Concerns on using ketamine therapy as a treatment for major depressive disorder

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ABSTRACT

The use of ketamine therapy to cure those with major depressive disorder is currently a controversial topic in the medical field. Ketamine is a pain reliever, it acts as a noncompetitive inhibitor of N-methyl-D-aspartic (NMDA) receptors, and it is typically used as anesthesia. Ketamine is a controlled and addictive substance that is commonly abused, and if it becomes more accessible it could potentially pose a risk for future addiction development. Here, I performed an in-depth literature review on the side effects and warnings for ketamine usage and compared those with some of the reported benefits. The goal of this research was to increase the understanding of the mechanisms for ketamine's negative effects on mental states, and to increase consumer awareness on the benefits and disadvantages of choosing ketamine to treat depression. In my research I found that 48-61% of people using SPRAVATO® brand ketamine treatment experienced sedation, 61-84% experienced derealization, depersonalization, and saw hallucinations. It is also seen after five years of use at similar dosage has caused a loss of gray matter in the brain, as well as decreasing the integrity of the white matter. This causes instability in the brain's processes, such as learning and processing stimuli. The next most common side effects in patients under the age of 24 included nausea and vomiting, feeling intoxicated, vertigo, anxiety, and suicidal thoughts. In conclusion, a safer alternative to ketamine would be an antidepressant that improves the natural reuptake of neurotransmitters in the brain, rather than introducing a controlled substance.

DOSAGE AND INTENDED EFFECTS

For MDD treatment purposes, ketamine is most commonly dosed at 0.5mg/kg of body weight, and this can vary down to 0.1 mg/kg to 0.75 mg/kg, usually done intravenously (IV). Higher doses are more likely to cause adverse side effects (Rosenbaum 2022). The most common dose of ketamine intravenously (IV) for 5 to 10 minutes of anesthesia/dissociation is 1 to 2 mg/kg body weight. Ketamine's half life is about 45 minutes, and that is why for therapy purposes it has to be repeated every 2-3 days, for as low as 40 minutes each day. The goal is to give the patient their next dose before the previous dose fully wears off. Ketamine is not a long term fix for the symptoms however, as once treatment is stopped, the MDD symptoms come back (Farber 2018).

Now, the usual illicit dose of ketamine can range from 50mg to 100mg per usage, which can last over the course of a few days. If I were to be prescribed the standard 0.5 mg/kg dose right now to be delivered every 2 to 3 days, I would be given 80mg of ketamine. This falls in the range of illicit usage, especially over the extended period of time , and this is why it's a major health risk to be prescribing ketamine as a treatment for MDD.

KETAMINE BACKGROUND AND SIDE EFFECTS

Why do people choose ketamine?

Studies show that fifteen to thirty percent of patients diagnosed with major depressive disorder (MDD) do not have a reaction to antidepressants that target the monoaminergic systems (Farber 2018). Monoaminergic systems include the serotonin and dopamine pathways, two of the main hormones responsible for feeling good, and are often the two imbalanced chemicals in people with MDD (Farber 2018). Since these systems are not responsive, NMDA antagonists are currently being researched as a treatment alternative, and ketamine is one of the most studied examples so far (Farber 2018). Despite all the potential for therapeutic effects, about 50% of patients do not show improvement or positive results under this type of therapy (Herrara-Melendez et. al 2021).

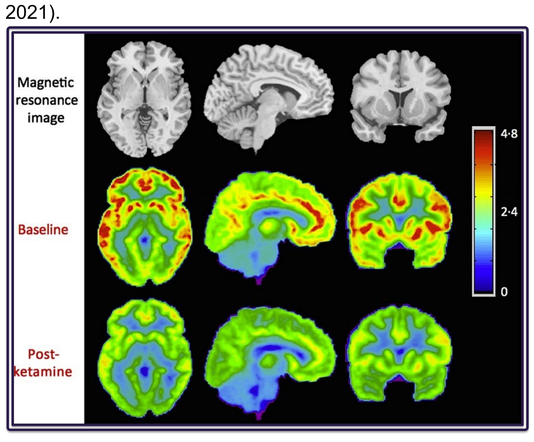


Figure 1: Image shows magnetic resonance imaging (MRI) and brain activity before and after ketamine treatment. People with MDD have hyperactive brains, as shown by the red in the baseline. Once treatment was administered, all red is depleted and the brain then functions at a lower power. (Drewninany et. Al 2014).

