and visual learning/short-term memory. None of the other MCCB test results were significantly altered from baseline. Cognitive tests dependent upon speed and learning are known to improve with ECT (Mohn and Rund, 2016a;2016b; Bodnar et al., 2016; Maric et al., 2016; Kessler et al., 2014; Semkowska and McLoughlin, 2010), and this is the first time this improvement has been shown to be sustained across 2 years. Although there was a deterioration in the test of reasoning/problem solving in 33% of the cases (despite an unaltered mean score), the frequency distribution (Table 5) of the changes from baseline to follow-up confirmed the general picture of overall cognitive improvement in most test results, even those that did not turn out as statistically altered in the ANOVAs. A note of caution is in order concerning the improvement in attention/vigilance, though. The CPT-IP is the final test of the MCCB, and six participants did not perform it due to fatigue after an hour long

assessment session. Had these individuals persisted, a lower mean CPT-IP score at follow-up could have been the result.

It may be argued that our results are influenced by test-retest effects. However, the MCCB was assembled partly in order to permit repeated testing, presenting alternate versions of tests most vulnerable to practice effects (Nuechterlein et al., 2008). Moreover, the MCCB has shown limited practice effects across 4 weeks (Roseberry and Hill, 2014). With assessments over longer intervals, we do not expect this type of bias to occur in our data.

At baseline, the healthy control group outperformed the depression patients on 7 of the 10 neurocognitive tests. Two years after ECT, the performance gap had been reduced to 5 of 10 tests. The test results that had been restored to the mean healthy control level at 2-year follow-up were the TMT-A and BVMT-R, assessing processing speed and visual learning. Again, this finding is in accordance with previous reports of these functions being improved after ECT (Mohn and Rund, 2016a;2016b; Bodnar et al., 2016; Maric et al., 2016; Kessler et al., 2014; Semkowska and McLoughlin, 2010; Falconer et al., 2010). It is worth noting, though, that the depression group was still cognitively disadvantaged relative to the controls on half the MCCB test scores 2 years after ECT. We speculate that this is the result of a general, small to moderate cognitive deficit in depression disorder patients (Lee et al., 2012), which is unlikely to improve significantly with conventional treatment (Trivedi and Greer, 2014).

4.2 Remission and neurocognitive function

Throughout our study period, the remission rates increased significantly, reaching 62.9% 2 years after ECT. This number is comparable to rates observed by Dombrowski et al. (2005) immediately after treatment, Sienaert et al. (2010) 6 weeks after treatment, and Verwijk et al.

(2015) 6 months after treatment. Among our patients, the rate of relapse (defined as needing a new series of ECT) was low: *n*=6 before the 6-week follow-up test and *n*=2 between the 6-month and the 2-year assessment. Although these data correspond to the general finding of the risk of relapse being greatest within the first 6 months after ECT (Jelovac et al., 2013), these numbers do not reach the >50% rates that are commonly observed during this time interval (Jelovac et al., 2013; Martinez-Amoroso et al., 2012; van Beusekom et al., 2007). During the entire study period, all our patients received some form of treatment, however, either regular psychotherapy, psychoeducation, antidepressant medication, or a combination thereof. This continued contact with the specialist health care system is likely to be the main reason for the low relapse rates of our participants.

At the same time, the remission rate at 6 weeks (27%) was lower than found by others (Brus et al., 2017; Sienaert et al., 2010). We believe our much smaller sample size and different ways of measuring remission to be the main explanations for this discrepancy. Additionally, we did not have information about the duration of the depressive episode for which our participants were treated with ECT. This factor, as well as concurrent psychosis or anxiety symptoms, for which we could not provide statistical control, may have contributed to our relatively low early remission rate. A further unexpected finding was that even though the rate of remission improved drastically from 6 weeks to 2 years, the MADRS sum score did not change significantly. Probably this was due to alterations in symptom severity in subgroups of patients that we did not have sufficient power to detect.

