Does Chronic Ketamine Administration Cause Hyperalgesia in Mice?

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Introduction

Ketamine is a synthetic drug used as an anesthetic as it can produce analgesic effects and is now being used as an antidepressant meaning it could potentially be used in a new population of patients. When discussing ketamine it's important that we understand drug addiction as ketamine has been abused as a party drug for its psychoactive effects like hallucinations and feelings of euphoria.
Drug addiction is a three stage cycle that consists of binge/intoxication, withdrawal/negative affect and preoccupation/anticipation. Other drugs, particularly opioids, cause an increase in pain sensitivity during withdrawal which is thought to contribute to the addiction cycle through negative reinforcement. Previous studies have shown that NMDA receptors are upregulated following chronic ketamine exposure. It's unclear if ketamine causes hyperalgesia.

Impact:

The purpose of this experiment is to understand the effects of chronic ketamine use in mice and answer whether mice will experience hyperalgesia from long term ketamine administration. By answering this question, we will understand the long term effects of ketamine use, we will understand its misuse potential and it will give more information towards potential guidelines for medical use of ketamine.

Methods:

The mice received intraperitoneal ketamine or saline Injections meaning in their body cavities, 2 times a day over a period of two weeks. The starting dosage for each injection was 10 mg/kg. We then increased the dosage to 20 and 30 mg/kg. After the initial injection, we used the hot plate to see if ketamine is producing an analgesic effect. When using the hot plate, and we looked for thermal pain reflexes which can be seen through jumping, withdrawal of the paw or paw licking. After chronic administration of ketamine, we withdrew the drug and tested the mice on cold plates to see if there were behavioral differences between the saline and ketamine mice. For the cold plate test, typical reactions would be jumping. The reason we used a cold plate was to see if ketamine caused hyperalgesia.

Methods:

C-57BL/6 Mice, 8 Male 8 Female
- intraperitoneal (IP) ketamine Injections
- Cold/Hot Plate:(2℃/55℃)

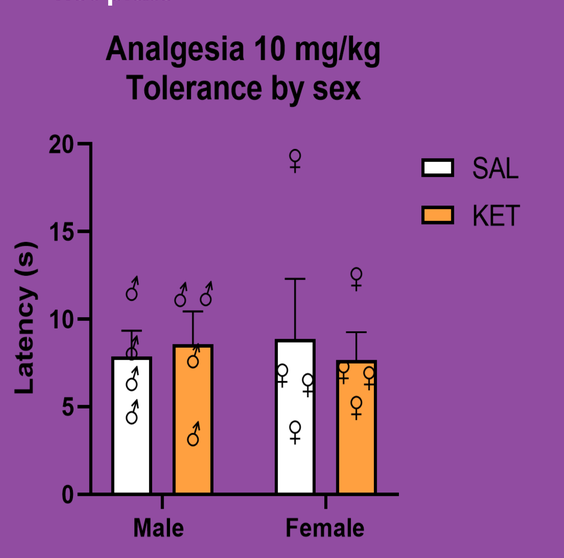
Reactions: Jumping, paw flicking, paw licking, paw on wall.

Hot/Cold plate

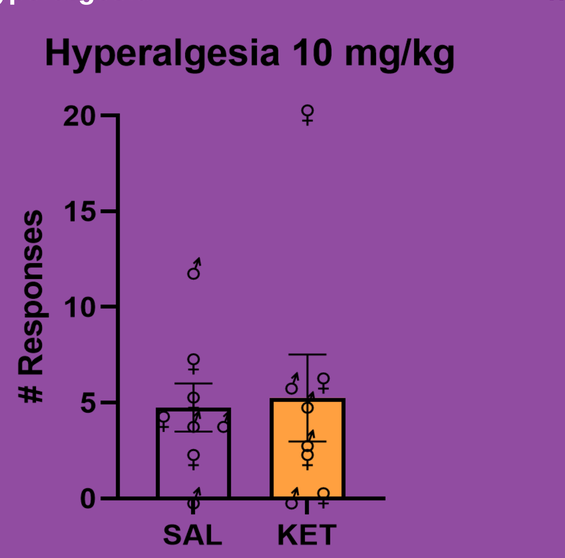
Results

10mg/kg of KET causes analgesic effect

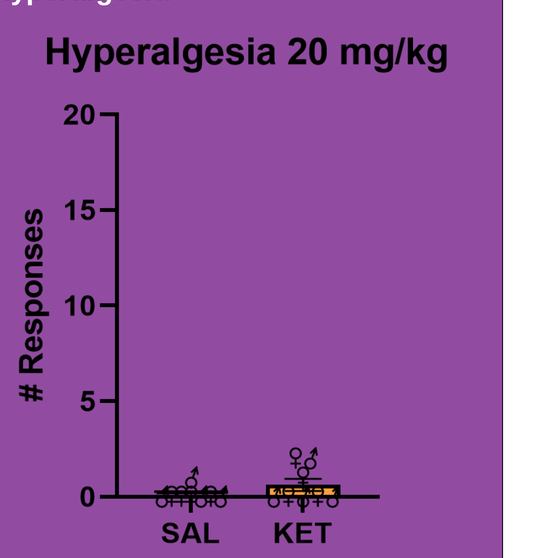
10mg/kg of KET causes tolerance to hot plate



10mg/kg of KET doesn't cause hyperalgesia



20mg/kg of KET doesn't cause hyperalgesia



Conclusion:

From this experiment, ketamine may not cause hyperalgesia despite previous literature on its misuse potential.

Confounding Factors:

1)Small sample size
2)Mice became comfortable on the plates
3)Stress induced analgesia

Future Work:

- How does ketamine effect sexes differently?
- Do experiment again with higher dosages and longer injections

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