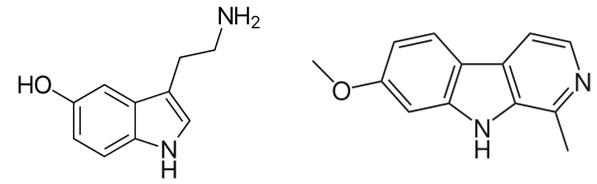


Exploration of Ayahuasca's Mechanisms in the Treatment of Stimulant Use Disorder

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Abstract

Stimulant use disorder presents an enormous epidemic in our society; further research on new treatment methods remains necessary. Ayahuasca (an entheogenic medicinal plant extract distinguished by the serotonergic psychedelic N,N-dimethyltryptamine in combination with a monoamine oxidase inhibitor) may potentially be such a treatment for stimulant use disorder. Four theories hypothesize the biochemical, physiological, psychological, and transcendent mechanisms describing ayahuasca's potential as a therapeutic treatment. To investigate ayahuasca's potential as a mechanism of treatment, we propose a placebo-controlled experimental design comprising of 50 participants who are moderate daily consumers of methamphetamine. We expect that ayahuasca treatment will result in reduced substance use, explained by biophysiological and psychotranscendent mechanisms. Specifically, we hypothesize that the ayahuasca condition's participants will have a lower concentration of methamphetamine in their bloodstream, which will be explained via a reduced average variability of dopamine, a reduced concentration of dopamine in the mesolimbic pathway, an increase in behavioral health, and an increase in measures of self-transcendence. If the results of this experiment support our hypotheses, this research study would be evidence that ayahuasca is an effective mechanism of treatment for stimulant use disorder. Adjustment of N,N-dimethyltryptamine's schedule is necessary for ayahuasca therapy to be a viable treatment method. Future studies should consider ayahuasca's efficacy in relation to various substance use disorders compared to conventional pharmacological substance treatment methods. Finally, we propose that future research should test the relationship between ayahuasca treatment and the demographic characteristics of the participants.

Methods

Sample

- 50 moderate methamphetamine users ($N = 50$) who consume between (0.2 – 0.5) grams of methamphetamine per day will be recruited for this study. Participants over the age of 21 will be recruited through local advertisements on the internet through websites such as Craigslist's, Facebook, and Bluelight.
- Applicants will be given a questionnaire to pre-screen their characteristics for attributes that are unacceptable to the study. The questionnaire will consist of eight inclusion questions and seventeen filler questions; this is to reduce the applicants suspicion about our methods.

Measures

Inclusion questions: 8 items developed for this study to identify participants who meet eligibility criteria; "Do you consume more than (0.5) grams of methamphetamine per day?"

Dopamine variability: Participants will undergo two 72 hours PET scan sessions to determine the average variability of dopamine in the limbic system (12 measurements of dopamine per session in which participants will view methamphetamine cues every other measurement period and control cues every other session). PET measurements will be observed through competition between endogenously released dopamine and raclopride a selective antagonist of dopamine receptors. A drop in signal would indicate a increase of dopamine released by transport vesicle into the synaptic cleft. Variability will be operationalized as the standard deviation of dopamine over the 24 sessions.

Mesolimbic pathway dopamine concentration: Participants will undergo two 72 hours PET scan sessions to determine the average concentration of dopamine in the nucleus accumbens of the mesolimbic pathway (12 measurements of dopamine per session in which participants will view methamphetamine cues prior to every other measurement period). PET measurements will be observed through competition between endogenously released dopamine and raclopride a selective antagonist of dopamine receptors. Concentration will be operationalized as the average value of dopamine concentration over the 24 sessions.

Psychological health: 20 items from Kopta and Lowry's (2002) Behavioral Health Questionnaire-20; "How satisfied have you been with your life?"

Self-transcendence: 15 items from Haugan, Rannestad, Garasen, Hammervold, and Espenes' (2012) self-transcendence scale; "Being involved with other people or in my community when possible."

Concentration of methamphetamine: Laboratory blood analysis of methamphetamine levels in blood plasma.

Procedure

- We will use an independent group study using a pretest-posttest waitlist-control design with one experimental ayahuasca condition and a placebo condition.
- Randomization using matched pairs will be used to distribute the 50 participants ($N = 50$) in to two groups of 25 ($n = 25$), one group for each condition.
- Participants will undergo two ayahuasca treatment sessions, two PET scanning sessions, and respond to two self-report scales.
- The study will be conducted over four weeks, a pretest measurement of methamphetamine in the participants bloodstream will be collected after participants are assigned to their group and a posttest will be conducted at the end of the four weeks.
- The ayahuasca sessions will consist of two separate ceremonies for the experimental condition, perform by two indigenous Shipibo shamans. The tea will be distributed in three eight-ounce servings, to be consumed over the course of the 10-hour therapy.
- The placebo group will participate in an identical ceremony, performed by another shipibo shaman. However, the shaman will not distribute ayahuasca to the placebo group. Instead, the shaman will distribute melatonin in the form of a tea as a placebo to the group.