There were no statistically significant differences in neurocognitive function between those patients who were in remission from their depressive episode and those who were not at any time point across the 2-year study period. We are aware of only one study that has compared

remitters and non-remitters on cognitive function after ECT. For bipolar type II patients in their depressive phase, Kessler et al. (2014) reported that the overall cognitive function score of the MCCB was significantly higher in the remitted group as compared to the non-remitters 6 weeks after treatment. Possibly, the difference in sub-diagnosis within the affective disorder spectrum may explain these divergent findings. Our finding adds to reports of improved neurocognitive function above the affective symptom remission after antidepressant medication treatment (Bortolato et al., 2016; Gonda et al., 2015). Future studies should link the neurocognitive effects of ECT to direct measures of functional outcome, such as time to return to work or studies.

In contrast to the results from the neuropsychological testing, the non-remitted patients reported significantly higher subjective cognitive problems, assessed with the EMQ, at every measurement point compared to the remitted participants. We have previously shown that the depression severity level and the EMQ score are correlated after ECT, but that the MCCB test results and the EMQ score are not (Mohn and Rund, 2016a;2016b). The same relationship was revealed in the current study. These findings suggest that cognitive problems in daily life in patients who have undergone ECT result from residual depression symptoms and not the treatment they have received.

Several studies of the relationship between cognitive test results on the one hand and depression severity scores on the other have found small (*F*'s +/- 4.00), but statistically significant associations between these variables (Maric et al., 2016; Sackeim et al., 2007). We chose the direct comparison method using remission status as the grouping variable, because a mere reduction in symptom load from a high to a less severe level is usually not a sufficient

indicator of functional outcome (Brus et al., 2017). An important aim of depression treatment is to make the patient able to resume as many tasks of independent living as possible, such as going to work or school, interacting with family and friends, and performing household chores. Therefore, full remission status should be the preferred outcome measure and not a simple reduction in symptoms, although the latter also eases the burden of suffering. Moreover, there are no consensus criteria for remission according to the MADRS. We used the same level (≤ 12) as Kessler et al. (2014) in order to generate data comparable to another ECT follow-up project using the Norwegian MCCB. With a stricter cut-off level, our statistical analyses may have generated slightly different results.

As we realize that this cut-off method may hide important associations in the data set, and in order to investigate our previous findings of significant relationships between depression symptom level and cognitive function (Mohn and Rund, 2016a;2016b), we also performed correlation analyses between the MADRS, EMQ, and MCCB test scores. We found the same results as previously i.e., a significant, positive correlation between the MADRS and the EMQ score after ECT, but no relationships or even non-significant trends between MADRS or EMQ on the one hand and MCCB test scores on the other. This strengthens our suggestions that cognitive complaints after ECT results from residual depression, and not cognitive damage.

In summary, the studies from our own research group as well as others point to a general positive neurocognitive effect of ECT in depressive disorder patients. There are several possible mechanisms that explain this phenomenon. First, there is a rapidly growing body of evidence for ECT boosting cognitive function by inducing neuroplastic changes in specific

brain structures involved in learning and memory, such as the hippocampus (Nordanskog et al., 2010), the cerebellum (Depping et al., 2017), or in the temporal cortex in general (van Eijndhoven et al., 2016; Sartorius et al., 2016; Wang et al., 2018). A second possibility is cognitive improvement resulting from the antidepressant effects of ECT. Impaired cognitive function is common during depression (Mohn and Rund, 2016c; Lee et al., 2010), and cognitive improvement may be a natural consequence of symptom remission. Third, these two processes may occur in tandem, ECT has been found to act directly on cognitive performance as well as indirectly via decreased depression scores (Bosboom and Deijnen, 2006).

We believe our results best support the first hypothesis of ECT inducing cognitive improvement through neuroplastic changes. The main reason is our finding of no significant differences in neurocognitive function between the remitted and non-remitted patients, indicating that the depression level had little influence on the cognitive test results after ECT. Future studies of cognitive remission in addition to affective symptom remission (Bortolato et al., 2016) after ECT should be combined with investigations of neuroplastic changes.

4.3 Strengths

There are certain unique features that permit us strong confidence in our main finding of improved neurocognitive function after ECT. First, we employed the longest follow-up period of cognitive monitoring after ECT to date. Second, our non-participation rate (38%) was lower than in most other studies in this field. Third, our control sample consisted of pairwise matched individuals according to gender, age, and education level. Fourth, the MCCB is a comprehensive test battery assessing ecologically valid cognitive functions highly relevant for daily life. It is mainly intended for use in schizophrenia spectrum disorders, but is suitable for

affective disorders as well (Mohn and Rund, 2016c; Murrough et al., 2015; Kessler et al., 2014).

