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PULSE

A Monthly Update on Advances in Neuromodulation

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Pre-ECT Clinical Variables Predict Individual Outcomes After ECT for Moderate to Severe Depression

Meghan Y. Reddy, MD reviewing Semple et al., Br. J. Psychiatry, 2024 Sep

This national registry study identified predictors of ECT response and remission and used machine learning to predict individual remission with 61% accuracy. Response and remission were associated with older age, psychotic symptoms, prior ECT response, psychomotor retardation, and lack of medication resistance.

ECT is a highly effective treatment for moderate to severe depression, but clinically applicable predictive models remain limited. Prior studies, often limited by small sample sizes and clinical heterogeneity, have identified population-level predictors but lack specificity. This study addressed these gaps using national registry data to identify sensitive and specific predictors of ECT response.

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This national cohort study analyzed data from the Scottish ECT Audit Network (2009-2018), including patients with acute unipolar depression and baseline MADRS scores ≥18. Response and remission were defined as a ≥50% reduction in MADRS from baseline and a post-ECT score ≤10, respectively. Group-level associations were evaluated using linear and logistic regression, and two predictive models for individual-level outcomes were developed using a linear kernel support vector machine with nested cross validation. Model 1 included only pre-ECT clinical variables, while Model 2 added early treatment response data using CGI-Improvement scores after two treatments (CGI-I2).

The study analyzed 2074 treatment episodes involving 1392 patients, with a mean age of 59.4 years (standard deviation [SD] = 15.7) and a male-to-female ratio of 1:1.94. Patients received an average of 9.1 ECT treatments per episode (SD = 5.3). Depression subtypes included 34% with psychotic symptoms and 51% with recurrent depression. Common indications for ECT were severe distress (28%), psychomotor retardation (24%), and suicidal ideation (26%). The mean baseline MADRS score was 38.8 (SD = 8.6), which decreased to 13.6 (SD = 11.7) post-ECT. Response and remission rates were 73% and 51%, respectively. Linear regression revealed that better outcomes were associated with older age, psychotic symptoms, and prior response to ECT ($p < 0.001$), while worse outcomes were linked to greater baseline MADRS and CGI-I2 scores, as well as greater sadness, poorer sleep, suicidal thoughts, medication resistance, higher total dose, and a greater number of treatments ($p < 0.05$ for all factors). Logistic regression identified strong predictors of response and remission, respectively, as severe distress (OR = 1.77 and 1.27, $p < 0.001$ and 0.014); urgent necessity for ECT (OR = 1.6 and 1.08, $p = 0.024$ and not significant [ns]); psychotic symptoms (OR = 1.53 and 1.48, $p < 0.001$ for both); psychomotor retardation (OR = 1.38 for both, $p = 0.01$ and 0.002); and prior response to ECT (OR = 1.33 and 1.45, $p = 0.006$ and < 0.001). Negative predictors of response and remission included medication resistance (OR = 0.59 and 0.63, $p < 0.001$ for both); more treatments (OR = 0.98 and 0.95, $p = 0.026$ and < 0.001); and higher total dose (OR = 1.0 and 1.0, ns and $p = 0.007$). The individual patient predictive accuracy was 60.4% (AUC = 0.63, 95% CI: 0.61–0.66) for model 1 and 61% (AUC = 0.65, 95% CI: 0.62–0.68) for model 2, with positive and negative predictive values for model 2 of 60.9% and 61.2%, respectively (not reported for model 1).

Impact: This national registry study highlights the potential of clinical and early treatment variables to predict ECT outcomes for moderate to severe depression. Predictors such as psychotic symptoms, prior response to ECT, and psychomotor retardation were strongly associated with positive outcomes, while medication resistance was linked to worse outcomes. Predictive modeling demonstrated modest accuracy but highlights opportunities remain for improvement. Limitations include its retrospective, non-randomized design, lack of reporting on adverse events, and focus on a Scottish cohort, which may limit generalizability. Future prospective studies should include safety outcomes, validate predictive models, and examine more diverse populations to enhance generalizability and clinical utility.

