The Association between the Recreational Use of Hallucinogens and Major Depression

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Introduction

- The clinical use of hallucinogens like psilocybin and ketamine has shown promising results in improving symptoms of mental disorders like major depression (Artin et al., 2021). Psilocybin therapy is used in clinical research as a form of treatment for patients who experience major depression and show little improvement on antidepressants or other forms of psychotherapy.
- Patients who experience major depression and have gone through multiple treatments of one of the hallucinogenic therapies show improvement in their depressive symptoms (Kalfas et al., 2023). Placebo controlled trials also show improvement in depressive symptoms after therapy (Sloshower et al., 2023)
- Clinical trials with psychedelic-assisted psychotherapy show promising results in treatment-resistant depression, where positive effects last several months after treatment (Artin et al., 2021). Clinical trials do not account for a patient who is both depressed and has engaged in the recreational use of psilocybin or related drugs on their own.

Research Questions

- Is there a relationship between the recreational use of hallucinogens (non-clinical) and major depression?
- Does this association change based on sex assigned at birth?

Methods

Sample

- Participants over the age of 18 who reported using hallucinogens (n=2276) were drawn from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC).
- The total sample includes a population of 43,903 participants who are all above the age of 18 and non-institutionalized
- The sample includes people of different ages, gender identities, and mental health conditions. NESARC was an observational study done in person with an interviewer.

Measures

- Major depression was quantified using the NIAAA, Alcohol Use Disorder and Associated Disabilities Interview Schedule – DSM-IV (AUDADIS-IV).
- The major depression module includes questions on clinical DSM diagnosis of major depression (two-level, categorical)
- The hallucinogen section of the dataset contains questions concerning the overall engagement with hallucinogenic drugs, measured with the question "Ever Used Hallucinogens" (two-level, categorical)

Results

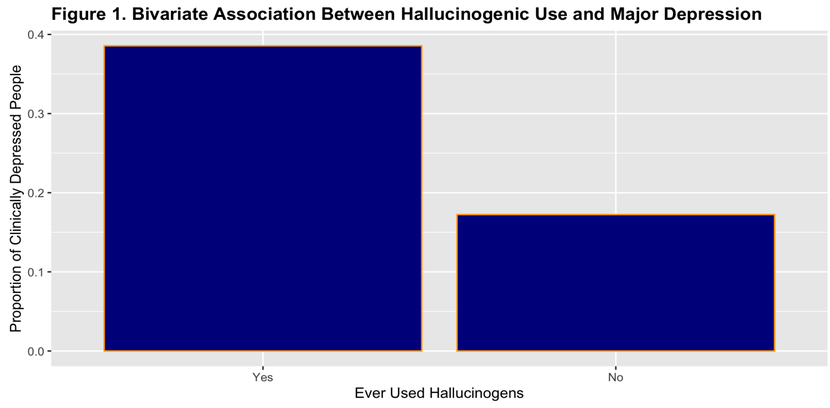
Univariate

- 5.10% of the total population engaged with hallucinogenic drugs at some capacity
- 18.32% of the total population met the DSM-IV criteria for major depression
- 42.9% of the total population is male, 57.1% is female

Bivariate

- Chi-Squared analysis showed that **subjects who used hallucinogens were significantly more likely to be depressed** (38.56%) compared to those who did not use hallucinogens (17.23%), X^2=626.05, 1 df, p<2.2 e^{-16}.
- As anticipated, **hallucinogenic use was significantly associated with** DSM-IV qualifications for **major depression** OR=0.33 (0.30-0.36). Odds Ratio indicates that who have used hallucinogens have an expected odds of not having depression that is 3.03 times higher than those who do.
- Overall, **subjects who are depressed had higher engagement with hallucinogens** compared to non-depressed subjects (Fig. 1).

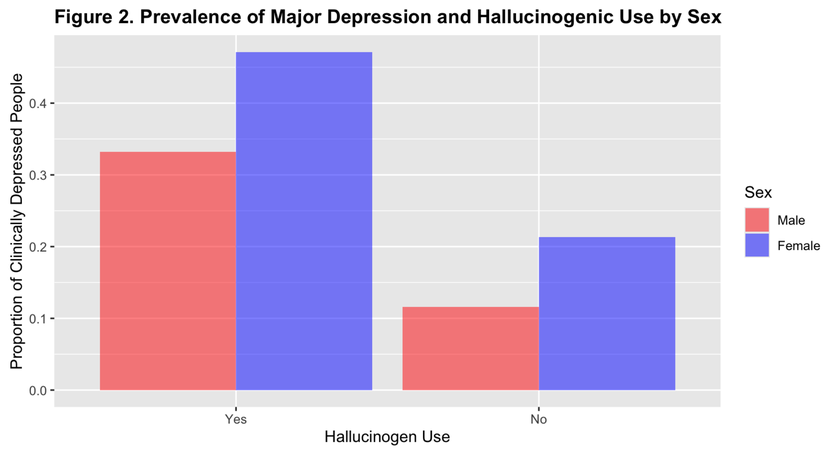
Figure 1. Bivariate Association Between Hallucinogenic Use and Major Depression



Multivariate

- **Major depression and hallucinogen use were still significantly associated** after controlling for sex (not confounding).
- The interaction between number of depressed people at each hallucinogen level was higher among the biological female population compared to the biological male population (Fig. 2).
- Females had an expected **odds of having depression that is 2.03 times higher than males.**
- Logistic regression analysis showed a significant relationship between **hallucinogen use and sex and major depression**

Figure 2. Prevalence of Major Depression and Hallucinogenic Use by Sex



Discussion

- **There is a significant relationship between major depression and hallucinogenic use.** Individuals who have used hallucinogens are more likely to have major depression compared to those that do not.
- Those assigned Female at birth are more likely to have major depression (2 times higher) compared to their male counterparts.
- Findings **contradict** current **clinical research on hallucinogenic drugs used to treat major depression.** Clinical research predicts a significantly lower likelihood of having major depression after hallucinogen therapy (like psilocybin and ketamine treatment).
- While sex and hallucinogen use predict major depression, sex does not confound the relationship between hallucinogen use and major depression.
- Further research might:
  - Specify specifically **what** recreational hallucinogenic drugs are being used.
  - Account for other confounding variables like age, other mental health conditions, family history, etc.
  - Time as a variable (before and after the use of hallucinogens over a specific time frame).
  - Larger sample size of hallucinogen users.

References

- Artin, H., Zisook, S., & Ramanathan, D. (2021). How do serotonergic psychedelics treat depression: The potential role of neuroplasticity [Review]. World Journal of Psychiatry, 11(6), 15. https://doi.org/10.5498/wjp.v11.i6.201
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- Sloshower, J., Skosnik, P. D., Safi-Aghdam, H., Pathania, S., Syed, S., Pittman, B., & D'Souza, D. C. (2023). Psilocybin-assisted therapy for major depressive disorder: An exploratory placebo-controlled, fixed-order trial. Journal of Psychopharmacology, 37(7), 698-706. https://doi.org/10.1177/02698811231154852