4.4 Limitations

The main shortcoming of our study is the relatively small sample size, upon which multiple statistical testing was performed. Moreover, our low N did not permit separate analyses of subgroups based in gender, age, comorbidity, and electrode placement. In addition, we could not perform analyses of the possible influence of mood stabilizing and anticonvulsant medication on neurocognitive function, as we had too few participants in these groups. Until our results are replicated with larger samples allowing control for such possible confounders, the present data should be interpreted with some caution.

Relatedly, our significance level of 0.05 may have increased the risk of Type I errors. However, we chose not to use Bonferroni or other types of correction for multiple testing, for the following reasons: First, Bonferroni corrections increase the risk of Type II errors, and we wished to uncover relevant group or time differences that will be selected for future large, nation-wide studies of the effects and side-effects or ECT. Second, the current paper is a follow-up of our previous studies (Mohn and Rund, 2016 a; 2016b), where we did not correct for multiple testing. In such cases, it is recommended to refrain from correction (Perneger, 1998). As our present results strongly resemble those of our previous reports (Mohn and Rund, 2016a; 2016b), we are confident that our findings are not the artifacts of statistical coincidences.

Second, although all patients received brief-pulse stimulation, other aspects of the ECT technique was not standardized, but tailored to each patient's clinical characteristics. Unilateral electrode placement may cause less cognitive side effects than bilateral placement (Kolshus et al., 2017; Kumar et al., 2016; Prudic, 2008), but others have found no such differences (Sienaert et al., 2010).

Third, we did not assess autobiographic memory, a cognitive domain that is assumed to be particularly impaired after ECT (Sackeim et al., 2007). The reasons for this are twofold: We wanted to spare a severely ill patient group additional time-consuming testing, and the psychometric properties of the most common tests of autobiographic memory are still not sound enough to generate valid and reliable data (Jelovac et al., 2016).

Fourth, we did not perform follow-up testing of the control group, but rely on the baseline scores for comparison. This is a suboptimal way of assessing cognitive changes, although neurocognitive function is remarkably stable across this time interval in adults (Mohn et al., 2012; Nuechterlein and Green, 2006).

A fifth limitation is the fact that our participants were able to give their informed consent to ECT as well as to participation in this study. Our results may not generalize to those whose depression level is so high that they are unable to participate in research. Moreover, 8 of the eligible participants contacted at baseline were not included in the project. Therefore, our results may not describe the cognitive function of all depressive disorder patients treated with ECT in our region at this time period.

Sixth, there were several clinicians involved in the diagnostic process, and although they were all experienced specialists in psychiatry or clinical psychology and highly familiar with the diagnostic instruments, we can not exclude reliability problems, as no calibration was performed for the present study. However, we did substantiate each diagnosis with extensive information from each patient's case file.

Further, no systematic assessment of treatment resistance to conventional methods (medication and psychotherapy) was made before the patients were referred to ECT. Different criteria for assigning depressive disorder patients to ECT in different countries may explain some of the discrepant results between our study and those of others, although our results are largely in accordance with previous findings.

Role of funding source

This study was supported by grants to Dr. Rund (no. 2009044 and no. 2011/125) from the Helse Sør-Øst (Health South East) Regional Hospital Trust and Vestre Viken Hospital Trust. The funding source has not contributed to the performance of the study or preparation of this article.

Contributors

Dr. Mohn designed the study, performed the neurocognitive assessments and the statistical analyses, and drafted the paper. Dr. Rund participated in the design of the study, the interpretation of the results, and in the drafting of the paper. Both authors approved of the final version of the paper.

Acknowledgements

Hilde Jakobsen, RN, Gro Liebeck, RN, and Drs Jovan Randjelovic, John E. Berg, Phelix Blayvas, Therese Torgersen Bigseth, and Arne Thorvik are gratefully acknowledged for recruiting the patients for this study.

Conflict of interest

None.

References

Benedict, R.H.B., 1997. Brief Visuospatial Memory Test – Revised. Psychological Assessment Resources, Odessa, FLA.

van Beusekom, B.S., van den Broek, W., Birkenhäger, T., 2007. Long-term follow-up after successful electroconvulsive therapy for depression. A 4- to 8-year naturalistic follow-up study. J ECT 23, 17-20.