Semple DM, Suveges S, Steele JD. Electroconvulsive therapy response and remission in moderate to severe depressive illness: a decade of national Scottish data. Br J Psychiatry. 2024;225(6):547-555. doi:10.1192/bjp.2024.126

Stimulus Dose with RUL-ECT Impacts Memory and Executive Functioning in TRD

Amanda Mengotto, MD reviewing Rummel L, Göke K, Philipsen A, Hurlemann R, Kiebs M. Front Psychiatry 2024 Sep

This prospective case-control study examined the effects of RUL-ECT on autobiographical and verbal memory in patients with TRD, with a focus on the influence of stimulus dose. The findings revealed that while RUL-ECT significantly impaired autobiographical memory, it also improved executive functions and working memory. Higher stimulus doses were associated with greater verbal memory impairment, highlighting a dose-dependent cognitive impact.

ECT is a highly effective treatment for TRD, but its use is often limited by concerns about cognitive side effects, particularly retrograde amnesia. While ECT has been associated with autobiographical memory impairments, right unilateral (RUL)-ECT is associated with fewer cognitive side effects. However, the nuanced effects of RUL-ECT on specific cognitive domains and the association with stimulus dose are less well characterized. This study examined how stimulus dose

modulates cognitive outcomes, especially autobiographical and verbal memory.

This prospective observational case-control study assessed the cognitive effects of RUL-ECT in patients with TRD, defined as failure to respond to at least two antidepressant trials. A healthy control group, matched for age and sex, underwent neuropsychological testing along with the patients at two time points: before the first ECT session and within one week after the final session. Assessments included the Autobiographical Memory Interview (AMI), the Verbal Learning and Memory Test (VLMT), and five tasks from the Cambridge Neuropsychological Test Automated Battery (CANTAB) assessing executive function and working memory. Depression severity was measured using the HAM-D. Statistical analysis included linear mixed models and multiple regression to examine the effects of treatment and the relationship between mean stimulus charge and cognitive outcomes.

RUL-ECT was highly effective in reducing depressive symptoms, with HAM-D scores declining from 19.7 ± 4.1 to 6.6 ± 4.4 ($p < 0.01$). Patients who underwent RUL-ECT (n = 21) exhibited significant impairments in autobiographical memory at both time points ($p < 0.01$), with a significant group-by-time interaction indicating worsening post-treatment compared to healthy controls (n = 19; $p < 0.01$). However, stimulus charge was not significantly associated with AMI performance ($\beta = -0.01$, $p = 0.96$). In contrast, RUL-ECT was associated with improvements in a subset of executive function and working memory tasks assessed by the CANTAB ($p = 0.03$), with a significant group-by-time interaction ($p = 0.01$) indicating greater post-treatment improvements in RUL-ECT patients than in controls. Interestingly, the effects of RUL-ECT on verbal memory were dose-dependent, with higher mean stimulus charge predicting worse delayed recall on the VLMT delay task ($\beta = -1.08$, $p = 0.03$); however, trends observed for other cognitive measures did not remain significant after correction for multiple comparisons. While baseline VLMT scores were significantly lower in TRD patients compared to controls ($p < 0.05$), the absence of a significant group-by-time interaction ($p > 0.01$) suggests that verbal memory decline followed an expected trajectory but was not mitigated—and may even have been exacerbated—by RUL-ECT.

Impact: This prospective case-control study provides important insights into the differential effects of RUL-ECT on various cognitive domains. The findings support the existing evidence that RUL-ECT may impair autobiographical memory; however, the improvements in executive function and working memory observed in this study suggest that RUL-ECT has a more nuanced impact on cognition than previously understood. The dose-dependent relationship observed between higher stimulus charge and verbal memory impairment suggests that clinicians can optimize ECT protocols through careful titration to minimize cognitive side effects. Nevertheless, the disappearance of several significant associations following multiple testing correction, along with the short post-treatment follow-up, underscores the need for further research with larger cohorts and longer-term evaluations to fully elucidate the cognitive impact of ECT.

