

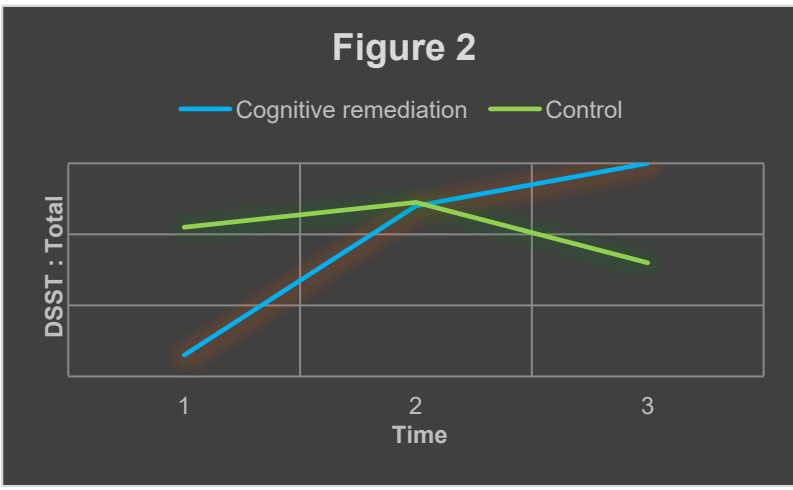
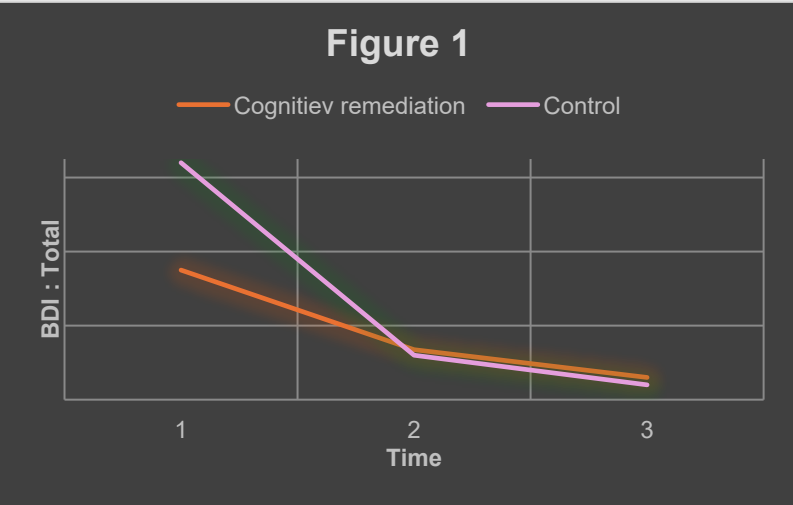
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Conclusions: This multicenter study demonstrates that CR yields sustained improvements in self-reported depression, subjective cognitive impairment, executive function, and processing speed at 3-month follow-up. Although some outcomes showed non-significant trends favoring CR, these findings support its potential as an adjunctive intervention for MDD, warranting further investigation in real-world settings.

Introduction: Major Depressive Disorder (MDD) is among the most prevalent psychiatric conditions worldwide. Cognitive impairment is a core feature, often persisting after remission and worsening with relapses. Cognitive Remediation (CR) is a structured psychosocial intervention targeting cognition and psychosocial functioning. This study reports the 3-month follow-up (T2) results of a previously conducted RCT, which assessed outcomes at baseline (T0) and post-treatment (T1).

Objectives: To evaluate the sustained effects at 3 months (T2) of computerized CR versus an active control (computer games, CG) in adults with MDD experiencing a Major Depressive Episode (MDE), focusing on cognitive performance, depressive symptoms, and functioning.

Methods: This single-blind, multicenter RCT randomized patients to either CR, delivered by trained therapists, or CG. Outcomes were measured with validated instruments by blind assessors at T0, T1, and T2. Mixed models for repeated measures (MMRM) with an intent-to-treat analysis were applied. Inclusion criteria required ≥ 8 years of education; exclusions included neurological disorders, severe head injury, or intellectual disability. Drop-out was defined as > 5 days interruption of antidepressant therapy or ≥ 2 consecutive missed sessions with declared discontinuation.



Results: Of 142 screened patients, 101 were randomized (CR n = 52, CG n = 49), and 81 completed the study through T2 (CR n = 45, CG n = 36). At the 3-month follow-up, CR showed superior outcomes in self-reported depression (BDI, Figure 1, $p = 0.003$), subjective cognitive impairment (PDQ-5, $p = 0.007$), executive function (TMT-B, $p = 0.032$), and processing speed (DSST, Figure 2, $p = 0.009$), with significantly greater improvements compared to CG. No significant between-group differences were observed for clinician-rated depression (MADRS, $p = 0.112$) or verbal memory (CVLT, $p = 0.083$), although CR patients showed greater within-group improvements. While no statistically significant effects were found for TMT-A ($p = 0.349$) or Clinical Global Impression (CGI-S, $p = 0.458$), CR patients exhibited trends toward improved processing speed (TMT-A, $p = 0.055$) and a more pronounced reduction in clinical severity (CGI-S), suggesting potential non-specific benefits of the intervention.

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