Blair, J.R., Spreen, O, 1989. Predicting premorbid IQ: a revision of the National Adult Reading Test. Clin. Neuropsychol. 3, 129-136.

Bodnar, A., Krzywotulski, M., Lewandowska, A., Chlopocka-Wozniak, M., Bartkowska-Sniatkowska, A., Michalak, M., Rybakowski, J.K., 2016. Electroconvulsive therapy and cognitive functions in treatment-resistant depression. World. J. Biol. Psychiatry doi:10.3109/15622975.2015.1091501

Bora, E., Harrison, B.J., Yucel, M., Pantelis, C., 2013. Cognitive impairment in euthymic major depressive disorder: a meta-analysis. Psychol. Med. 43, 2017-2026.

Bortolato, B., Miskowiak, K.W., Köhler, C.A., Maes, M., Fernandes, B.S., Berk, M., Carvalho, A.F., 2016. Cognitive remission: a novel objective for the treatment of major depression? BMC Med. 14, 9.

Bosboom, P.R., Deijnen, J.B., 2006. Age-related cognitive effects of ECT and ECT-induced mood improvement in depressive patients. Depr. Anx. 23, 93-101.

Brandt, J., Benedict, R.H.B., 2001. The Hopkins Verbal Learning Test – Revised. Psychological Assessment Resources, Odessa, FLA.

Brus ,O., Cao, Y., Gustafsson, E., Hultén, M., Landen, M., Lundberg, J., 2017. Self-assessed remission rates after electroconvulsive therapy of depressive disorders. Eur. Psychiatry 45, 154-160.

Cornblatt, B.A., Risch, N.J., Faris, G., Friedman, D., Erlenmeyer-Kimling, L., 1988. The continuous performance test, identical pairs version (CPT-IP): I. New findings about sustained attention in normal families. Psychiatry Res. 26, 223-238.

Depping, M., Nolte, H.M., Hirjak, D., Palm, E., Hofer, S., Stieltjes, B., Maier-Hein, K., Sambatero, F., Wolf, R.C., Thomann, P.A., 2017. Cerebellar volume change in response to electroconvulsive therapy in patients with major depression. Progr. Neuro-Psychopharm. Biol. Psychiatry 73, 31-35.

Dombrowski, A.Y., Mulsant, B.H., Haskett, R.F., Prudic, J., Begley, A.E., Sackeim, H.A., 2005. Predictors of remission after electroconvulsive therapy in unipolar major depression. J. Clin. Psychiatry 66, 1043-1049.

van Eijndhoven, P., Mulders, P., Kwekkeboom, L., van Oostrom, I., van Beek, M., Janzing, J., Schene, A., Tendolkar, A., 2016. Bilateral ECT induces bilateral increases in regional cortical thickness. Transl. Psychiatry 6, e874.

Falconer, D.W., Cleland, J., Fielding, S., Reid, I.C., 2010. Using the Cambridge Neuropsychological Test Automated Battery (CANTAB) to assess the cognitive impact of electroconvulsive therapy on visual and visuospatial memory. Psychol. Med. 40, 1017-1025.

Gold, J.M., Carpenter, C., Randolph, C., Goldberg, T.E., Weinberger, D.R., 1997. Auditory working memory and Wisconsin Card Sorting test performance in schizophrenia. Arch. Gen. Psychiatry 54, 159-165.

Gonda, X., Pompili, M., Serafini, G., Carvalho, A.F., Rihmer, Z., Dome, P., 2015. The role of cognitive dysfunction in the symptoms and remission from depression. Ann. Gen. Psychiatry 14, 27.

Jelovac, A., Kolshus, E., McLoughlin, D.M., 2013. Relapse following sucessful electroconvulsive therapy for major depression: A meta-analysis. Neuropsychopharm. 38, 2467-2474.

Jelovac, A., O'Connor, S., McCarron, S., McLoughlin, D.M., 2016. Autobiographical memory specificity in major depression treated with electroconculsive therapy. J ECT 32, 38-43.

Keefe, R.S.E., 1999. Brief assessment of cognition in schizophrenia (BACS). Duke University Medical Center, 1999, Durham, NC.

