Chapter 5

Early complete remitters after electroconvulsive therapy: profile and prognosis

Harm-Pieter Spaans¹
Esmée Verwijk¹
Max L. Stek²
King H. Kho¹
Filip Bouckaert¹
Rob M. Kok¹
Pascal Sienaert¹

¹ Parnassia Psychiatric Institute, The Hague, The Netherlands
² GGZ inGeest, Amsterdam, The Netherlands
³ University Psychiatric Center – KU Leuven, campus Kortenberg, Kortenberg, Belgium

Under review Journal of ECT
Chapter 5

Abstract

Objective: To investigate the prevalence, characteristics and prognosis of depressive patients who show early complete remission after right unilateral (ultra)brief pulse electroconvulsive therapy (ECT).

Methods: Early Complete Remitters (ECR) were those patients who were rated 1 on the Clinical Global Impression scale (maximum score 7) within 4 ECT sessions and achieved remission (MADRS score<10). ECR were compared with Late Complete Remitters (LCR), which fulfilled the same criteria after 9 to 12 ECT sessions and with the non-remitters/non-responders (NR).

Results: Of the 87 patients who completed the index treatment phase, 50 (57.5%) achieved remission. Of these remitters 12 (14%) were ECR, and 9 (10%) were LCR. ECR were characterized by a higher mean age (71.0 years vs. 53.9; \(p=0.008\)), a shorter current depressive episode (mean 5.8 months vs. 15.4 months; \(p=0.042\)), more psychotic features (75% vs. 22%; \(p=0.030\)), and were treated more often with brief pulse ECT (\(p=0.030\)) compared to the LCR. Although not significant, cognitive performances of ECR were lower than that of LCR at baseline with a large effect size: Autobiographical Memory Interview (\(p=0.099\); \(d=0.83\)), Amsterdam Media Questionnaire (\(p=0.114\); \(d=0.84\)) and Letter fluency (\(p=0.071\); \(d=0.95\)). The ECR group had a lower relapse rate during 6 months follow-up: 10% (1/10) vs 62.5% (5/8) \(p=0.043\). No significant differences in demographic and clinical characteristics were found between LCR (n=9) and NR (n=27).

Conclusions: Older patients with a psychotic depression and a profile of cognitive slowing have a high chance of achieving complete remission within four ECT sessions, with a favorable six-month prognosis.
Introduction

Electroconvulsive therapy (ECT) is an effective treatment for depression with a fast onset of action. In most studies, remission is achieved after 6 to 8 treatment sessions, i.e. 2 to 4 weeks depending on the treatment schedule. Speed of response to ECT has been positively associated with higher age, shorter duration of the depressive episode, the presence of psychotic symptoms and bipolarity, and negatively with higher depression severity, co-morbidity and treatment resistance. Treatment schedule, electrode position, and technical aspects like seizure threshold, total charge, waveform, pulse width, and pulse frequency, might also impact on the speed of recovery.

Some authors report that the first session of a series of treatments contributes the most to the total improvement. Apart from this observation, many clinicians share the experience of patients responding almost immediately after starting an ECT course, although published reports of remission after a single or a few treatments are rather scarce. Thomas and Kellner report remission of a patient with depression and obsessive-compulsive disorder after a single right unilateral (RUL) treatment with a stimulus intensity of only 5%. Keisling describes a dramatic improvement after one ECT session in a 40-year-old woman with psychotic and depressive symptoms. Her diagnosis is not mentioned, but the clinical description suggests a psychotic depression with catatonia, a state in which a prompt recovery is the rule rather than the exception. Aside from ECT, a swift and robust remission of depressive symptomatology is also reported after treatment with sleep deprivation, lithium, and ketamine. It can be hypothesized that the underlying conditions and distinct mechanisms of action involved in this fast remission are different from the more gradual response to antidepressant medication.

