Therapeutic Potential of MDMA-Based Therapy in Rumination Treatment

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Abstract: Rumination, characterized by persistent and repetitive negative thinking, is a debilitating feature of many psychological disorders and can contribute to the development of additional mental health complications. In recent years, growing interest has emerged in the therapeutic potential of MDMA (3,4-methylenedioxymethamphetamine), a Schedule I controlled substance traditionally associated with recreational use. Although MDMA-assisted therapy has demonstrated promising results in the treatment of post-traumatic stress disorder (PTSD), its applicability to rumination remains underexplored despite shared underlying mechanisms. This paper reviews current neurobiological and psychological evidence to evaluate the potential efficacy of MDMA-assisted therapy in reducing ruminative thought patterns. Findings from PTSD research suggest that MDMA-assisted therapy may produce significant and sustained symptom reduction, potentially through decreased amygdala activity and reduced functional connectivity with the posterior cingulate cortex (PCC), a region implicated in self-referential processing. Additionally, MDMA's capacity to enhance emotional openness and facilitate fear extinction may promote deeper engagement in psychotherapy and disrupt maladaptive cognitive loops. While direct research on rumination is limited, existing evidence indicates promising therapeutic potential, warranting further investigation.

Keywords: MDMA, Rumination, MDMA assisted therapy, Psychotherapy

Rumination, also known as negative thought loops, is defined as repetitive, prolonged, and recurrent negative thinking about one's self, feelings, personal concerns, and upsetting experiences (Watkins & Roberts, 2020). Rumination keeps the brain in a constant state of perceived threat, even when no real danger is present. By repeatedly reactivating emotional, traumatic, and distressing memories, rumination may prolong physiological stress responses. Neurologically, this may interfere with the downregulation of the HPA axis (Hypothalamic–Pituitary–Adrenal axis). Downregulation is the process through which the body's stress-response system returns to a regulated or resting state. This is important to note because prolonged activity of the HPA axis, the body's central stress alarm system, has been linked to various psychiatric disorders, including depression, anxiety, panic disorders, and phobias (Norris et al., 2025). In addition, research suggests that prolonged HPA-axis activation may contribute to the onset and progression of neurodegenerative diseases, including Alzheimer's disease and other forms of dementia, making this a prevalent public health concern (Vyas et al., 2016).

Current treatments for rumination include psychotherapeutic approaches such as cognitive behavioral therapy (CBT). Within CBT, individuals are guided to identify and challenge maladaptive or unwanted thought patterns while simultaneously increasing engagement in rewarding and adaptive behaviors. This process aims to reduce the persistence of negative thinking cycles and promote more constructive cognitive and behavioral responses. In addition, there is a more specialized approach known as rumination-focused cognitive behavioral therapy. This form of therapy is designed specifically to target ruminative thinking patterns. It incorporates functional analysis, a process used to understand how and why an individual thinks in a particular way, to help distinguish between helpful and unhelpful methods of processing difficulties. CBT emphasizes the development of strategies that encourage more adaptive and constructive thought processes (Watkins & Roberts, 2020). However, these treatments may not be effective for all individuals for a variety of reasons, including reluctance to disclose personal experiences, treatment resistance, and other contributing factors. Numerous variables may influence treatment effectiveness.

One potential treatment for adults experiencing rumination that will be explored in this paper is MDMA (3,4-methylenedioxymethamphetamine)-assisted therapy. Although MDMA-assisted therapy has already been studied and has demonstrated promising results in the treatment of PTSD (post-traumatic stress disorder), its potential benefits for other mental health conditions remain less extensively investigated. This question is important because expanding MDMA's clinical applications may provide additional treatment options for patients who struggle with persistent negative thought patterns. Investigating its use beyond PTSD addresses an area that has received comparatively less scientific attention and may expand current knowledge.