Kessler, U., Schoeyen, H.K., Andreassen, O.A., Eide, G.E., Malt, U.F., Oedegaard, K.J., Morken, G., Sundet, K., Vaaler, A.E., 2014. The effect of electroconvulsive therapy on

neurocognitive function in treatment-resistant bipolar disorder depression. J. Clin. Psychiatry 75, e1306-1313.

Kolshus, E., Jelovac, A., McLoughlin D.M., 2017. Bitemporal v. high-.dose right unilateral electroconvulsive therapy for depression: a systematic review and meta-analysis of randomized controlled trials. Psychol. Med. 47, 518-530.

Kumar, S., Mulsant, B.H., Liu, A.Y., Blumberger, D.M., Daskalakis, Z.J., Rajji, T.K., 2016. Systemic review of cognitive effects of electroconvulsive therapy in late-life depression. Am. J. Geriatr. Psychiatry 24, 547-565.

Lam, R.W., Kennedy, S.H., McIntyre, R.S., Khullar, A., 2014. Cognitive dysfunction in major depressive disorder: Effects on psychosocial functioning and implications for treatment. Can. J. Psychiatry 59, 649-654.

Lee, R.S.C., Hermens, D.F., Porter, M.A., Redoblado-Hodge, M.A., 2012. A meta-analysis of cognitive deficits in first-episode major depressive disorder. J. Aff. Dis. 140, 113-124.

Maric, N.P., Stojanovic, Z., Andric, S., Soldatovic, I., Dolic, M., Spiric, Z., 2016. The acute and medium-term effects of treatment with electroconvulsive therapy on memory in patients with major depressive disorder. Psychol. Med.
doi: http://dx.doi.org/10.1017/S0033291715002287

Martinez-Amoroso, E., Cardoner, N., Soria, V., Galvez, V., Menchon, J.M., Urretavizcaya, M., 2012. Long-term treatment strategies in major depression: A 2-year prospective naturalistic follow-up after successful electroconvulsive therapy. J ECT 28, 92-97.

Mayer, J.D., Salovey, P., Caruso, D.R., 2002. Mayer-Salovey-Caruso Emotional Intelligence Test. MHS Publishers, Toronto, ON.

Mohn, C., Rund, B.R., 2016a. Significantly improved neurocognitive function in major depressive disorders 6 weeks after ECT. J. Aff. Dis. 202, 10-15.

Mohn, C., Rund, B.R., 2016b. Maintained improvement of neurocognitive function in major depressive disorders 6 months after ECT. Frontiers Psychiatry doi.org/10.3389/fpsyt.2016.00200

Mohn, C., Rund, B.R., 2016c. Neurocognitive profile in major depression disorders: relationship to symptom level and subjective memory complaints. BMC Psychiatry 16, 108.

Mohn, C., Sundet, K., Rund, B.R., 2012. The Norwegian standardization of the MATRICS Consensus Cognitive Battery. J. Clin. Exp. Neuropsychol. 34, 667-677.

Montgomery, S.A., Åsberg, M., 1979. A new depression scale designed to be sensitive to change. Br. J. Psychiatry 134, 382-389.

Murrough, J.W., Burdick, K.E., Levitch, C.F., Perez, A.M., Brallier, J.W., Chang, L.C., Foulkes, A., Charney, D.S., Mathew S.J., Iosefscu, D.V., 2015. Neurocognitive effects of

ketamine and association with antidepressant response in individuals with treatment-resistant depression: A randomized controlled trial. Neuropsychopharmacol. 40, 1084-1090.

Nordanskog, P., Dahlstrand, U., Larsson, M.R., Larsson, E.M., Knutsson, L., Johanson, A., 2010. Increase in hippocampal volume after electroconvulsive therapy in patients with depression: a volumetric magnetic resonance imaging study. J ECT 26, 62-67.

Nuechterlein, K.H., Green, M.F., 2006. MCCB. MATRICS Consensus Cognitive Battery. Manual. MATRICS Assessment Inc, Los Angeles, CA.

Nuechterlein, K.H., Green, M.F., 2009. MATRICS Consensus Cognitive Battery, Norwegian Version. (BR Rund, KS Sundet, trans.) MATRICS Assessment Inc, Los Angeles, CA.