Rummel L, Göke K, Philipsen A, Hurlemann R, Kiebs M. Role of stimulus dose on neuropsychological functioning after electroconvulsive therapy in patients with major depressive disorder. Front Psychiatry. 2024 Sep 26;15:1443270. doi: 10.3389/fpsyt.2024.1443270.

Targeted Cognitive Assessments Reveal Domain-Specific Effects of ECT

Meghan Y. Reddy, MD reviewing Guo et al., Asian J Psychiatr., 2024 Aug

This systematic review and meta-analysis evaluated the results from 30 studies on post-ECT cognitive assessments in patients with MDD, identifying 11 tools effective for short-term assessment (≤10 days post-ECT) and 10 tools for long-term assessment (≥1 month post-ECT), with six tools reliable in both timeframes. These findings support the use of domain-specific cognitive tools for clinical evaluations.

ECT is a rapid and highly effective treatment for severe depression, yet concerns about post-ECT cognitive impairment limit its use. While prior research consistently found short-term cognitive impairments with recovery over time, studies using bilateral ECT and broad cognitive screens (e.g., Mini-Mental Status Exam [MMSE], MoCA) may have overestimated impairment. Most research has focused on optimizing ECT parameters to minimize cognitive risk, but less attention has been given to optimizing assessment tools that can improve clinical decision-making.

This prospectively registered systematic review and meta-analysis followed PRISMA guidelines and searched major databases for studies published through November 12, 2023. Studies were included if participants were diagnosed with MDD, were treated with at least 6

sessions of ECT, and had baseline cognitive assessments. Cognitive outcomes were categorized as short-term (up to 10 days post-treatment) and long-term (≥1 month past treatment). A random effects model employing the I^2 test was used due to the high degree of methodological heterogeneity. Sensitivity analyses evaluated the robustness and stability of the results, and GRADE classification was applied to determine the strength of evidence for recommended cognitive assessment tools.

A total of 30 studies (20 RCTs, 10 quasi-experimental) met inclusion criteria, encompassing a total of 2,462 patients with MDD. While overall cognitive function did not significantly change post-ECT, subgroup analyses revealed specific domain-level changes. Short-term effects (≤10 days post-ECT) included statistically significant impairments in memory and learning (SMD = 0.47; 95 % CI, 0.09-0.85) and verbal ability (SMD = 0.75; 95 % CI, 0.01-1.50), with improvements in attention and processing speed (SMD = −0.35; 95 % CI, -0.69 to -0.02). Long-term effects (≥1 month post-ECT) included improvements in memory and learning (SMD = −0.36; 95 % CI, -0.57 to −0.16), verbal ability (SMD = −0.59; 95 % CI, -1.1 to -0.08), and visuospatial ability (SMD = −0.59; 95 % CI, -0.17 to -0.01), while other domains showed no significant changes. Using the GRADE classification, six tools were identified as reliable for both short- and long-term cognitive assessment: the Controlled Oral Word Association Test, the Abbreviated Mental Test, the Color-Word Interference Test Item 3, the Global Self-Evaluation of Memory, the Trail Making Test, and the Symbol Coding Test. Five additional tools were identified as useful only in the acute period (11 total), while four additional tools were identified as useful only for long-term evaluation (10 total). Notably, MMSE and MoCA were included in some studies but failed to meet GRADE criteria for sensitivity and reliability.