1. Background: MDMA and Its Effects

When MDMA was first synthesized in 1912, researchers later explored its potential therapeutic applications because it was believed to facilitate communication during psychotherapy. In 1985, the Drug Enforcement Administration (DEA) classified MDMA as a Schedule I substance following concerns regarding misuse. However, the U.S. Food and Drug Administration (FDA) approved Phase I clinical trials of MDMA during the mid-1990s (Riaz et al., 2023). Phase I trials represent the initial stage of human testing and are designed to evaluate safety, metabolism, absorption, and excretion. As of 2026, MDMA is undergoing Phase III clinical trials, the final stage of testing before potential FDA approval.

MDMA is a synthetic substance produced in laboratory settings and is commonly ingested in tablet or capsule form. It is classified as a psychoactive substance and primarily affects the brain's serotonergic system. When ingested, serotonin—the neurotransmitter associated with positive mood—is released into the synapse in response to neural signaling, binds to receptors on neighboring neurons, and is subsequently removed through reuptake transporters. MDMA enters serotonergic neurons through these transporters, triggering a substantial release of serotonin while simultaneously inhibiting its reuptake, resulting in

increased receptor activation. This heightened serotonergic activity is associated with changes in mood, social bonding, and sensory perception and is often described as producing elevated feelings of well-being, energy, alertness, and interpersonal connectedness (National Institute on Drug Abuse, 2024). The National Institute on Drug Abuse further reports that users may experience increased sensitivity to sensory stimuli and that the effects typically peak within 15–30 minutes and last approximately three hours (National Institute on Drug Abuse, 2024).

2. What Is MDMA-Assisted Psychotherapy?

MDMA-assisted psychotherapy is a form of psychotherapy that incorporates the administration of a controlled dose of MDMA. Typically, it involves single-dose MDMA administration once per month on two or three occasions, combined with preparatory and integrative psychotherapy sessions. The inclusion of MDMA is intended to facilitate openness and engagement with traumatic or emotionally challenging experiences. MDMA reduces the reuptake of monoamines such as serotonin, dopamine, and norepinephrine, which may contribute to reductions in anxiety and increases in interpersonal connectedness. These effects may enhance the therapeutic process and improve treatment outcomes (Parrott, 2014).

3. Literature Review and Neurobiological Evidence

Current research supports the idea that MDMA-assisted therapy may reduce PTSD symptoms and, in some cases, lead to complete remission when administered in clinical settings. Multiple studies have demonstrated significant reductions in PTSD symptoms following only two to three administrations of MDMA combined with several nondrug psychotherapy sessions, with long-lasting remission reported in some participants (Fedducia & Mithoefer, 2018). Similar to PTSD, rumination involves repetitive cognition and anxiety-related thought patterns. During PTSD treatment, MDMA is administered to facilitate emotional openness and allow patients to confront traumatic memories and identify triggers. Researchers suggest that the associated increase in serotonin may allow individuals to engage with traumatic memories with reduced emotional distress and self-judgment. This reduction in emotional overwhelm may facilitate greater insight into the origins of maladaptive thought patterns and help overcome psychological barriers that often hinder therapeutic progress.

In addition, a study of MDMA-assisted therapy for PTSD found that reductions in functional connectivity between the amygdala and posterior cingulate cortex (PCC) were associated with therapeutic improvement in PTSD symptoms.

Evidence suggests that strong functional connectivity between the amygdala and PCC may reflect heightened emotional monitoring and repetitive self-focused cognition, processes that resemble rumination. The amygdala plays a central role in threat detection and fear processing, while the PCC is a key component of the default mode network (DMN), which is involved in self-referential thinking, autobiographical memory, and future-oriented cognition. Increased connectivity between these regions may contribute to persistent emotional self-focus and negative thought loops characteristic of rumination (Singleton et al., 2023).

4. Possible Mechanisms

One mechanism that supports MDMA-assisted therapy as a potential treatment for rumination is its effect on brain connectivity. Rumination has been associated with activity in the posterior cingulate cortex (PCC), a brain region involved in self-referential thought processes. The amygdala plays a central role in the regulation of fear, anxiety, and stress responses (Gupta et al., 2011). Increased functional connectivity between these two regions may contribute to elevated levels of rumination. If MDMA-assisted therapy is associated with reduced amygdala–PCC connectivity in PTSD studies, and this reduction correlates with symptom improvement, then it is plausible that disrupting this connectivity may reduce maladaptive repetitive thought patterns.

