A case report SPECT study and rationale for the sequential administration of ibogaine and 5-MeO-DMT in a veteran with alcohol use disorder

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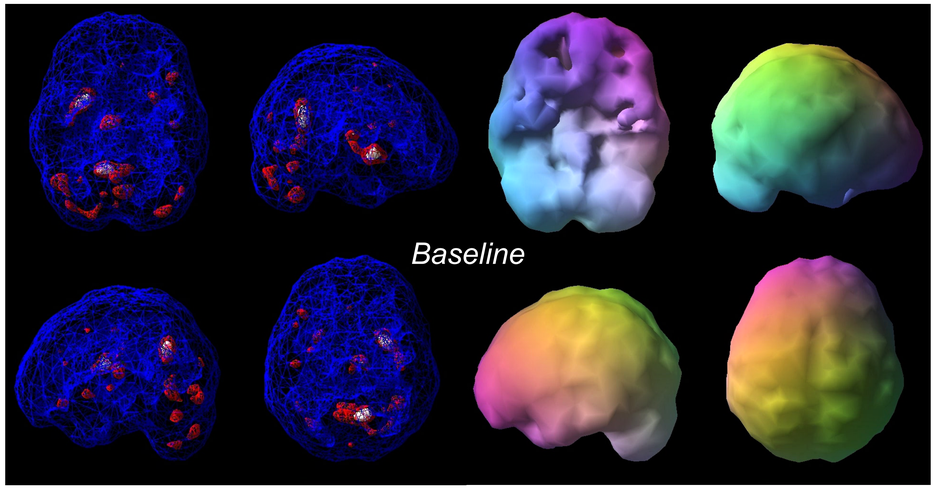
Introduction

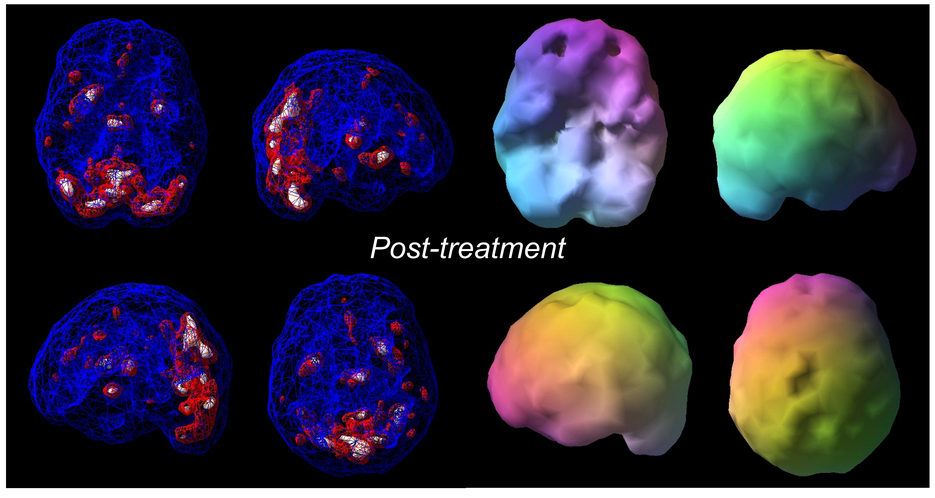
- Alcohol use disorders are the most prevalent form of Substance Use Disorder among military personnel.
- The Food and Drug Administration approved medications to treat alcohol use disorder, such as disulfiram, naltrexone, and acamprosate, have demonstrated limited efficacy, and more effective treatments are warranted against this deadly condition.
- Ibogaine is a plant-derived psychedelic dissociative compound that is administered internationally in controlled settings and demonstrates addiction-interrupting properties with alcohol through upregulation of GDNF in the ventral tegmental area (VTA), long-acting effects on DAT and SERT, and by engendering novel psychological insights.
- 5-MeO-DMT is a potent serotonergic tryptamine found in high concentrations in the bufotoxin of the Colorado River Toad that occasions transformative mystical experiences of comparable intensity to high dose psilocybin, and demonstrates anti-addictive and neuroregenerative properties via 5HT1A and 5HT2A agonism, and downregulation of metabotropic glutamate receptor 5.
- To date there are no published imaging reports of either compound in humans.

