

Rumination-Focused Cognitive Behavioral Therapy Versus Mindfulness-Based Cognitive Therapy in Treatment-Resistant Major Depressive Disorder: A Controlled Empirical Analysis of Ruminative Response Styles and Prefrontal Inhibitory Dysregulation

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Abstract. Treatment-resistant major depressive disorder (TR-MDD) presents a substantial clinical burden, particularly when ruminative response styles perpetuate maladaptive prefrontal inhibitory dysregulation. This controlled empirical analysis examined 112 adults diagnosed with TR-MDD (DSM-5 criteria), randomized to either Rumination-Focused Cognitive Behavioral Therapy (RFCBT) or Mindfulness-Based Cognitive Therapy (MBCT) across a 16-week protocol. Primary outcomes included scores on the Ruminative Response Scale (RRS), Hamilton Depression Rating Scale (HDRS-17), and neurocognitive indices of executive inhibition measured via the Sustained Attention to Response Task (SART). RFCBT demonstrated significantly superior reductions in brooding rumination ($d = 0.74$, $p < .001$) and HDRS-17 scores compared to MBCT. Neurocognitive inhibitory deficits showed partial mediation of treatment outcomes. These findings support RFCBT as a preferential protocol for TR-MDD with prominent ruminative phenomenology.

Keywords: treatment-resistant major depressive disorder, rumination-focused cognitive behavioral therapy, ruminative response styles, prefrontal inhibitory dysregulation, mindfulness-based cognitive therapy, brooding rumination, executive inhibition, Hamilton Depression Rating Scale, neurocognitive mediation

Introduction

Major depressive disorder (MDD) remains one of the most prevalent and debilitating psychiatric conditions worldwide, affecting an estimated 280 million individuals globally as of 2024 (World Health Organization, 2024). Among its most clinically challenging presentations is treatment-resistant major depressive disorder (TR-MDD), operationally defined as the failure to achieve adequate symptomatic remission following at least two adequate pharmacological trials of differing mechanistic classes. TR-MDD accounts for approximately 30–40% of all MDD diagnoses and is associated with markedly elevated rates of suicidality, functional impairment, and healthcare resource utilization. Despite decades of psychopharmacological advancement, the integration of targeted psychotherapeutic protocols into TR-MDD management remains insufficiently systematized, representing a critical gap in both clinical practice and empirical literature. A particularly prominent transdiagnostic mechanism implicated in the perpetuation of TR-MDD is maladaptive rumination—defined within the Response Styles Theory framework (Nolen-Hoeksema, 1991) as repetitive, passive, self-focused cognitive processing directed toward one's distress, its causes, and its consequences. The Ruminative Response Scale (RRS) distinguishes two functionally distinct subtypes: brooding, a moody, comparative pondering associated with heightened depressogenic vulnerability, and reflective pondering, a more problem-solving-oriented mode. Neurobiologically, chronic brooding rumination has been associated with aberrant prefrontal cortex (PFC) inhibitory dysregulation, specifically implicating the dorsolateral and ventromedial PFC in deficient top-down suppression of amygdala-driven affective hyperreactivity. This neurocognitive substrate distinguishes TR-MDD from non-treatment-resistant presentations and underscores the necessity of rumination-targeted psychotherapeutic intervention. Two manualized psychotherapeutic modalities have demonstrated preliminary efficacy in targeting ruminative processes: Rumination-Focused Cognitive Behavioral Therapy (RFCBT), developed by Watkins et al. (2007), which employs concrete thinking induction, functional analysis of rumination triggers, and compassionate imagery rescripting; and Mindfulness-Based Cognitive Therapy (MBCT), a structured 8-week group program integrating mindfulness meditation practices with cognitive behavioral principles. Both modalities theoretically target overlapping yet mechanistically distinct aspects of ruminative dysregulation; however, no adequately powered, controlled head-to-head comparison exists within a rigorously defined TR-MDD sample assessed concurrently across self-report, clinician-rated, and objective neurocognitive domains. The present study addresses this lacuna through a 16-week randomized controlled design in which adults meeting DSM-5 criteria for TR-MDD were allocated to RFCBT or MBCT. This paper is

organized as follows: Section 2 details the participant recruitment and diagnostic screening protocols; Section 3 describes the randomization and intervention delivery procedures; Section 4 presents primary and secondary outcome analyses including RRS brooding subscale scores, HDRS-17 ratings, and SART-derived inhibitory indices; and Section 5 discusses clinical implications, mediational pathways, and recommendations for integrating RFCBT within stepped-care TR-MDD frameworks.

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