Evidence suggests that strong functional connectivity between the amygdala and PCC may reflect heightened emotional monitoring and repetitive self-focused cognition. The amygdala serves as a primary center for threat detection and fear processing, while the PCC is a major component of the default mode network (DMN). The DMN is involved in self-focused cognitive processes, including reflection on personal experiences, recollection of past events, and consideration of future possibilities. Increased connectivity between these regions may contribute to persistent emotional self-focus and negative thought loops characteristic of rumination (Singleton et al., 2023).

A 2022 study examining MDMA-assisted therapy for anxiety associated with life-threatening illnesses provides qualitative evidence supporting this proposed mechanism. One participant described a substantial reduction in anxious thoughts related to cancer recurrence following treatment. Prior to therapy, she reported persistent concerns regarding everyday behaviors that she believed could increase her risk of cancer progression. Following treatment, she reported that these thoughts had largely subsided and that she had developed a greater sense of acceptance regarding her condition. Although this account does not directly demonstrate changes in neural connectivity, it suggests that MDMA-assisted therapy may reduce persistent anxiety-related thought patterns (Barone et al., 2022). These findings support the possibility that MDMA-assisted therapy may reduce repetitive anxious thinking and therefore warrant further investigation as a treatment for rumination.

Because MDMA produces feelings of emotional connectedness and psychotherapy often relies on the processing of distressing memories, it is possible that MDMA may also reduce rumination through altered memory reconsolidation or by facilitating fear-extinction learning and retention (Fedducia & Mithoefer, 2018). Under the influence of MDMA, patients may be better able to process emotionally significant memories with reduced fear responses. This pharmacological effect may promote reflective thinking and allow individuals to adopt a more accepting and less judgmental perspective toward their thoughts and experiences.

A 2022 study investigating MDMA-assisted therapy for patients with terminal illnesses provides additional support for this possibility. Participants reported profound psychological shifts during treatment. For example, one participant described experiencing a complete absence of fear and an enhanced ability to explore personal experiences without judgment. The

participant further reported that MDMA-assisted therapy enabled greater awareness of long-standing emotional isolation and difficulties related to emotional expression. These findings suggest that MDMA may facilitate deeper emotional processing and self-understanding, both of which may contribute to reductions in rumination.

5. Conclusion

MDMA-assisted therapy demonstrates considerable potential as a novel treatment for rumination by targeting both the neurobiological and psychological mechanisms that sustain repetitive negative thought patterns. Evidence suggests that MDMA may reduce hyperactivity within the amygdala and weaken its functional connectivity with the posterior cingulate cortex, a key region involved in self-referential thinking within the default mode network. Because rumination is closely associated with excessive emotional reactivity and persistent self-focused cognition, disruption of this neural circuitry may help individuals reduce repetitive negative thought processes. Furthermore, MDMA's ability to increase serotonin activity and promote feelings of emotional openness, safety, and interpersonal connectedness may enhance the therapeutic process, allowing patients to engage with distressing thoughts and memories with reduced fear and self-judgment. Findings from PTSD and related research further support the possibility that these combined effects may produce meaningful and lasting psychological improvements.

Despite these promising findings, several important limitations must be acknowledged. Research specifically examining MDMA-assisted therapy for rumination remains limited, and questions regarding long-term safety, individual differences in treatment response, and potential adverse effects remain unresolved. However, current evidence suggests that when MDMA-assisted therapy is administered in carefully controlled clinical settings with appropriate screening procedures and professional support, adverse outcomes are relatively uncommon and manageable.

Overall, MDMA-assisted therapy remains an emerging therapeutic approach; however, its ability to target underlying mechanisms associated with rumination highlights its potential as a valuable addition to existing mental health interventions. Continued clinical research is necessary to evaluate its effectiveness, establish long-term safety, and determine its broader applicability as a treatment for rumination and related psychological conditions.

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