



# Summary

### **Neurocognitive performance in electroconvulsive therapy**

The main scope of this thesis was to study the nature and extend of changes across multiple domains of neurocognitive functioning in depressed patients after ECT. The evolution of these changes was followed up within six months after the last ECT and the variability concerning cognitive performance between patients was explored. Ultrabrief pulse and brief pulse right unilateral (RUL) ECT were compared regarding the efficacy and cognitive side effects hypothesizing that ultrabrief pulse ECT has less severe cognitive side effects.

In *Chapter 2* prospective studies using right unilateral (ultra) brief pulse index electroconvulsive therapy were reviewed. The severity and persistence of neurocognitive side effects immediately (one to seven days post ECT), between one and six months and after six months post ECT were assessed by calculating effect sizes using Cohen's *d*. Only ten studies fulfilled the inclusion criteria and provided detailed information to compute effect sizes. The results indicate loss of autobiographical memory and impairment of verbal fluency, anterograde verbal and non-verbal memory immediately after brief pulse ECT. To a lesser extent impairment of working memory and reduced speed of processing is found.

Loss of autobiographical memory is still present between one and six months after brief pulse ECT, although it improves in this period. Other neurocognitive impairments after brief pulse ECT seem to be transient. Verbal fluency normalized to baseline performance within six months post ECT whereas anterograde verbal and non-verbal memory normalized or even improved. Speed of processing improved within six months after ECT. Based on two of the ten included studies the results suggest that right unilateral ultrabrief pulse ECT causes less decline in autobiographical and anterograde memory after ECT than right unilateral brief pulse ECT.

In *Chapter 3*, global cognitive function, memory and executive function were assessed in 42 depressed elderly ( $\geq 55$  years) patients. Assessments were done before ECT treatment started and one week and six months after ECT. Our data offered no evidence of decline for any of the neurocognitive tests after ECT, given its power to detect differences. In our severely depressed elderly patients, neurocognitive performance improved or did not change after ECT. No associations between cognitive functioning and electrode placement, total number of treatment sessions, age and the severity of depression on time of cognitive measurement were found.

In *Chapter 4* we compared the efficacy and cognitive side effects of high dose unilateral brief pulse ECT with high dose unilateral ultrabrief pulse ECT in the treatment of major depression. From April 2007 until March 2011, we conducted a prospective, double blind, randomized multicenter trial in 3 tertiary psychiatric hospitals and all patients with a depressive disorder according to *DSM-IV* criteria were eligible. The Autobiographical Memory Interview and Amsterdam Media Questionnaire were the primary outcome measures for retrograde amnesia. Other cognitive domains included category fluency (semantic memory) and Letter fluency (lexical memory). Of the 116 patients, 75% completed the study. There was a significant difference in remission rate between the brief pulse group (68.4%) versus the ultrabrief group (49.0%) and the brief pulse group needed fewer treatment sessions to achieve remission. No significant group differences were found in the evaluation of the cognitive assessments post ECT. The results clearly indicated that the efficacy and speed of remission in high-dose brief pulse right unilateral ECT twice weekly was superior to those seen in high-dose ultrabrief pulse right unilateral ECT. Equal cognitive side effects as defined by retrograde amnesia, semantic memory and lexical memory were found.

In *Chapter 5* the results of the naturalistic follow up of the randomized multicentre trial are described. We compared the differences in relapse rate and cognitive performance (retrograde amnesia, semantic memory and lexical memory) three and six months after index ECT with unilateral brief pulse ECT or ultrabrief pulse ECT.

Of the 50 patients who remitted after index ECT 44 were monitored for follow up. Relapse at three months follow-up was equal between the brief pulse group (25%) and ultrabrief pulse group (25%). Relapse at six months showed also no significant difference between the brief pulse group (43.5%) and ultrabrief pulse group (35%). Cognitive assessments showed no significant differences between BP and UBP groups, except for an advantage for the BP group with respect to the autobiographical incident questions at three months follow-up. We therefore concluded that patients that achieved remission after right unilateral brief pulse or ultrabrief pulse ECT showed similar relapse rates after three and six months and cognitive advantage of UBP over BP ECT in follow up was absent.

In *Chapter 6* we evaluated the changes in retrograde amnesia for (auto)biographical memory and executive functioning of depressed patients treated with right unilateral ECT. Assessments were done one week, 3 and 6 months after the last ECT session. The group of patients receiving ECT at any time during the follow up was compared



to the group of patients not receiving any ECT after the index episode and the level of cognitive performances was compared with normative data of a representative normal population. One week post ECT biographical memory (public events) improved, autobiographical memory did not change and executive functioning declined. Compared to the pre-ECT condition, cognitive performances improved during 6 months follow up but the performance of the patients still receiving ECT did not change during this 6 months follow-up. Compared to a representative normal population, cognitive performance of remitted patients was still below average level after six months.

Because most of our knowledge about cognitive functioning after ECT is based on results analysed at group level, inter-individual variability in neurocognitive performances may be overlooked. This may limit the clinical interpretation of the results of most studies on cognitive functioning after ECT. In *Chapter 7*, we investigated inter-individual variability in neurocognitive performances after ECT in two cohorts, representative for ECT practice. We compared subgroups of patients whose cognitive function declined significantly after ECT with those who improved significantly. We found that neurocognitive side effects after ECT showed inter-individual variability: 29% of the patients clinically relevant declined and 26% clinically relevant improved on one or more tests. Decline of the autobiographical memory and on fluency tests were associated with more treatment sessions.