Impact: This systematic review and meta-analysis refines our understanding of ECT's cognitive effects, demonstrating that while overall cognitive function remained stable post-treatment, domain-specific changes can be detected in the short- and long-term. In the acute phase, impairments in memory, verbal ability, and executive function were detected, while over time, cognitive function improved in key areas such as memory, verbal fluency, and visuospatial ability. Prior studies may have overestimated impairment by relying on broad cognitive screens (e.g., MoCA, MMSE) designed for dementia rather than domain-specific post-ECT cognitive changes. Additionally, the studies evaluated here primarily used optimized ECT protocols (e.g., right unilateral ultrabrief pulse) associated with fewer cognitive side effects. While this suggests that modern ECT may mitigate cognitive risks, comprehensive cognitive monitoring remains essential to detect subtle impairments and guide clinical decision-making. A key limitation of this study is methodological heterogeneity, and the mechanisms underlying post-ECT cognitive changes remain unclear. Future long-term research is needed to refine cognitive assessment strategies and explore mechanisms of cognitive recovery post-ECT.

Guo Q, Wang Y, Guo L, Chen C, Han S, Shang S. Evaluating cognitive assessment tools for patients with major depressive disorder receiving electroconvulsive therapy: A systematic review and meta-analysis. Asian J Psychiatr. 2024;100:104169. doi:10.1016/j.ajp.2024.104169

ECT and Psychiatric Rehospitalization: Higher Rates May Reflect Illness Severity

Amanda Mengotto, MD reviewing Rahangdale A, Ferraro J. BMC Psychiatry 2024 Oct

This retrospective national database study investigated the relationship between ECT and psychiatric rehospitalization rates in patients with severe mental illness. It found that ECT is associated with higher rehospitalization rates and longer stays, particularly in patients with severe mental illnesses, such as psychosis and schizophrenia. While these findings suggest an association between ECT use and higher rehospitalization rates, the study acknowledges that ECT is typically reserved for patients with more severe conditions.

ECT is one of the most effective treatments for severe, treatment-resistant psychiatric disorders. While it is well known for providing rapid symptom relief, its impact on longer-term rehospitalization rates remain debated. Previous studies in international settings suggested that continuation or maintenance ECT (CM-ECT) may reduce rehospitalization rates. However, no large-scale study in a U.S.

hospital system had examined the relationship between ECT use and psychiatric rehospitalization risk across various disorders.

This study analyzed a retrospective dataset of inpatient encounters between 2016 – 2022 from HCA Healthcare Behavioral Health Units located across the United States. Adults (≥18 years old) hospitalized for major depressive disorder (MDD), bipolar disorder, schizophrenia, or schizoaffective disorder were included. Rehospitalization rates within one year of discharge were compared between patients who received ECT and non-ECT patients with the same diagnosis. Subgroup analyses evaluated the impact of diagnosis, sex, and race, and statistical analyses included Fisher's Exact Test and the Wilcoxon Rank Sum Test to compare categorical and continuous variables, respectively.

Of the 38,109 patients included in the analysis, 637 received ECT. Patients who underwent ECT had a significantly higher psychiatric rehospitalization rate (37.5%) compared to those who did not receive ECT (20.7%; $p < 0.001$). The mean length of stay upon rehospitalization was also notably longer in the ECT group (14.5 days) versus the non-ECT group (6.4 days; $p < 0.001$). Subgroup analysis revealed that patients diagnosed with psychotic disorders had the highest rehospitalization rates and longer stays; the rehospitalization rates among patients diagnosed with schizophrenia was 87.28%, with schizoaffective disorder it was 73.77%, and with bipolar disorder with psychotic features it was 65.6%. Additionally, while some differences in rehospitalization rates were observed based on age, sex, and race, the study did not report statistical tests of these relationships. The mean age of readmitted patients (45.5 years) was lower than that of the ECT group overall (59.5 years). White patients were overrepresented among those receiving ECT (85.6% of ECT recipients vs. 71.4% of the total patient population), while Black patients were underrepresented (7.7% of ECT recipients vs. 20.4% overall). Among rehospitalized patients, 23.7% were Black. Women accounted for a larger proportion of ECT recipients (60.1%), while men made up a greater share of readmitted patients (56.07%). Measures of the strength of association between ECT treatment and rehospitalization rates, such as the Phi Coefficient (0.0529) and Cramer's V (0.0529), indicate that while the relationship is statistically significant, it is not particularly strong.