Nuechterlein, K.H., Green, M.F., Kern, R.S., Baade, L.E., Barch, D.M., Kraemer, H., 2008. The MATRICS consensus cognitive battery, part I: test selection, reliability, and validity. Am. J. Psychiatry 165, 203-213.

Obbels, J., Verwijk, E., Vansteelandt, K., Dols, A., Bouckaert, F., Schouws, S., Vandebulcke, M., Emsell, L., Stek, M., Sienaert, P., 2018. Long-term neurocognitive functioning after electroconvulsive therapy in patients with late-life depression. Acta Psychiatr. Scand. 138, 223-231.

Perneger, T.V., 1998. What's wrong with Bonferroni corrections? BMJ 316, 1236-1238.

Prudic, J., 2008. Strategies to minimize cognitive side effects with ECT: Aspects of ECT technique. J ECT 24, 46-51.

Roseberry, J.E., Hill, S.K., 2014. Limited practice effects and evaluation of expectation for change: MATRICS Consensus Cognitive Battery. Schiz. Res. 159, 188-192.

Sackeim, H.A., Prudic, J., Fuller, R., Keilp, J., Lavori, P.W., Olfson, M., 2007. The cognitive effects of electroconvulsive therapy in community settings. Neuropsychopharmacol. 32, 244-254.

Sartorius, A., Demiracka, T., Böhringer, A., von Hohenburg, C.C., Aksay, S.S., Bumb, J.M., Kranaster, L., Ende, G., 2016. Electroconvulsive therapy increases temporal gray matter volume and cortical thickness. Eur. Neuropsychopharm. doi: 10.1016/j.euroneuro.2015.12.036

Semkovska, M., McLoughlin, D.M., 2010. Objective cognitive performance associated with electroconvulsive therapy for depression: A systematic review and meta-analysis. Biol. Psychiatry 68, 568-577.

Sienaert, P., Vansteelandt, K., Demyttenaere, K., Peuskens, J., 2010. Randomized comparison of ultra-brief bifrontal and unilateral electroconvulsive therapy for major depression: cognitive side-effects. J. Aff. Dis. 122, 60-67.

Sunderland, A., Harris, J.E., Gleave, J., 1984. Memory failures in everyday life following

severe head injury. J. Clin. Neuropsychol. 6, 127-142.

Trivedi, M.H., Greer, T.L., 2014. Cognitive dysfunction in unipolar depression: Implications for treatment. J. Aff. Dis., 152-154, 19-27.

UK ECT Review group, 2003. Efficacy and safety of electroconvulsive therapy in depressive disorders: a systematic review and meta-analysis. Lancet 361, 791-808.

United States War Department, 1944. Army Individual Test Battery: Manual of Directions and Scoring. War Department, Adjutant General's Office, Washington, DC.

Verwijk, E., Comijs, H.C., Kok, R.M., Spaans, H.-P., Stek, M.L., Scherder, E.J.A., 2012. Neurocognitive effects after brief pulse and ultrabrief pulse unilateral electroconvulsive therapy for major depression: A review. J. Aff. Dis. 140, 233-243.

Verwijk, E., Spaans, H.P., Comijs, H.C., Kho, K.H., Sienaert, P., Bouckaert, F., Obbels, J., Scherder, E.J.A., Stek, M.L., Rob, M.K., 2015. Relapse and long-term cognitive performance after brief pulse or ultrabrief pulse right unilateral electroconvulsive therapy: A multicenter naturalistic study. J. Aff. Dis. 184, 137-144.

Wang, J., Wei, Q., Yuan, X., Jiang, X., Xu, J., Zhou, X., Tian, Y., Wang, K., 2018. Local functional connectivity density is closely associated with the response of electroconvulsive therapy in major depressive disorder. J. Aff. Dis. doi: 10.1016/jad.2017.09.001

Wechsler, D., 1997. Wechsler Memory Scale, third ed. The Psychological Corporation, San Antonio, TX.

White, T., Stern, R.A., 2003. Neuropsychological Assessment Battery. Psychological Assessment Resources, Odessa, FLA.

WHO, 1993. The ICD-10 classification of mental and behavioural disorders. Diagnostic criteria for research. World Health Organization, Geneva.