Obviously a quick relief of depression and suicidality can save lives, alleviates the personal and the caregivers’ burden, shortens admissions, and reduces costs. Absence of residual symptoms or subsyndromal symptomatology after improvement with medication, has been shown to predict a lower risk of relapse and recurrence. In parallel, fewer residual symptoms after ECT probably also predict lower relapse rates. Therefore gaining insight into the factors influencing a fast and full remission is of great importance, as well as understanding of the patients characteristics associated with this particular response pattern.

In the present study we tried to identify patients who achieved full remission within two weeks after the start of ECT, and the characteristics that may discriminate this
subgroup from patients that achieve remission after a higher number of treatments, or do not remit at all.

Methods

Participants and treatment

Patients who participated in a prospective, double blind, randomized multicenter ECT trial comparing efficacy and cognitive side effects of twice weekly right unilateral (RUL) brief pulse (BP; 1.0 ms) ECT and RUL ultrabrief pulse (UBP; 0.3 ms) stimulation at eight times seizure threshold with a naturalistic six months follow up were included in the current analysis. Treatment was delivered by a constant current device (spECTrum 5000 Q, MECTA corp., Tualatin, OR) with a maximum stimulus level of 1152 mC using RUL d’Elia electrode placement.

Participants were 18 years or older suffering from a unipolar or bipolar depressive disorder (with or without psychotic features) according to DSM-IV TR criteria. The diagnosis was confirmed using the Mini-International Neuropsychiatric Interview. Participants were treated as inpatients during the RCT but could be discharged in the follow up phase.

Remission was defined as a Montgomery-Åsberg Depression Rating Scale (MADRS) score <10 at 2 consecutive weekly assessments by blind, independent raters. After finishing the treatment phase, patients entered an open naturalistic follow up period with assessments at three and six months. During follow up adjustment of patients’ medication was at the discretion of the treating psychiatrist.

All patients provided informed consent. The Institutional Review Boards of the respective centers in The Hague, Delft and Leuven approved the study, which was conducted according to the Declaration of Helsinki (Netherlands National Trial Register number 1304).

Early Complete Remission, Late Complete Remission and Non-Remitter / Non-Response

Early Complete Remitters (ECR) were defined as patients: a) with a score of 1 out of 7 (=normal, not at all ill) on the Clinical Global Impressions (CGI) scale within 2 weeks of treatment (≤ 4 ECT sessions) and b) who achieved remission during the treatment course. We compared the ECR with a contrasting group defined as Late Complete Remitters (LCR) containing patients fulfilling the same criteria in week 5 or 6 during
the last two weeks of the trial (9 to 12 ECT sessions). Those who achieved neither remission nor response irrespective of CGI within 12 ECT sessions were termed the nonremitter / non-responder (NR) group. Response was defined as a fifty percent or more decrease from baseline MADRS score.

Assessments

Clinical assessment and demographic features
At baseline, the following socio-demographic and clinical data were collected: age, gender, level of education, treatment condition, previous depression, duration of the index major depressive episode, bipolarity, psychotic features, early or late-onset, depression severity, history of ECT treatment, number of admissions, medication resistance score as assessed with a modified Antidepressant Treatment History Form (ATHF) and number of antidepressants used to treat the current depression.

Depression severity and relapse criteria

Blind MADRS rating
For blind assessment of efficacy, trained nurses rated the severity of depression using the MADRS, at baseline and weekly during the ECT course until the end of the randomized study-period. After finishing the ECT course follow up assessments were scheduled after three and six months. Relapse was defined as a MADRS score >15, readmission due to depressive relapse, restart of ECT or suicide.

Clinical global impression scale
We tried to capture the clinical aspects of the severity of depression by using the clinical judgment of the treating physician, represented in the score of the CGI scale. On a weekly basis during the treatment phase and at three and six months follow up, the patients were rated by their responsible physician. Clinical judgment was based on information derived from a standardized clinical MADRS interview, after which the CGI was applied.

