

An open-label safety and feasibility pilot trial of ketamine-assisted psychotherapy for methamphetamine use disorder (KAPPA)

Kathryn Fletcher^a, Nadine Ezard^{a,b}, Krista Siefried^{a,b}, Harriet MacDonald^a, Liam Acheson^{a,b}, Gillinder Bedi^c, Alexandre Guerin^c, Elizabeth Knock^b, Michael Millard^d, Robert May^b, Jonathan Brett^{e,f}, Jess Doumany^g, Celia Morgan^{h,i}, Brendan Clifford^{a,b}

Ketamine-assisted psychotherapy for methamphetamine use disorder

- Australia leads the world in methamphetamine use and dependence.¹ Frequent use is linked to mental health issues, insomnia, cardiovascular problems, cognitive deficits and risk of psychosis.^{2,3}
- No approved pharmacological treatments exist for methamphetamine use disorder (MAUD). Current care relies of psychosocial interventions like Cognitive Behavioural Therapy (CBT), which have modest effectiveness.⁴
- Preliminary evidence suggests ketamine-assisted psychotherapy (KAP) can reduce substance use and improve mental health outcomes.^{5,6} This approach has not been tested in MAUD.

Objectives

- 1 Assess the safety and feasibility of subanaesthetic ketamine combined with CBT for adults with MAUD.
- 2 Explore changes in methamphetamine use, cravings, withdrawal symptoms, quality of life and treatment satisfaction.

Methods

Design: Open-label, single-arm clinical trial.

Participants: 20 adults with DSM-5-TR criteria for MAUD, recruited from St Vincent's Hospital, Sydney (outpatient setting).

Assessment periods: Safety and feasibility over 8 weeks, secondary outcomes over 24 weeks.

Intervention: Three subcutaneous doses of ketamine (0.75mg/kg to 0.9mg/kg) + four sessions of CBT over a 4-week period.

Intervention

Ketamine

- Dissociative anaesthetic, glutamatergic n-methyl-d-aspartate (NMDA) receptor antagonist.
- 3 x subanaesthetic doses, delivered subcutaneously each week.

CBT

- Strategies to enhance motivation to change use, skills to cope with craving, manage triggers for use, relapse prevention.
- 4 x sessions (once weekly) within 24-48 hours following ketamine to coincide with peak ketamine-induced synaptogenesis.