Side Effects:

Physical

- High blood pressure, which leads to faster heart rate, chest pain, anxiety, and headaches.
- Less gray matter in the brain
- Less integrity of white matter
- Pollakiuria, dysuria, micturition urgency, nocturia, ulcerative cystitis, suprapubic pain

Mental

- Psychosis and schizophrenia-like symptoms
- Nociception and brain tissue damage (at low routine doses)
- Difficulty with memory, emotional, and cognitive functions.
- Dissociation, dizziness, nausea, sedation, vertigo, hypoesthesia, anxiety, lethargy, increased blood pressure, vomiting, and feeling drunk

THE DEVELOPING FRONTAL LOBE

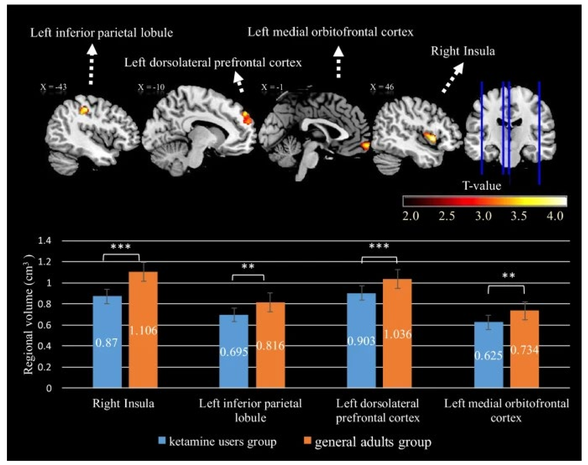


Figure 2: Here the consistent usage of ketamine from 34 adults who used over an average of 5 years is compared to a control group who never used ketamine. Although hard to put a specific number, the usual illicit dose of ketamine can range from 50mg to 100mg per usage, which can last over the course of a few days.(Hung et. Al 2020)

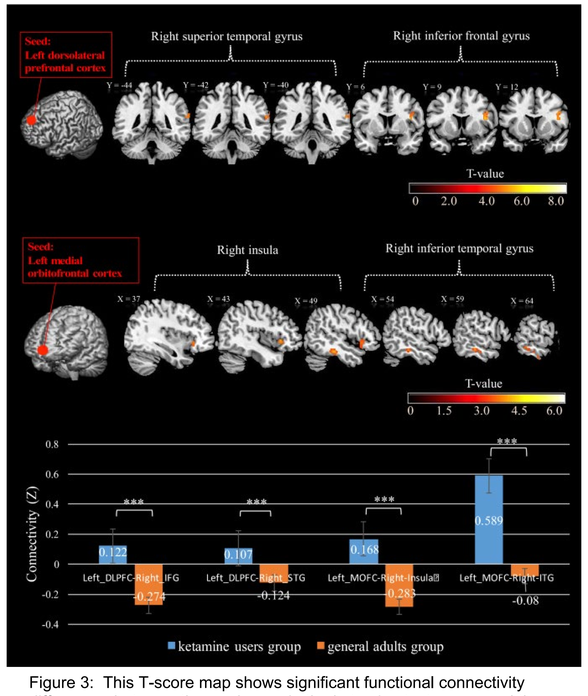
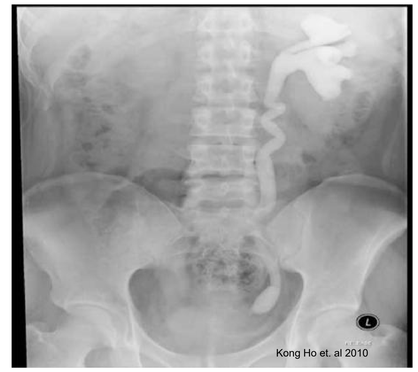


Figure 3: This T-score map shows significant functional connectivity differences between those who are in the ketamine test group, and those in the control group. Functional connectivity can be assessed with a resting-state functional MRI, or rs-fMRI, which will measure the blood oxygen level dependent signals (BOLD) when the patient is at a resting state. As seen in the control (orange) group, there are far less BOLD signals, meaning there's less reliance on signals depending on blood oxygen.
The BOLD signal will reflect changes in deoxyhemoglobin driven by localized changes in brain blood flow and blood oxygenation. By the process of neurovascular coupling, these are tied to underlying neuronal activity.

DRUG COMPANY WARNINGS

The ketamine treatment itself is known to cause many urinary tract issues, including but not limited to suprapubic pain and a lack of expression from kidneys.



CONCLUSIONS

While ketamine is capable of providing a relaxed state in the mind, it is not a safe alternative to other antidepressant treatments. Overall, the possible physical and psychological side effects are a large risk in exchange for the treatment. Alternatives, such as traditional antidepressants, have similar risks in terms of suicidal ideation but they lack the psychological derealization and addictive risks (NHS 2021 Feb 5), and appear to be less of a risk than ketamine.