Cognitive assessment
Cognitive assessment was performed by a neuropsychologist or supervised trainee neuropsychologist, who were blind to the treatment condition. The assessments were obtained within a week prior to the first ECT, one week after finishing the randomized treatment course and at follow up after three months and six months post-ECT.
Kopelman’s Autobiographical Memory Interview (AMI)\textsuperscript{33, 34} was used to assess retrograde amnesia for personal events. The Amsterdam Media Questionnaire (AMQ)\textsuperscript{34} was used to assess retrograde amnesia for impersonal events. For the evaluation of retrograde amnesia the total AMI and AMQ scores were used. Other cognitive domains included semantic memory (Category fluency- animals and professions)\textsuperscript{35} and an aspect of executive functioning (Letter fluency - “D”, “A”, “T”).\textsuperscript{35}

**Statistical analysis**
We compared Early Complete Remitters (ECR) with Late Complete Remitters (LCR) on demographic and clinical characteristics at baseline and for relapse in follow up. For the analysis of the baseline cognitive performance we used the raw AMI total score and AMQ score. Normative scores (scores corrected for age and education) were used for the Category fluency and the Letter fluency. One extreme outlier in the Letter fluency test was a participant who refused further testing and turned out to be a LCR. This participant was excluded from the initial analyses. Additionally we compared the LCR with the non-remitters, non-responders (NR) for baseline characteristics. We used two-tailed \(t\) tests, Mann-Whitney \(U\) tests, Pearson’s chi-square tests or Fisher’s Exact tests where appropriate. In order to quantify clinical relevance of the cognitive data, we calculated the Cohen’s \(d\) effect size (ES). Effect sizes were interpreted as suggested by Cohen\textsuperscript{36}: 0.2 – 0.5 is considered a small effect, 0.5 – 0.8 a medium effect and \(\geq 0.8\) a large effect. Due to the small sample sizes we did not attempt multivariate analysis. Results were considered statistically significant at a \(p\)-value less than 0.05. All tests were two-sided. Statistical analyses were done using IBM SPSS statistics for Windows version 20.

**Results**
Of the 87 patients who completed the acute treatment phase, 50 (57.5\%) achieved remission. Of these remitters 12 (14\%) were ECR, and 9 (10\%) were LCR. Also, 27 patients (31\%) neither remitted nor responded (NR group). The mean MADRS ratings of the physician and independent raters in week two were 2.6 (s.d. 2.5) and 3.5 (s.d. 4.0) respectively for the ECR (data not shown).

**Demographic and clinical characteristics**
Demographic and clinical characteristics of Early Complete Remitters, Late Complete Remitters and non-remitters/non-responders are shown in Table 1. The ECR group
had a significantly higher mean age, a shorter duration of the current depressive episode, more often a psychotic depression and were more often treated with brief pulse stimulation. There were no significant differences between the three groups considering gender, level of education, baseline depression severity (MADRS), bipolarity, treatment-refractoriness (ATHF) and age of onset.

The cognitive performances at baseline showed no statistically significant differences between the ECR and the LCR groups on the AMI, AMQ, Category fluency and on the Letter fluency (LF). However, although the differences of AMI, AMQ and LF were not statistically significant, the clinical relevance of the differences was illustrated by a large ES (Table 1). The respective ES's for the differences of the Category fluency for animals and the Category fluency for professions were small.

The comparison of the cognitive performances between LCR and NR showed no significant differences, although with a high ES for AMQ.

Regarding prognosis during 6 months follow up the ECR demonstrated a significantly lower relapse rate than the LCR.

**Discussion**

Our study confirmed the clinical impression that ECT can result in a dramatic improvement early in the treatment course in a substantial number of patients (14%). In addition, our results suggested that this subgroup of patients has a better long-term prognosis. In the following paragraphs we discuss the characteristics of these early complete remitters.

**Age, treatment condition (BP, UBP), episode duration, psychotic features**

The early complete remitters had a higher age, were more often treated with brief pulse ECT, had a shorter current depressive episode, and more often had psychotic features compared with the late complete remitters. These results are in line with other studies in which a higher age,7, 37 the use of a brief pulse width,12 a shorter episode duration11, 38 and the presence of psychotic features3, 7 have been shown to predict remission. However, although the late complete remitters were also remitters, they still differed significantly in these characteristics from the early complete remitters.

