

Ketamine-Assisted Psychotherapy

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Background:

Ketamine was approved by the FDA as an anesthetic in 1970. Over the past several decades, randomized controlled trials have provided growing evidence that ketamine can rapidly improve mood and other emotional symptoms for some people, especially when other treatments have not helped. Many clinicians now see ketamine-assisted psychotherapy (KAP), as an important emerging option in mental health care. People considering medication as a treatment for anxiety or depression might consider the more effective results of Ketamine-Assisted Psychotherapy.

Biological changes:

Ketamine modulates glutamate, a key neurotransmitter involved in learning, memory, and synaptic plasticity. At lower, sub-anesthetic doses, ketamine can function as an analgesic, anti-obsessional, and antidepressant agent, and research suggests it may enhance neuroplasticity and support the brain's capacity to form and reorganize neural connections. Because of this, ketamine has sometimes been described as a kind of “fertilizer” for new brain connections.

Ketamine can quiet overactive circuits involved in worry and rumination. It typically reduces activity in the “default mode network,” the brain network most closely associated with self-referential thinking and the sense of ego. With this network dialed down, ketamine can release large amounts of unconscious material all at once, which may feel profound but also overwhelming.

Ketamine's Effects:

Ketamine tends to reduce the sense of self while also dampening cortical awareness, which often softens the impact of material that surfaces. Traumatic experiences may come into awareness, but the emotional intensity can be more manageable, making ketamine a gentler introduction to non-ordinary states of consciousness for many people. As a dissociative medicine, ketamine can produce one of the more striking alterations in consciousness that people encounter in their lives.

Ketamine has a relatively clear dose–response curve, which allows treatment to be tailored to the type of experience desired:

- Mild dose: verbal, lightly dissociated, able to talk and engage.

- Moderate dose: some verbal capacity, but largely inward
- High dose: non-verbal, deeply dissociated, often with strong visionary or mystical qualities.

Visits:

A typical in-office ketamine session, from check-in to departure, is usually under two hours. Acute changes in the default mode network and increases in neuroplasticity peak during the session but can persist for roughly a day. This period can be an especially effective window for psychotherapy. Low-dose lozenges often produce a “twilight” state that can enhance access to painful material while maintaining enough grounding to explore and process it. Ego defenses are softened but not absent, which can help people tolerate difficult insights and work through longstanding wounds more deeply. This combination can accelerate psychotherapeutic change.

In KAP, higher doses of ketamine are sometimes used to induce a more profound non-ordinary state, with experiences resembling those reported with classical psychedelics, including altered perceptions, mystical-type experiences, and feelings of ego dissolution. These states can be powerful catalysts for change, but they can also be destabilizing if someone is not well prepared, adequately screened, and strongly supported during and after the experience. Preparation, set and setting, and careful integration are essential.

Psychotherapy is woven throughout the KAP process. Either immediately after the acute effects of ketamine subside, and/or in the days and weeks that follow, clients engage in counseling or psychotherapy to reflect on the experience in the context of their history, values, and goals. The therapeutic work focuses on:

- Stabilizing and sustaining positive behavioral changes.
- Integrating psychological material and insights.
- Processing trauma and entrenched patterns.
- Improving relationships and sense of connection.
- Strengthening self-awareness and self-compassion.

Many people who pursue KAP struggle with self-doubt, negative self-beliefs, and persistent thought patterns that keep them feeling stuck. When used appropriately, this model can help people feel more connected to themselves and others, often with a renewed sense of meaning and possibility.

Medical and Psychological Screening

A thorough psychological and medical evaluation is essential to determine whether ketamine-assisted psychotherapy is appropriate and reasonably safe for a given individual. Ketamine is not suitable for everyone. In many practices, the following are considered disqualifying or strong cautions:

1. Not being ready or willing to engage in deep therapeutic work.
2. Pregnancy or breastfeeding.
3. Poorly controlled or untreated hypertension or significant cardiovascular disease.
4. Poorly controlled or untreated hyperthyroidism.
5. Acute mania or hypomania.
6. A history of psychosis or schizophrenia, bipolar or mania.
7. Known allergy to ketamine or a history of ketamine dependence or misuse.
8. Recent traumatic brain injury.
9. Severe obstructive sleep apnea or significant respiratory disease.
10. Obesity at a level that meaningfully increases anesthetic risk (often judged on a case-by-case basis).
11. An active substance use disorder or ongoing addiction.
12. History of recurrent bladder inflammation (cystitis.)
13. Poor reality testing.

Anyone considering KAP should discuss the potential benefits, risks, and alternatives with a qualified medical prescriber and psychotherapist, and should only receive ketamine in a safe, legally compliant, medically supervised setting that includes preparation and integration support.

References:

<https://www.tandfonline.com/doi/full/10.1080/02791072.2019.1587556#abstract>

<https://pmc.ncbi.nlm.nih.gov/articles/PMC12294355/>

<https://pmc.ncbi.nlm.nih.gov/articles/PMC9207256/>

<https://pmc.ncbi.nlm.nih.gov/articles/PMC11613527/>

<https://pmc.ncbi.nlm.nih.gov/articles/PMC9542929/>

<https://www.sciencedirect.com/science/article/abs/pii/S0165032725006020>

<https://www.nature.com/articles/s41398-024-03033-4>

<https://www.columbiapsychiatry.org/news/ketamine-rapidly-improves-cognitive-function-making-those-suicidal-crisis-less-likely-harm-themselves>

<https://pubmed.ncbi.nlm.nih.gov/30995364/>

<https://www.sciencedirect.com/science/article/pii/S0165032725019081>

<https://www.sciencedirect.com/science/article/abs/pii/S1876201824002648>

<https://www.nature.com/articles/s41591-024-03063-x>

<https://www.sciencedirect.com/science/article/abs/pii/S0022395624001341>