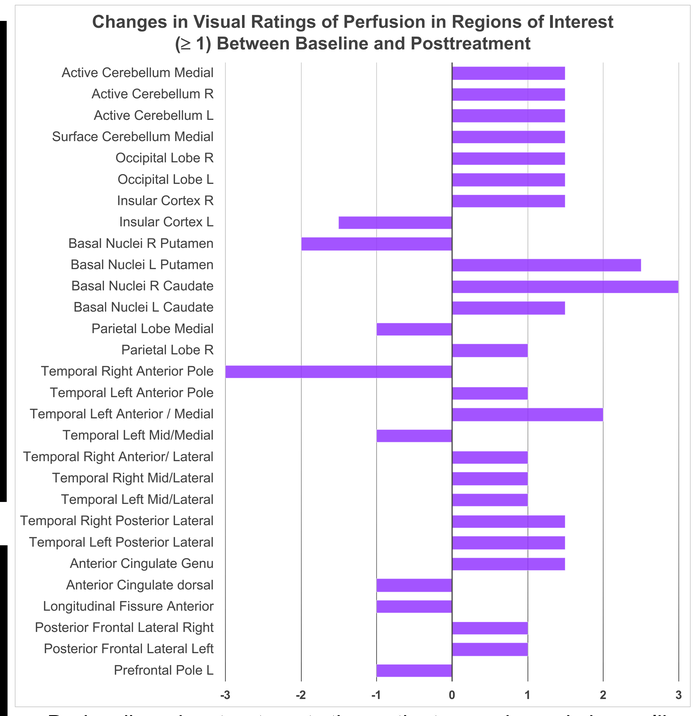
Methods

- A 31-year-old male military veteran (Air Force) with moderate alcohol use disorder and prior history of PTSD sought treatment at an inpatient clinic in Mexico that utilized a sequential protocol in a 4-day program.
- He was administered ibogaine hydrochloride (1550mg, 17.9mg/kg) on day 1, followed by vaporized 5-MeO-DMT (bufotoxin source 50mg, estimated 5-MeO-DMT content, 5–7mg) on day 3.
- SPECT examinations were performed in a resting state at baseline at 48 h prior to ibogaine administration and at follow-up 5 days post-ibogaine administration/3 days after 5-MeO-DMT.
- 99m Tc hexamethylpropylene amine oxime (Ceretec) was injected after the initial equilibration period. A tomographic brain study was performed using a high resolution Picker (Phillips) Prism XP 3000 triple-headed gamma camera with fan beam collimators. Data were acquired in 128x128 matrices, yielding 120 images per scan with each image separated by 3 degrees spanning 360 degrees. The tomographs were displayed using a standardized linear color scale, rendered in the Odyssey step-20 scale, which scales all voxels to the brain maximum and assigns each a color gradient based upon its percentile of activity. Each color step represents a (not necessarily linear) five-percentile-point change in rCBF.
- Image renderings include a surface view, looking at the top 45% of brain activity, and an internal active view where the most active 15% and 8% of the brain are rendered. Active scans where blue color = 55%, looking at top 45% of brain perfusion, red = top 15%, and white = top 8% of cerebral blood flow in that subject's brain compared to their whole brain perfusion. A healthy control shows full even, symmetrical perfusion with most active area in the cerebellum.

Results







- During ibogaine treatment, the patient experienced dream-like visions that included content pertaining to his alcohol use and resolution of past developmental traumas. He described his treatment with 5-MeO-DMT as a peak transformational and spiritual breakthrough.
- On posttreatment SPECT neuroimaging, general increases in brain perfusion were noted in bilateral caudate nuclei, left putamen, right insula, as well as temporal, occipital, and cerebellar regions compared to the patient's baseline scan.
- The patient reported improvement in mood, cessation of alcohol use, and reduced cravings at 5 days post-treatment, effects which were sustained at 1 month, with a partial return to mild alcohol use at 2 months.

Conclusions

- Serial administration of ibogaine and 5-MeO-DMT resulted in increased perfusion in multiple brain regions broadly associated with alcohol use disorders and known pharmacology of both compounds, which coincided with a short-term therapeutic outcome.
- Phase 1 studies are required to investigate the safety of both compounds in controlled designs.
- 5-MeO-DMT and ibogaine are plant-based substances that possess multiple therapeutic properties, yet, remain scheduled in the most strict drug classifications in the United States and Europe making research highly restrictive, limited and cost prohibitive

References and Funding

**Poster from prior published article which includes all references*: Barsuglia, J. P., Polanco, M., Palmer, R., Malcolm, B. J., Kelmendi, B., & Calvey, T. (2018). A case report SPECT study and theoretical rationale for the sequential administration of ibogaine and 5-MeO-DMT in the treatment of alcohol use disorder. Progress in Brain Research. http://doi.org/10.1016/bs.pbr.2018.08.002

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