A higher age,7 the use of brief pulse ECT,6, 12 and the presence of psychotic features39 also predicted a higher speed of response and remission. Since the early complete remitters form a subset of those with a high speed of remission, it is expected that the characteristics of ECR overlap with the predictors of higher speed of remission.
Table 1: Demographic and clinical characteristics of Early Complete Remitters, Late Complete Remitters and Non-Remitters / Non-Responders

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Early Complete Remitters</th>
<th>Late Complete Remitters</th>
<th>p(^a)</th>
<th>ES (d)</th>
<th>Non-remitters/responders</th>
<th>p(^b)</th>
<th>ES (d)</th>
<th>p(^c)</th>
<th>ES (d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographical characteristics</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, mean years (sd; range)</td>
<td>71.0 (12.8; 46-92)</td>
<td>53.9 (13.7; 31-79)</td>
<td>0.008</td>
<td></td>
<td>53.4 (16.3; 26-78)</td>
<td>0.002</td>
<td></td>
<td>0.966</td>
<td></td>
</tr>
<tr>
<td>Gender, female, n (%)</td>
<td>8 (66.7)</td>
<td>5 (55.6)</td>
<td>0.673</td>
<td></td>
<td>16 (59.3)</td>
<td>0.734</td>
<td></td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Education level, median; interquartile range</td>
<td>4.4</td>
<td>5.5; 4</td>
<td>0.115</td>
<td></td>
<td>5.0; 2 (n=26)</td>
<td>0.073</td>
<td></td>
<td>0.771</td>
<td></td>
</tr>
<tr>
<td>Clinical characteristics</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BP treatment, n (%)</td>
<td>9 (75)</td>
<td>2 (22.2)</td>
<td>0.030</td>
<td></td>
<td>8 (29.6)</td>
<td>0.014</td>
<td></td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Previous depression, n (%)</td>
<td>9 (75)</td>
<td>5 (55.6)</td>
<td>0.397</td>
<td></td>
<td>18 (66.7)</td>
<td>0.719</td>
<td></td>
<td>0.693</td>
<td></td>
</tr>
<tr>
<td>Current episode (months), mean (sd, range)</td>
<td>5.8 (4.0; 1-15)</td>
<td>15.4 (11.8; 3-36)</td>
<td>0.042</td>
<td></td>
<td>24.5 (27.5; 1-120)</td>
<td>0.002</td>
<td></td>
<td>0.349</td>
<td></td>
</tr>
<tr>
<td>Unipolar, n (%)</td>
<td>12 (100)</td>
<td>7 (77.8)</td>
<td>0.171</td>
<td></td>
<td>24 (88.9)</td>
<td>0.539</td>
<td></td>
<td>0.581</td>
<td></td>
</tr>
<tr>
<td>Psychotic, n (%)</td>
<td>9 (75)</td>
<td>2 (22.2)</td>
<td>0.030</td>
<td></td>
<td>12 (44.4)</td>
<td>0.996</td>
<td></td>
<td>0.432</td>
<td></td>
</tr>
<tr>
<td>Early onset depression (&lt;55), n (%)</td>
<td>8 (66.7)</td>
<td>8 (88.9)</td>
<td>0.338</td>
<td></td>
<td>20 (74.1)</td>
<td>0.709</td>
<td></td>
<td>0.648</td>
<td></td>
</tr>
<tr>
<td>History of ECT, n (%)</td>
<td>5 (41.7)</td>
<td>2 (22.2)</td>
<td>0.642</td>
<td></td>
<td>6 (22.2)</td>
<td>0.262</td>
<td></td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Total admissions, mean (sd, range)</td>
<td>3.3 (2.5; 1-10)</td>
<td>4.8 (4.2; 1-12)</td>
<td>0.347</td>
<td></td>
<td>3.0 (2.0; 1-9)</td>
<td>0.747</td>