Interpretation

Literature Review

Biochemical: Ayahuasca's anti-addictive properties are attributed to N,N-dimethyltryptamine's global impact on the neurotransmitters released by dopaminergic and serotonergic neurons. N,N-dimethyltryptamine's affinity with serotonin receptors elicits agonism in the 5HT2A receptor, which releases GABA, inhibiting the release of dopamine. Ayahuasca's monoamine oxidase inhibitor prevents the remaining dopamine reabsorbed by the pre-synaptic membrane from being eliminated. Ayahuasca stabilizes the concentration of dopamine in the reward center of the brain, between elevated levels of dopamine associated with addictive behavior and low levels of dopamine associated with withdrawals.

Physiological: Ayahuasca's anti-addictive properties are attributed to N,N-dimethyltryptamine's reduction of dopamine concentration in the nucleus accumbens. Ayahuasca's inhibitory interference on dopamine within the nucleus accumbens alters genetic expression of D1 receptors, triggering the upregulation of these receptors. This increase in D1 receptors elicits an increased efficacy of dopamine in the mesolimbic system, which reduces the cravings and withdrawals associated with self-administration of a euphoric substance.

Psychological: Ayahuasca enables the processing of significant conscious and unconscious experiences promoting the resolutions of suppressed emotions and an improvement in resiliency in a phenomenon known as ego death. Ayahuasca increases thought and speed facilitation to new associations, which promotes reflection on personal issues. The death of the ego provides a resolution to the three-horned dilemma between the ego, id, and superego dissolving internal trauma in the unconscious that are responsible for addiction. Substance abuse is a reparative attempt to cope with internal conflict related to the psychodynamic theory. Ayahuasca therapy promotes an oceanic feeling of connectedness to the universe, which can resolve psychodynamic issues regarding the environment.

Transcendent: Ayahuasca facilitates peak experiences, which can change a person's beliefs, values, and worldview promoting connection to their environment. Social preoccupation with individualism in our society often leads to social isolation, and addiction is a disruption of social integration resulting in a lack of social connections.

Culture

Substance use disorders are a complicated intersection of social and psychological dynamics. The major determinants of substance use disorders pertain to the disturbance of social connections elicited by trauma and the environment.

Many of the people who consume substances are rational and functional members of our society. Racism and stereotypes have further degraded our societies perspective about drugs. These concepts do not properly reflect the reality of the substance use issue in our society.

The Drug Enforcement Administration's current prohibitional regulation is an inappropriate suppression of human rights.

People who suffer from substance use disorders are discouraged from obtaining treatment as they are threatened by prosecution.

Hypotheses

Hypothesis 1: Participants in the ayahuasca condition will have a lower concentration of methamphetamine in their bloodstream at the end of the four-week experiment compared to the participants in the placebo condition.

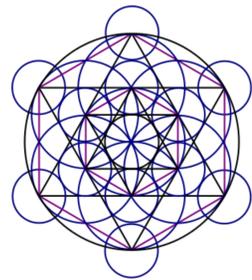
Hypothesis 2: The reduced concentration of methamphetamine among those in the ayahuasca compared to the control condition will be explained via biochemical mechanisms (i.e., lower average variability of dopamine in the limbic system).

Hypothesis 3: The reduced concentration of methamphetamine among those in the ayahuasca compared to the control condition will be explained via physiological mechanisms (i.e., lower average concentration of dopamine in the nucleus accumbens).

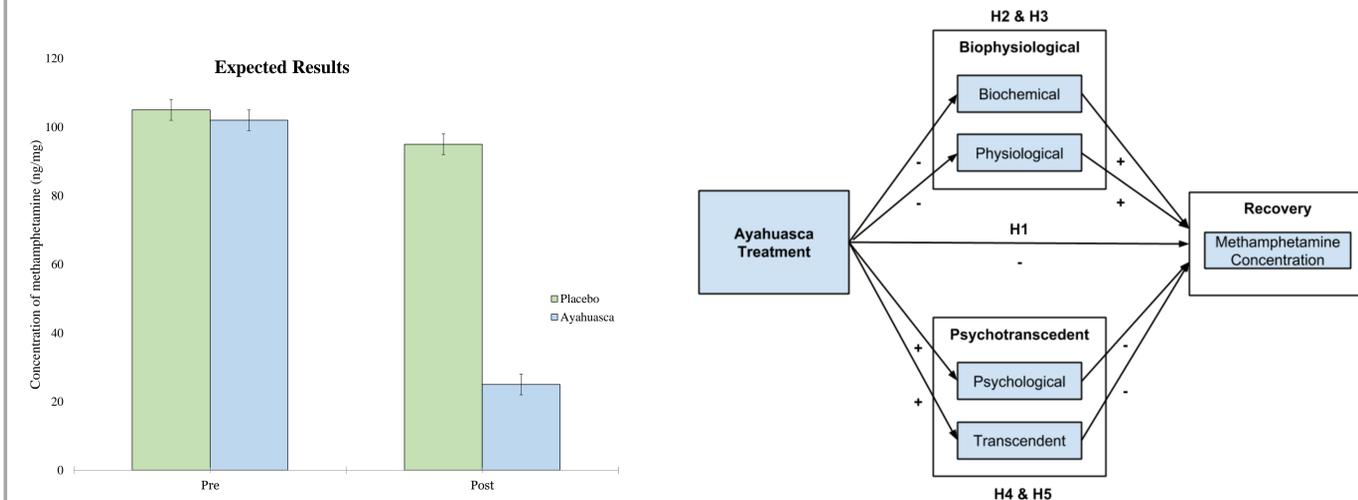
Hypothesis 4: The reduced concentration of methamphetamine among those in the ayahuasca compared to the control condition will be explained via psychological mechanisms (i.e., higher self-reported behavioral health).