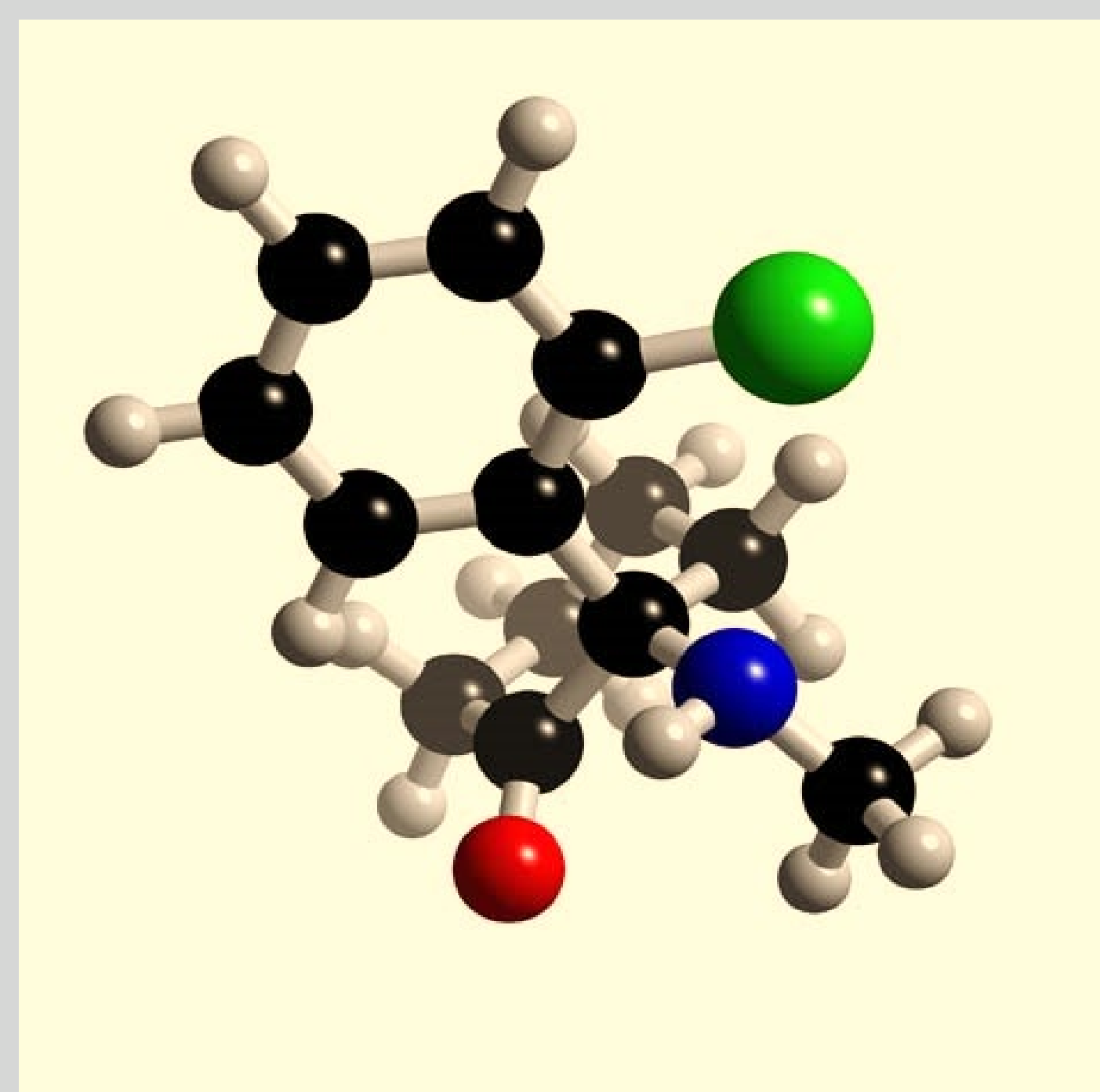


Fig 1. Ketamine

Why Ketamine + CBT for MAUD?

- 1 Enhances neurogenesis and neuroplasticity in animal models,⁷ which supports learning.
- 2 Reduces stimulant craving.
- 3 Alleviates low mood through rapid antidepressant action, with may promote therapeutic engagement in those experiencing withdrawal-related dysphoria.



Criteria	Inclusion	Exclusion
Age	≥18 years of age	
Consent	Able to provide informed consent	
Compliance	Willing and able to comply with all study requirements	
Diagnosis	Meets DSM-5-TR criteria for methamphetamine use disorder	Meets DSM-5-TR criteria for current or past use disorder for ketamine or analogues
Drug Screen	Positive urine drug screen for methamphetamine	Prescribed or non-prescribed use of ketamine in the previous four weeks
Treatment seeking	Seeking treatment to cease or reduce methamphetamine use	Currently enrolled in another treatment trial for MAUD
Psychiatric conditions	Mild to moderate coexisting depression, anxiety, or transient psychotic symptoms	Current psychotic disorder, acute suicidality, or bipolar disorder
Substance use disorders	Stable opioid use disorder on opioid agonist treatment	Current moderate or severe substance use disorders (except tobacco, caffeine, or cannabis)
Other	Willing to register as a client of the St Vincent's Hospital Sydney Stimulant Treatment Program	Likely or planned surgery, travel, incarceration, or other engagements during the study
Pregnancy		Currently pregnant or breastfeeding
Medical conditions		Severe liver, kidney, or bladder disease, elevated cerebrospinal fluid pressure, severe cardiovascular disease, heart failure, poorly controlled hypertension

Progress to date

- Ethics approval obtained from St Vincent's Hospital Sydney Human Research Ethics Committee (2023/ETH00530).
- Consumer group consultations indicate that those seeking to reduce methamphetamine use are supportive and interested in trialling this novel treatment approach.
- Recruitment will commence shortly. Study results will inform the development of a later randomised controlled trial.

For further information about the KAPPA trial contact k.fletcher@unsw.edu.au

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Discussion

- This is the first study to investigate the safety and feasibility of KAP for MAUD, an important first step towards establishing a novel, potentially effective treatment for this underserved group.
- Secondary outcomes were selected with a harm-reduction and person-centered lens, including reduction in methamphetamine use, cravings, withdrawal symptoms, and improved quality of life.
- The use of a standardised manual-based CBT alongside a low-cost subcutaneous ketamine dosing protocol allows for ready reproducibility.

References

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