<td></td>
<td>0.237</td>
<td></td>
</tr>
<tr>
<td>ATHF, median (interquartile range)</td>
<td>3.2 (n=1)</td>
<td>4.2</td>
<td>0.280</td>
<td></td>
<td>4.0; 2 (n=23)</td>
<td>0.427</td>
<td></td>
<td>0.759</td>
<td></td>
</tr>
<tr>
<td>No. treatments for current episode, (mean, sd, range)</td>
<td>2.5 (1.0; 1-5)</td>
<td>2.0 (1.5; 0-4)</td>
<td>0.370</td>
<td></td>
<td>2.1 (1.3; 0-4)</td>
<td>0.358</td>
<td></td>
<td>0.830</td>
<td></td>
</tr>
<tr>
<td>Baseline MADRS mean (sd, range)</td>
<td>29.3 (7.7; 16-43)</td>
<td>30.7 (5.6; 21-38)</td>
<td>0.647</td>
<td></td>
<td>33.3 (8.2; 17-47)</td>
<td>0.158</td>
<td></td>
<td>0.381</td>
<td></td>
</tr>
<tr>
<td>Number of ECT sessions, mean, (sd, range)</td>
<td>5.2 (1.3; 4-7)</td>
<td>11.0 (0.2; 9-12)</td>
<td>&lt;.001</td>
<td></td>
<td>11.6 (1.2; 7-12)</td>
<td>&lt;.001</td>
<td></td>
<td>0.215</td>
<td></td>
</tr>
<tr>
<td>Relapse within 6 months FU</td>
<td>1 (10)</td>
<td>5 (62.5)</td>
<td>0.043</td>
<td></td>
<td>N/A</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AMI total mean (sd, range)</td>
<td>45.3 (0.2; 22.5-57.5)</td>
<td>52.8 (7.6; 40.5-62.0)</td>
<td>0.099</td>
<td>0.83</td>
<td>49.2 (9.3; 18.5-62)</td>
<td>0.268</td>
<td>0.41</td>
<td>0.345</td>
<td>0.42</td>
</tr>
<tr>
<td>Characteristics</td>
<td>Early Complete Remitters (n=12)</td>
<td>Late Complete Remitters (n=9)</td>
<td>Non-remitters/responders (n=27)</td>
<td>p&lt;sup&gt;a&lt;/sup&gt;</td>
<td>ES (d)</td>
<td>p&lt;sup&gt;b&lt;/sup&gt;</td>
<td>ES (d)</td>
<td>p&lt;sup&gt;c&lt;/sup&gt;</td>
<td>ES (d)</td>
</tr>
<tr>
<td>---------------------------------------------</td>
<td>--------------------------------</td>
<td>------------------------------</td>
<td>-------------------------------</td>
<td>----------</td>
<td>--------</td>
<td>----------</td>
<td>--------</td>
<td>----------</td>
<td>--------</td>
</tr>
<tr>
<td>AMQ total, mean (sd; range)</td>
<td>19.9 (9.8; 6-41) (n=10)</td>
<td>27.4 (8.0; 16-38) (n=7)</td>
<td>19.9 (9.5; 6-37) (n=23)</td>
<td>0.114</td>
<td>0.84</td>
<td>0.993</td>
<td>0.068</td>
<td>0.85</td>
<td></td>
</tr>
<tr>
<td>Category fluency, animals, normative (T-score), mean (sd; range)</td>
<td>29.9 (7.3; 16-42) (n=11)</td>
<td>34.4 (9.6; 16-42) (n=7)</td>
<td>37.8 (11.8; 23-69) (n=24)</td>
<td>0.295</td>
<td>0.50</td>
<td>0.050</td>
<td>0.78</td>
<td>0.503</td>
<td>0.21</td>
</tr>
<tr>
<td>Category fluency, professions, normative (T-score), mean (sd; range)</td>
<td>33.4 (7.9; 19-45) (n=11)</td>
<td>33.7 (8.8; 21-48) (n=7)</td>
<td>33.6 (0.6; 5-60) (n=24)</td>
<td>0.933</td>
<td>0.04</td>
<td>0.943</td>
<td>0.02</td>
<td>0.984</td>
<td>0.01</td>
</tr>
<tr>
<td>Letter fluency, normative (T-score), mean (sd; range)</td>
<td>37.3 (7.4; 29-35) (n=11)</td>
<td>44.1 (7.2; 34-57) (n=7)</td>
<td>43.1 (14.8; 19-77) (n=23)</td>
<td>0.071</td>
<td>0.95</td>
<td>0.227</td>
<td>0.50</td>
<td>0.864</td>
<td>0.09</td>
</tr>
</tbody>
</table>

