

Official Title:

Investigating the Synergistic Potential of Music as an Adjunct to Ketamine Therapy for Chronic Noncancer Pain

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Statistical analyses

This study aims to examine the potential synergistic effects of intravenous (IV) ketamine infusions and listening to self-selected music for patients with chronic noncancer pain.

Aim 1: To investigate the effect of listening to self-selected music during IV ketamine infusion therapy on pain intensity in the short-term, when compared to therapist-selected music or silence. We hypothesize that pain relief will be significantly greater when participants are exposed to self-selected music during the IV ketamine infusions, when compared to therapist-selected music or silence.

The impact of IV ketamine infusion while listening to preferred music will be assessed by comparing its effects on short-term pain intensity relief (24 hours post-infusion) to those of IV ketamine infusion while listening to therapist-selected music and silence. A repeated-measures analysis of variance (ANOVA) will be used, with time (pre vs. post) and condition (preferred, therapist-selected, silence) as main effects, and the time \times condition interaction as the main effect of interest. The order in which participants were exposed to the conditions will be statistically controlled for to account for potential order effects. Planned contrasts between conditions will be conducted to test our *a priori* hypotheses.

Our second aim (**Aim 2**) is to estimate the duration of pain relief following each of the ketamine infusion conditions (usual care, silence, self-selected and therapist-selected music). To evaluate differences in the duration of pain relief across conditions, similar repeated-measures ANOVAs as in Aim 1 will be conducted separately at each follow-up time point, replacing the 24-hour post-infusion pain rating with the pain rating from each of the time points (daily from days 1 to 7, then weekly from weeks 2 to 5). This approach will allow us to determine the time points in which pain intensity differences between conditions remain significant, and when those differences begin to subside.

All analyses will be conducted using R and R Studio, following an intention-to-treat (ITT) approach. Descriptive statistics and exploratory graphical techniques will be used to evaluate statistical assumptions. Assumptions of normality, sphericity, and homoscedasticity will be checked using residual plots and appropriate diagnostic tests. If assumptions of repeated-measures ANOVA are violated or if data are missing not at random, linear mixed-effects models may be used for sensitivity analyses. Where necessary, transformations of dependent variables will be considered. The level of significance will be set at $\alpha = 0.05$.

All remaining analyses will be exploratory.