

HEART ALCHEMY INSTITUTE · CLINICAL RESEARCH SERIES

# Ketamine-Assisted Psychotherapy (KAP)

## *Current Research Findings & Clinical Applications*

Preparation · Medicine Sessions · Integration

PTSD · Burnout · Existential Distress · TBI · Grief

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## Executive Summary

Ketamine-Assisted Psychotherapy (KAP) represents one of the most significant paradigm shifts in modern mental health treatment. By combining the rapid-acting neurobiological effects of ketamine with structured psychotherapeutic support — specifically preparation and integration sessions — KAP offers a comprehensive, evidence-based approach to healing that transcends the limitations of conventional pharmacotherapy and psychotherapy practiced in isolation. This document synthesizes current peer-reviewed research on the efficacy of KAP in treating Post-Traumatic Stress Disorder (PTSD), burnout (encompassing depression and anxiety), existential distress, Traumatic Brain Injuries (TBIs), and complicated grief. The evidence consistently indicates that the integration of psychotherapy with ketamine administration significantly enhances and prolongs therapeutic outcomes compared to pharmacological intervention alone.

Heart Alchemy Institute is committed to offering KAP within a rigorous, compassionate, and evidence-informed framework. This document is intended to provide prospective clients with a clear understanding of the scientific foundation underlying this transformative modality.

## 1. Introduction: The Emergence of Ketamine-Assisted Psychotherapy

Ketamine was first synthesized in 1962 and approved by the U.S. Food and Drug Administration (FDA) in 1970 as a dissociative anesthetic. For decades, it served primarily in emergency medicine and surgical settings due to its excellent safety profile, rapid onset, and minimal respiratory depression. Over the past two decades, a growing body of research has revealed ketamine's remarkable potential as a rapid-acting antidepressant, anxiolytic, and facilitator of profound psychological change — effects that extend far beyond its original anesthetic applications.<sup>1</sup>

The pivotal discovery that a single subanesthetic intravenous infusion of ketamine could produce rapid and robust antidepressant effects — often within hours — in patients with treatment-resistant depression sparked a revolution in psychiatric research.<sup>2</sup> The FDA's 2019 approval of esketamine (Spravato) for treatment-resistant depression further legitimized ketamine's role in psychiatry.<sup>3</sup>

KAP emerged as a distinct and more comprehensive treatment model that goes beyond purely pharmacological administration. Drawing from the traditions of psychedelic-assisted psychotherapy, KAP positions the ketamine experience within a structured therapeutic container that includes preparation, the dosing session itself, and integration.<sup>4</sup> This model recognizes that the subjective, psychological, and spiritual dimensions of the ketamine experience are not merely side effects to be managed, but are central to its therapeutic efficacy.<sup>5</sup>

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## 2. Mechanisms of Action: How Ketamine Heals

### 2.1 Neurobiological Mechanisms

**NMDA Receptor Antagonism and Glutamatergic Modulation:** Ketamine's primary pharmacological action is as a non-competitive antagonist of the N-methyl-D-aspartate (NMDA) receptor, a key glutamate receptor present in over 60% of all brain synapses. By blocking NMDA receptors, ketamine triggers a cascade of downstream effects that ultimately promote synaptic plasticity and antidepressant responses.<sup>6</sup>

**Neuroplasticity and BDNF Upregulation:** Ketamine rapidly stimulates neuroplasticity and upregulates Brain-Derived Neurotrophic Factor (BDNF), a protein critical for neuronal survival and growth.<sup>8,9</sup> This neuroplastic window, peaking approximately 24–48 hours after administration, is the optimal period for psychotherapeutic integration — the brain is in a heightened state of receptivity to new learning and cognitive restructuring.<sup>10</sup>

**Default Mode Network Modulation:** Ketamine differentially modulates large-scale neural networks, including the Default Mode Network (DMN) — associated with self-referential thought and rumination. By temporarily disrupting the hyperactive, self-critical patterns of the DMN that characterize depression, PTSD, and anxiety, ketamine creates a psychological opening for new perspectives and emotional processing.<sup>7</sup>

### 2.2 Psychological and Experiential Mechanisms

The subjective experience induced by ketamine — which can include altered states of consciousness, ego dissolution, heightened emotional access, and mystical-type experiences — is increasingly recognized as a key driver of therapeutic outcomes. Research has demonstrated that the intensity of mystical-type experiences correlates significantly with improvements across numerous psychiatric outcome measures.<sup>5,11</sup> These experiences provide the raw material for the psychotherapeutic work of integration.