BP = brief pulse; No. treatments = number of antidepressants used to treat the current depressive episode; ATHF = Antidepressant Treatment History Form; each medication trial was rated on a scale from 0 to 5. A threshold score of three indicated an adequate trial and was judged as treatment resistant. MADRS = Montgomery Åsberg Depression Rating Scale; N/A = not applicable; AMQ = Amsterdam Media Questionnaire; for all scores, higher scores mean better performance.

<sup>a</sup> Comparison Early Complete Remitters with Late Complete Remitters; student t-test, Fishers’ Exact, Mann Whitney test where appropriate

<sup>b</sup> Comparison Early Complete Remitters with Non-Remitters/Non-Responders; student t-test, Fishers’ Exact, Mann Whitney test where appropriate

<sup>c</sup> Comparison Late Complete Remitters with Non-Remitters/Non-Responders; student t-test, Fishers’ Exact, Mann Whitney test where appropriate

<sup>d</sup> The scoring system of Verhage (range 1-7; 1=less than 6 years education, 2=6 years, 3=7-8 years, 4=9 years, 5=10-14 years, 6=more than 14 years, 7=University)
Bipolarity
Speed of remission with ECT is reported to be higher in bipolar depression than in unipolar depression. Bipolar patients were not represented in the ECR sample and the total number of bipolar patients in the remission sample was low (n=8) and thus may have hampered statistical analysis.

Current depressive episode duration
In our sample, episode duration was significantly shorter in the ECR group. This is in accordance with the notion that a shorter episode duration has been shown to predict both remission and speed of remission, although there are some conflicting results. Patients with a longer episode duration often have had more medication trials and, as a consequence, have a higher degree of medication resistance. The shorter episode duration of the ECR in our sample would suggest less medication resistance, but the number of antidepressant treatments and ATHF score of the ECR differed not statistically from that of the LCR-group. This equal number of treatments, however, was given in a significantly shorter period of time, suggesting more frequent medication changes due to resistance or intolerance. Therefore we would argue that the shorter episode duration was the result of the specific severity profile of depression which prompted earlier referral for ECT.

Relapse
The 63% (95%CI 29-96) relapse of the LCR within 6 months is in line with the 50% relapse within 6 months in an intensively monitored medication continuation trial. The ECR presented a much more optimistic prognosis of 10% (95%CI 9-29) relapse. The relapse rates of ECR were significantly lower than relapse rates of LCR.
Residual symptoms are shown to predict relapse, but by definition ECR and LCR have no to very few residual symptoms.
Relapse has been associated with treatment resistance, but in our cohort there was no difference between ECR and LCR in the ATHF that rates the adequacy of antidepressant treatment. The number of antidepressants used to treat the current depressive episode was also equal in the ECR and LCR group. However, inadequate medication trials are not represented in the ATHF score. Thus if medication intolerance lead to inadequate medication trials in the ECR group, there could be a difference in treatment resistance between the ECR and LCR despite the equal number of antidepressants used to treat the current depressive episode. This difference in treatment resistance could possibly
be partly responsible for the lower relapse rates of the ECR, but also other factors e.g. somatic and psychiatric comorbidity may be involved.