WHO, 2010. Collaborating Center for Drug statistics Methodology. DDD Definitions and General Considerations. (http://www.whocc.no/atc_ddd_methodology/purpose_of_the_atc_ddd_system/)

Ziegelmayer, C., Hajak, G., Bauer, A., Held, M., Rupprecht, R., Trapp, W., 2017. Cognitive performance under electroconvulsive therapy (ECT) in ECT-naïve treatment-resistant patients with major depressive disorder. J ECT 33, 104-110.

Table 1. Demographic characteristics of the patient group *(N*=27)

Age (years)	45.9 (SD 11.7)	
Gender	*n* = 8 (29.6 %) men *n* = 19 (70.4 %) women	
Education		
Elementary school	*n* = 9 (33.3 %)	
High school	*n* = 9 (33.3 %)	
BA / BA+	*n* = 9 (33.3 %)	
Years since first onset of depression	18.4 (SD 10.5, range 3-40)	
Medication (in CDD)		
	Baseline	**2 years after ECT**
Antidepressants	1.3 (*n*=18)	1.4 (*n*=14)
Antipsychotics	0.6 (*n*=15)	0.8 (*n*=12)
Lithium	0.8 (*n*=3)	1.1 (*n*=4)
Anticonvulsants	0.5 (*n*=6)	1.3 (*n*=3)
No medication	*n*=1	*n*=5

BA: Bachelor degree. BA+: Bachelor degree or higher. Age and Years since onset in mean. CDD: Calculated dose of medication based on the prescribed dosage divided by the defined daily dosage. The numbers in the brackets of the Medication columns refer to the number of individuals using the type of medication.

Table 2. Neurocognitive (raw) scores of the MCCB in depression patients (*N*= 27) and healthy controls (*N*=27) at baseline.

	Depression Mean (SD)	**Controls** Mean (SD)	***F (p)***	η^2
Speed of Processing				
TMT-A	51.5 (26.5)	28.7 (8.6)	18.02, p<.001	.26
BACS	39.6 (13.3)	54.5 (10.6)	20.77, p<.001	.29
Fluency	21.0 (8.6)	27.2 (8.9)	10.21, p=.002	.16
Attention/Vigilance (CPT-IP) *	2.4 (0.5) (*n*=18)	2.7 (0.5) (*n*=26)	3.65, p=.029	.08
Working Memory				
SS-WMS	12.9 (3.2)	15.9 (2.5)	14.32, p<.001	.22
LNS	11.9 (4.2)	13.9 (2.4)	4.76, p=.034	.08
Verbal Learning (HVLT-R)	22.4 (6.2)	25.1 (5.1)	3.23, p=.078	.06
Visual Learning (BVMT-R)	20.4 (8.8)	25.5 (6.0)	6.06, p=.017	.10
Reasoning/Problem Solving (Mazes)	11.4 (7.9)	18.9 (4.5)	18.52, p<.001	.26
Social Cognition (MSCEIT)	92.6 (11.0) (*n*=23)	97.2 (8.9)	2.67, p=.109	.05

F: Significance test of group differences. η^2 : effect size. *: Mann-Whitney U test.

Table 3. Depression levels, subjective cognitive function, and MCCB (raw) test scores of the patient group before (baseline) and after ECT (*N*=27). Results of the linear mixed model analyses.