Impact: This retrospective nationwide database study suggests that inpatient psychiatric patients receiving ECT experience higher psychiatric rehospitalization rates and longer hospital stays when compared to other psychiatric inpatients. However, these higher rates could reflect the complexity and severity of their underlying conditions rather than a direct adverse effect of ECT itself. These findings are consistent with known high rates of relapse after ECT, underscoring the need for clinicians to carefully monitor patients post-ECT and consider adjunctive therapies or long-term management strategies to reduce the risk of relapse and rehospitalization. Despite its strengths, this study is limited by its retrospective design, reliance on electronic health records, and lack of data on illness severity, ECT treatment variations, and outpatient follow-up care—factors that may independently influence rehospitalization risk. Additionally, demographic disparities in ECT treatment were observed, but socioeconomic and systemic barriers to access were not analyzed. Future research is needed to explore the underlying factors driving these associations and to determine if there are modifiable variables in ECT protocols that could mitigate the increased rehospitalization risk.

Rahangdale A, Ferraro J. Electroconvulsive therapy (ECT) and psychiatric rehospitalization rates: a retrospective study. BMC Psychiatry. 2024 Oct 30;24(1):753. doi: 10.1186/s12888-024-06211-2.

cTBS (continuous theta burst stimulation)
DBS (deep brain stimulation)
dTMS (deep transcranial magnetic stimulation)
ECT (electroconvulsive therapy)
HFL (high frequency left, 10 Hz stimulation to left DLPFC)
HF-rTMS (high frequency repetitive transcranial magnetic stimulation; 10 Hz unless otherwise stated)
iTBS (intermittent theta burst stimulation)
MST (magnetic seizure therapy)
TBS (theta-burst stimulation; TMS delivered as triplet burst pulses at 50 Hz, repeated at 5 Hz)
TENS (transcutaneous electrical nerve stimulation)
TMS (transcranial magnetic stimulation)
rTMS (repetitive transcranial magnetic stimulation)
tDCS (transcranial direct current stimulation)
tACS (transcranial alternating current stimulation)
TPS (transcranial pulse stimulation)

BOLD (blood oxygen level dependent)
DTI (diffusion tensor imaging)
EEG (electroencephalography)
EMG (electromyography)
fMRI (functional magnetic resonance imaging)
MRI (magnetic resonance imaging)
MT (motor threshold)
RMT (resting MT)

ADHD (attention-deficit/hyperactivity disorder)
AUD (alcohol use disorder)
GAD (generalized anxiety disorder)
MDD (major depressive disorder)
OCD (obsessive compulsive disorder)
PTSD (post-traumatic stress disorder)
SUD (substance use disorder)
TRD (treatment resistant depression)

BAI (Beck Anxiety Inventory)
BDI (Beck Depression Inventory)
CGI (clinical global impression scale)
HAM-A (Hamilton Anxiety Rating Scale)
HAM-D / HDRS (Hamilton Depression Rating Scale)
MADRS (Montgomery-Asberg Depression Rating Scale)
MoCA (Montreal Cognitive Assessment)
PANSS (Positive and Negative Symptom Scale)
QIDS (Quick Inventory of Depressive Symptomatology)
YBOCS (Yale-Brown Obsessive Compulsive Scale)

ANOVA (analysis of variance)
AUC (area under the curve)
CI (confidence interval)
FDA (United States Food and Drug Administration)
ICA (independent component analysis)
ITT (intention to treat)
OR (odds ratio)
PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses)
RCT (randomized controlled trial)
ROC (receiver operating characteristic)
SMD (standard mean difference)

BA (Brodmann area)
DLPFC (dorsolateral prefrontal cortex)
DMPFC (dorsomedial prefrontal cortex)
M1 (primary motor cortex)
mPFC (medial prefrontal cortex)
OFC (orbitofrontal cortex)
SMA (supplementary motor area)