**Cognitive performance at baseline**

The cognitive performances at baseline did not differ significantly between the ECR and the LCR. However, the large effect sizes suggest a clinically relevant specific profile with predominantly lower performances of executive functioning with cognitive slowing related to the frontal-subcortical dysfunction. Apart from using baseline assessments to evaluate the development of cognitive side effects during ECT, this cognitive profile might help support the prediction of ECT outcome.

**Subtype of depression**

The psychotic features and cognitive slowing of the ECR subgroup correspond with the findings by Hickie et al. who investigated the outcome of ECT in melancholic and non-melancholic patients with the CORE (an observational score for rating psychomotor disturbance). The ‘Retardation’ and ‘Non-interactiveness’ subscale, as measured with the CORE, as well as psychosis did clearly predict outcome of ECT, but not age and depression severity as measured with a standard depression rating scale. Assessing depression severity using standard rating scales like the MADRS bears the risk that we miss a dimension important enough for adequate treatment choice and prognosis. A catatonia rating was not included in the study design and although patients with severe catatonia were not included, milder catatonia cannot be ruled out as a partial explanation for the early treatment effects. Indeed some authors have raised the issue of a categorical classification for subtypes of depression: melancholia, psychotic depression and catatonia. Lumping of depressive disorders into one major depression category may disguise the differences between subtypes resulting in an average improvement of 50% across antidepressant treatments and 60% for ECT.

In summary, with the higher age, psychotic features, shorter time to referral for ECT and a specific cognitive profile of the early complete remitters, a classical picture of a severe depression with psychotic and melancholic features emerges, with cognitive and possibly also motor inhibition.
Strength and limitations

This study supports the validity of a clinical notion of remarkably fast and full remission in patients with a recognizable profile of depression. Although one of the larger ECT studies to date, the number of early complete remitters was small which hampered statistical significance for some of the comparisons. The presence of this subtype will vary within the different treatment populations. Therefore the 14 percent of early complete remission cannot be generalized to other populations e.g. outpatients.

Another limitation is the validity of the concept of ‘complete remission’ defined as a score of 1 out of 7 on the Clinical Global Impressions scale, representing no symptoms of depression. The mean MADRS ratings of the physician and blind raters supported the clinical validity as this suggests only few residual symptoms, which had not to be mood related.

We did not control for the concomitant psychotropic medication as a confounder. Differences in prescribed co-medication between the ECR and LCR group may have resulted in both a faster treatment effect as well as in cognitive slowing.

The use of the raw scores of the AMI and AMQ may have introduced a bias, because these scores are negatively associated with age. However normative data stratified by age and education were used for the letter fluency.

Conclusions

A specific depression profile was found for early complete remitters. A higher age, psychotic features, a shorter episode duration and a dysexecutive profile with cognitive slowing at baseline were associated with complete remission of depression within two weeks and less relapse during six months follow up. These early complete remitters may represent a clinically distinct subtype of depression.

Clinical implications

- It is possible to identify patients with depression that will benefit fast and completely from ECT
- It is not possible to predict non-response in our study, based on the clinical characteristics at baseline
- Cognitive assessment, in particular letter fluency could be considered as outcome predictor for ECT
Early complete remitters after ECT

References

15. Thomas SG, Kellner CH. Remission of major depression and obsessive-compulsive disorder after a single unilateral ECT. *J ECT.* 2003; 19:50-51
Chapter 5

29. Montgomery SA, Åsberg M. A new depression scale designed to be sensitive to change. *Br J Psychiatry* 1979; 134:382-389
31. Sackeim HA. The definition and meaning of treatment-resistant depression. *J Clin Psychiatry* 2001; 62 Suppl 16:10-17
35. Luteijn F, van der Ploeg FAE. *Groninger Intelligentie Test (GIT)* [Groningen Intelligence Test (GIT)]. Lisse: Swets & Zeitlinger; 1983
43. Thase ME. Achieving remission and managing relapse in depression. *J Clin Psychiatry* 2003; 64 Suppl 18:3-7