Hypothesis 5: The reduced concentration of methamphetamine among those in the ayahuasca compared to the control condition will be explained via transcendent mechanisms (i.e., higher self-transcendence).

Tables and Figures



Procedure	Date of Experiment
Prescreening Questionnaire	2 weeks before experiment
Matched Pairs t-test	1 week before experiment
Blood Analysis Pretest	Day 1
PET Session 1	Day 1
Self-Report Pretest	Day 3
Ayahuasca Session 1	Day 4
Ayahuasca Session 2	Day 7
Blood Analysis Posttest	Day 25
PET Session 2	Day 25
Self-Report Posttest	Day 28



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Discussion

Conclusion

- Addiction should be treated as a health issue rather than a criminal issue. Appropriate methods to treat addiction disorders must consider behavioral issues that pertain to substances along with the physical issues. Effective treatment methods promote connections that inspire the dissolution of underlying issues of addicts. Noninterventional methods promote aspects that build relationships in the lives of addicted individuals. Treatments should discourage convictions and focus on rehabilitation. Criminal regulations elicit difficult community integration which ultimately promotes addiction.
- Humans are social creatures as described by the attachment theory; substance use disorders are a symptom of a disturbed social integration. Social disturbances can pertain to disruptions in connections with an individual's peers, environment, society, or even their own identity. Substances themselves are not the issue, the problem relies on the person's inability or unwillingness to process their own emotions.
- Substance use disorders are a reparative attempt to process internal conflicts or external disparities. When experiencing a lack of social integration, individuals will often find other methods to fulfill their instinctual desire for attachment. Substance use is a method that many individuals use to cope with their experienced lack of social connections.

- The limbic system has profound influence over basic emotions and drives which elicit an individual's resiliency to substance use disorders. The nucleus accumbens is a critical component of the limbic system's mesolimbic pathway, its terminals are the site of action for almost every recreational drug which causes a manifold increase in dopamine levels. Dopamine regulates reward- motivated behavior which also elicits an individual's resiliency to substance use disorders. Erratic levels of dopaminergic neurons are believed to be responsible for addiction.

Implications

- The implications of this theoretical research is to advocate for the potential benefits of ayahuasca therapy for patients suffering from stimulant use disorder. Ayahuasca's therapeutic potential is demonstrated by a reduction of methamphetamine use in the experimental participants.
- Evidence of a reduction in the consumption of methamphetamine in the experimental condition group would imply the efficacy of ayahuasca therapy on various substance use disorders.
- Adjustment of N,N-dimethyltryptamine's schedule is necessary for ayahuasca therapy to be a viable treatment method. Schedule V chemicals are medicinal substances with a low potential for abuse. Ayahuasca's inhibitory effects on of dopaminergic neurons indicates its low potential for abuse.
- Ayahuasca therapy can provide treatment for patients that are experiencing undesirable results from conventional methods. The addiction crisis in our society continues to escalate. To treat this epidemic efficiently, a liberal treatment perspective must be realized.

Future Directions

- Methamphetamine abuse represents a wide variety of substance use disorders to indicate ayahuasca's therapeutic potential. Methamphetamine was selected as the user's drug of choice because of its powerful affinity with dopamine. Future studies should research the efficacy of ayahuasca therapy with various substance use disorders.
- Racism influences youth who are exposed to drugs in their communities. The lack of connection seen by the disrespect of acknowledgement about the beliefs of minorities in our community is spurred by institutional racism. This institutional racism has misinformed the public about the potential harms of drugs. This concept elicits our inappropriate response to drug use in our society. Future studies should research the relationship between ayahuasca treatment and the participant's race.
- People experiencing poverty generally have fewer alternatives in their lives. The availability of drugs and the reduction of alternatives has a positive correlation with addiction. The self-administration of addictive substances can be eliminated with positive alternatives. Future studies should research the relationship between ayahuasca treatment and the participant's available resources.
- Finally, future studies should research the efficacy therapeutic treatments oriented to the biochemical, physiological, psychological and transcendent mechanisms of substance use disorders compared to conventional pharmacological treatment methods.