Verbal Memory and Inhibitory Control Predict Functional Capacity and Impairment in Major Depressive Disorder: A Secondary Analysis of the ReMIND SWITCH Trial

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1. Introduction

- Major Depressive Disorder (MDD) is a leading cause of disability worldwide.
- 30-60% of people with MDD exhibit cognitive impairment, which is associated with worse functional outcomes.
- The purpose of the present analysis was to examine whether cognition explains some of the relationship between depression with functional capacity (ability to perform everyday activities) and functional impairment (limitations in daily activities due to illness).
- We also examined whether certain cognitive domains are more associated with functional capacity or functional impairment in depression

2. Study Design

- Data was analyzed from the ReMIND SWITCH trial (NCT02272517; N = 101)
- Subjects were ≤ 65, met criteria for MDD, had a Montgomery-Asberg Depression Rating Scale (MADRS) ≥ 22 at baseline, Patient Health Questionnaire-9 item (PHQ-9) ≥ 14, Perceived Deficits Questionnaire-Depression (PDQ-D) > 25, and Digit Symbol Substitution (DSST) < 70
- Functional Capacity was measured with the UCSD Performance-Based Skills Assessment – Brief (UPSA-B); Functional Impairment was measured with the Functional Assessment Short Test (FAST)
- Cognition was measured with the DSST (processing speed), Rey Auditory Verbal Learning Test (RAVLT; verbal learning and memory), Stroop Color/Word Test (SCWT; inhibition), Trail-Making Test (TMT; cognitive flexibility), Simple Reaction Time/Choice Reaction Time (SRT/CRT; psychomotor speed)

3. Data Analysis

- A Global Cognitive composite was first created by taking the mean of the (standardized) cognitive tests
- Multiple regression models were used to examine the relationship between global cognition and functional capacity and functional impairment, controlling for depression severity and perceived cognitive problems
- Stepwise regression with backwards elimination was used to identify whether specific cognitive domains predict functional capacity and impairment
- Indirect effects analysis was used to examine whether cognition explains the relationship between depression and functional capacity and impairment

4. Global Cognition Predicts Functioning

	Capacity	Impairment
Variable	**β (P-Value)**	**β (P-Value)**
Global Cognition	**0.45 (< 0.001)***	**-0.30 (0.001)***
MADRS	-0.04 (0.733)	0.20 (0.046)
PDQ-D	0.00 (0.961)	**0.25 (0.011)***

**Significant after adjusting for multiple comparisons (P = 0.025)*

5. Cognitive Domains Predict Functioning

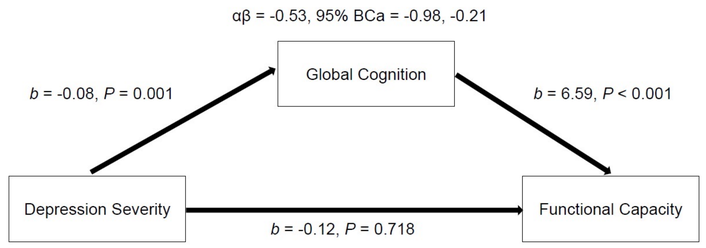
	Capacity	Impairment
Variable	**β (P-Value)**	**β (P-Value)**
DSST	--	--
RAVLT	**0.24 (0.016)***	--
SCWT	**0.35 (0.001)***	--
TMT-B	--	--
SRT/CRT	--	**-0.28 (0.002)***
MADRS	-0.05 (0.612)	**0.25 (0.011)***
PDQ-D	0.02 (0.845)	**0.22 (0.023)***

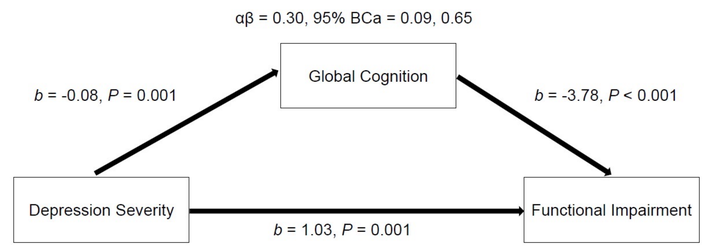
**Significant after adjusting for multiple comparisons (P = 0.025); cognitive predictor removed from model if P > 0.025*

6. Indirect Effects Analysis

- Indirect effects analysis (mediation) is used to examine whether the relationship between two variables occurs through another variable
- Here, mediation was tested by the product of coefficients (αβ), where α refers to the relationship between depression severity and cognition; β refers to the relationship between cognition and functional outcomes
- Statistical significance is evaluated by bootstrapping αβ; if the 95% confidence intervals do not contain zero, the indirect effect is considered statistically significant (here, Bias-corrected and accelerated bootstrapping with 5,000 replications was used)
- No formal effect size measure exists; here, we use proportion mediated (indirect effect of cognition divided by direct effect) to estimate the effect size

7. Indirect Effects Analysis





- The proportion of the relationship between depression and functional capacity explained by cognition is approximately 80%
- The proportion of the relationship between depression and functional impairment explained by cognition is approximately 23%

9. Conclusions

- Cognitive function is a robust predictor of functional outcomes in MDD
- Depression severity and self-reported cognitive complaints were only associated with functional impairment
- Verbal memory and inhibition on the Stroop were uniquely associated with functional capacity (ability to perform everyday activities), whereas psychomotor speed was uniquely associated with impairment (limitations in daily activity due to illness).
- Cognitive function explains part of the relationship between depression and functional outcomes
- Interventions that improve cognition in MDD or work for individuals with cognitive dysfunction with MDD will likely improve functional outcomes

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