	Baseline Mean (SD)	**6 weeks** Mean (SD)	**6 months** Mean (SD)	**2 years** Mean (SD)	***T* (*p*)**
MADRS	33.3 (8.6)	16.1 (7.7)	13.5 (8.1)	10.7 (5.5)	10.62, p<.001
EMQ	102.0 (39.0)	104.4 (42.2)	97.6 (42.3)	94.3 (39.4)	0.36, p=.733
Speed of Processing					
TMT-A	50.3 (27.4)	41.0 (23.2)	38.0 (18.4)	33.3 (12.5)	2.97, p=.004
Symbol coding	39.9 (14.0)	44.6 (12.4)	47.2 (13.4)	47.8 (11.2)	-2.08, p=.040
Fluency	21.4 (9.0)	22.1 (6.7)	24.7 (7.8)	23.6 (6.6)	-1.15, p=.254
Attention / Vigilance (*n*=21)					
CPT-IP	2.4 (0.5)	2.7 (0.5)	2.9 (0.4)	2.8 (0.5)	-2.28, p=.025
Working Memory					
SS-WMS	13.1 (3.2)	13.8 (3.4)	14.2 (3.6)	14.4 (3.0)	1.54, p=.127
LNS	12.0 (4.4)	12.5 (4.1)	12.5 (4.0)	12.3 (4.2)	-0.10, p=.920
Verbal Learning					
HVLT-R	22.6 (6.5)	23.9 (6.5)	24.1 (6.6)	25.0 (6.1)	-1.18, p=.242
Visual Learning					
BVMT-R	21.6 (8.7)	23.8 (8.2)	24.2 (7.8)	26.9 (5.9)	2.43, p=.017
Reasoning / Problem solving					
Mazes	12.3 (7.9)	13.5 (7.9)	15.1 (8.2)	15.8 (7.9)	1.46, p=.146
Social Cognition (*n*=23)					
MSCEIT	94.3 (8.3)	96.9 (8.5)	96.4 (8.4)	96.1 (9.1)	-0.88, p=.381

T: Significance test of time differences.

Table 4. Neurocognitive (raw) scores of the MCCB in depression patients 2 years after ECT (*N*= 27) and healthy controls at baseline (*N*=27)

	Depression Mean (SD)	**Controls** Mean (SD)	***F (p)***	η^2
Speed of Processing				
TMT-A	33.3 (12.5)	28.7 (8.6)	3.85, p=.055	.07
BACS	47.8 (11.2)	54.5 (10.6)	6.97, p=.011	.12
Fluency	23.6 (6.6)	27.2 (5.4)	6.07, p=.017	.10
Attention/Vigilance (CPT-IP)	2.8 (0.5) (*n*=21)	2.7 (0.5) (*n*=26)	0.20, p=.660	.01
Working Memory				
SS-WMS	14.4 (3.0)	15.9 (2.5)	4.71, p=.035	.08
LNS	12.3 (4.2)	13.9 (2.4)	4.57, p=.037	.08
Verbal Learning (HVLT-R)	25.0 (6.1)	25.1 (5.1)	0.26, p=.612	.01
Visual Learning (BVMT-R)	25.7 (6.5)	25.5 (6.0)	0.01, p=.931	.01
Reasoning/Problem Solving (Mazes)	15.8 (7.9)	18.9 (4.5)	5.29, p=.018	.10
Social Cognition (MSCEIT)	96.1 (9.1) (*n*=23)	97.2 (8.9)	0.74, p=.393	.02

F: Significance test of group differences.

Table 5. Change in neurocognitive function (MCCB raw scores) from baseline to 2 years after ECT in the depression patients (N=27).

	Worsened	**No change**	**Improved**
Speed of Processing			
TMT-A	*n*=2 (7.4%)	*n*=2 (7.4%)	*n*=23 (85.2%)
BACS	*n*=5 (18.5%)	*n*=1 (3.7%)	*n*=21 (77.7%)
Fluency	*n*=8 (29.6%)	*n*=1 (3.7%)	*n*=18 (66.6%)
Attention/Vigilance (CPT-IP) (*n*=21)	*n*=4 (19.0%)	*n*=1 (4.7%)	*n*=16 (76.2%)
Working Memory			
SS-WMS	*n*=5 (18.5%)	*n*=6 (22.2%)	*n*=16 (59.2%)
LNS	*n*=8 (29.6%)	*n*=3 (11.1%)	*n*=16 (59.2%)
Verbal Learning (HVLT-R)	*n*=7 (25.9%)	*n*=2 (7.4%)	*n*=18 (66.6%)
Visual Learning (BVMT-R)	*n*=5 (18.5%)	*n*=2 (7.4%)	*n*=20 (74.1%)
Reasoning/Problem Solving (Mazes)	*n*=9 (33.3%)	*n*=2 (7.4%)	*n*=16 (59.2%)
Social Cognition (MSCEIT) (*n*=23)	*n*=7 (30.4%)	*n*=1 (4.3%)	*n*=15 (65.2%)

Change is defined as +/- 1 raw score point of difference from the mean depression group level at baseline, except for CPT-IP, where change is defined as +/- 0.1 raw score point of difference.