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## 3. The KAP Therapeutic Framework: Preparation and Integration

The efficacy of KAP is deeply rooted in its structured therapeutic framework. Unlike standard ketamine infusion clinics that administer the medication without psychological support, KAP positions the ketamine experience within a comprehensive psychotherapeutic container. The standard KAP protocol involves three distinct phases.<sup>4,12</sup>

### 3.1 Preparation Sessions

Prior to ketamine administration, therapists conduct one or more preparation sessions. These establish a therapeutic alliance and foundation of trust, provide psychoeducation about ketamine's effects, and involve collaborative intention-setting. Drawing from the psychedelic therapy tradition, preparation sessions introduce patients to the concept of "set and setting" — the idea that the patient's mindset and the physical and relational context profoundly influence the nature and therapeutic value of the experience.<sup>10,13</sup>

### 3.2 The Dosing Session

During the ketamine session, the therapist provides a supportive, non-directive presence. The patient is typically in a comfortable, reclined position with an eye mask and carefully curated music to support inward exploration. The therapist monitors the patient's physical and psychological state, offering reassurance and gentle guidance as needed. Following the acute experience, the patient is encouraged to share their insights, emotions, and imagery with the therapist.<sup>4,13</sup>

### 3.3 Integration Sessions

Integration is widely considered the most critical component of KAP for achieving lasting therapeutic change. Integration sessions — typically held within 24–48 hours after the dosing session and continuing over subsequent weeks — are dedicated to helping the patient process, understand, and make meaning of their ketamine experience.<sup>12</sup> The goal is to translate the transient neuroplasticity and psychological breakthroughs induced by ketamine into enduring cognitive, emotional, and behavioral changes. Various psychotherapeutic modalities — including CBT, somatic therapy, narrative therapy, and mindfulness-based approaches — can be woven into integration work.<sup>10,14</sup>

## 4. KAP in the Treatment of Specific Conditions

### 4.1 Post-Traumatic Stress Disorder (PTSD)

PTSD is a chronic and debilitating condition affecting approximately 6–9% of the general population over their lifetime, with significantly higher rates among veterans, first responders, and survivors of sexual violence.<sup>15</sup> Characterized by intrusive memories, avoidance, negative alterations in mood and cognition, and hyperarousal, PTSD is frequently resistant to first-line treatments including SSRIs and trauma-focused psychotherapies.<sup>15,16</sup>

A 2023 systematic review with meta-analyses of six randomized controlled trials found that ketamine significantly reduced PTSD symptom scores compared to active controls, with benefits detectable as early as one day after treatment.<sup>16</sup> A 2024 systematic review further confirmed significant symptom improvements both 24 hours after the first infusion and at the conclusion of treatment.<sup>17</sup> A large retrospective effectiveness study of KAP across 11 Field Trip Health clinics (n=346) found large treatment effects sustained at 6 months, with 50–75% of participants achieving a minimal clinically important difference at 3 months.<sup>19</sup>

Outcome Measure	Effect Size (3 mo)	Effect Size (6 mo)	% Achieving MCID (3 mo)
Depression (PHQ-9)	d' = 0.86	d' = 0.73	75%

Anxiety (GAD-7)	$d' = 0.75$	$d' = 0.61$	50%
PTSD (PCL-6)	$d' = 0.80$	$d' = 0.65$	60%

Table 1: KAP treatment effects from Yermus et al. (2024). MCID = Minimal Clinically Important Difference.

## 4.2 Burnout, Depression, and Anxiety

Burnout is a syndrome of chronic workplace stress characterized by emotional exhaustion, depersonalization, and a reduced sense of personal accomplishment. It is particularly prevalent among healthcare workers, first responders, and individuals in high-demand professions, and frequently co-occurs with clinical depression and anxiety.<sup>20,21</sup>

A 2024 case series examined a group KAP program for frontline healthcare workers experiencing COVID-19-related burnout and PTSD. Results demonstrated significant reductions in burnout, PTSD, depression, and anxiety, with participants reporting improved emotional regulation and a renewed sense of meaning in their work.<sup>21</sup> A 2025 study of a 6-week community-based group KAP program for first responders (n=16) found significant reductions in trauma, anxiety, and depression symptoms ( $p < 0.002$ ).<sup>20</sup>

## 4.3 Existential Distress

Existential distress refers to profound suffering arising from confrontation with the fundamental conditions of human existence — mortality, meaninglessness, isolation, and freedom. It is particularly prevalent in patients facing life-threatening illness and individuals grappling with profound loss or identity crises.<sup>23</sup>

A review in the *Cleveland Clinic Journal of Medicine* (2025) noted a promising overall body of evidence supporting psychedelic-assisted therapies for alleviating existential distress and improving spiritual well-being at the end of life.<sup>24</sup>

A 2025 narrative review proposed a novel, time-limited KAP model specifically for palliative care populations, integrating preparatory and integrative psychotherapy with two ketamine dosing sessions and goals-of-care discussion.<sup>7</sup>

## 4.4 Traumatic Brain Injury (TBI)

TBI presents a complex clinical challenge, as neurological sequelae frequently co-occur with depression, anxiety, PTSD, and cognitive impairment. Historically, ketamine was used with caution in TBI patients due to concerns about intracranial pressure; however, a 2025 systematic review and meta-analysis concluded that ketamine is safe for TBI patients and does not adversely affect intracranial pressure when administered appropriately.<sup>27</sup>

A 2025 narrative review found that esketamine at subanesthetic doses demonstrated neuroprotective effects against TBI-induced neurological deficits in animal models, and that ketamine's anti-inflammatory and neuroplastic effects may support neurological recovery.<sup>28</sup> A 2024 clinical outcomes study found ketamine effective in reducing depression and PTSD in patients with comorbid TBI, regardless of TBI severity.<sup>26</sup>

## 4.5 Grief and Bereavement

Grief is a universal human experience, but for a significant minority — estimated at up to 10% of bereaved individuals — grief becomes prolonged and pathological. Prolonged Grief Disorder (PGD), recognized in the DSM-5-TR and ICD-11, is characterized by intense yearning for the deceased and significant functional impairment persisting for a

year or more after the loss.<sup>30</sup>

A 2024 narrative review from Johns Hopkins University identified psychedelics including ketamine as a promising treatment avenue for PGD, noting that psychedelics often produce subjective effects — transcendence, mystical experiences, a sense of oneness — that may be uniquely relevant to the existential distress of PGD.<sup>30</sup> A foundational case report documented the rapid resolution of complicated grief symptoms following a single IV infusion of ketamine.<sup>31</sup> Integration therapy is essential in grief work, providing space for patients to make meaning of their loss and develop a continuing bond with the deceased.<sup>32</sup>

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## 5. Safety, Contraindications, and Ethical Considerations

KAP has a well-documented safety profile when administered responsibly within established clinical guidelines. The most frequently reported adverse effects — including dissociation, nausea, headache, transient anxiety, and mild elevations in heart rate and blood pressure — are typically mild, transient, and resolve without intervention.<sup>13</sup>

Contraindications include a history of primary psychotic disorders, active substance use disorder (particularly involving ketamine or other dissociatives), uncontrolled hypertension, elevated intracranial or intraocular pressure, pregnancy, and aneurysmal or hemorrhagic vascular disease. A thorough medical and psychiatric evaluation is essential prior to initiating KAP.<sup>13</sup> The therapeutic use of ketamine within a structured KAP protocol, with appropriate screening and monitoring, is considered safe and well-tolerated.

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## Conclusion

The current body of scientific literature provides compelling support for the efficacy of Ketamine-Assisted Psychotherapy across a spectrum of challenging and often treatment-resistant psychological conditions. The synergistic effect of ketamine's neurobiological mechanisms — including NMDA receptor antagonism, enhanced neuroplasticity, BDNF upregulation, and modulation of large-scale neural networks — combined with the structured psychological support of preparation and integration sessions, offers a depth of healing that neither pharmacology nor psychotherapy can achieve in isolation.

At Heart Alchemy Institute, KAP is offered within a rigorous, compassionate, and evidence-informed framework that honors both the science and the profound human dimensions of this work. Our protocols are designed to maximize therapeutic outcomes through careful patient selection, thorough preparation, attentive support during dosing sessions, and comprehensive integration. We are committed to accompanying each client on their unique journey of healing with skill, care, and deep respect for the transformative potential of this modality.

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