

INTRODUCTION

- 300 million people suffer from depression globally each year.
- Cost is \$1 trillion on the global economy annually.
- Conventional pharmacological and psychosocial approaches are limited in their effectiveness.
- Psychedelics including psilocybin, ayahuasca, and LSD were studied for their antidepressive effects during the mid-20th century before legislation stopped research.
- There has been a resurgence of interest since the 1990s in psychedelics used as an adjunct to psychotherapy.
- There now exists a foundation of studies that look at the neurobiology, psychology and psychopharmacology of psychedelics to treat various forms of depression.

PSILOCYBIN

- Found in mushroom species.
- Acute effects are changes in perception, cognition and somatosensation.
- 2006 - double-blind RCT of 40 people found significant improvements in quality of life and overall happiness in psilocybin group vs control.
- Carhart-Harris and colleagues in UK have been pioneering the work into psilocybin assisted therapy for the past 10 years, and have found significant improvements in depressive symptoms in trials.
- Griffiths et al (2016) looked at 51 terminally ill cancer patients and found high dose of psilocybin produced large decreases in all measures of depression and anxiety, increases quality of life and reduced fear of death.
- Ross et al (2016) found that psilocybin produced immediate, substantial, and sustained improvements in anxiety and depression among 29 terminally-ill cancer patients.
- All studies showed improved quality of life.
- The more intense the psilocybin-induced mystical-experience the greater therapeutic benefits.

LSD

- Synthetic chemical made from a substance found in ergot, a type of fungus.
- During the 1950s and 1960s, roughly 40,000 people took part in clinical LSD trials, showing promising results in treating a range of conditions like depression.
- Mid-1960s to the mid-1970s, several trials involved 83 patients showed that LSD reduced depression and spiritual distress among cancer patients.
- Casser et al (2014) looked at LSD to treat anxiety and depression among 12 terminally-ill patients. Research reported sustained significant reductions in anxiety at the 12 month follow up among all participants.

AYAHUASCA

- Amazon region of Brazil, Peru, Colombia and Ecuador have used ayahuasca for therapeutic and spiritual purposes for centuries.
- The typical ayahuasca experience is introspective, and includes strong visuals, somatic reactions, personal memories, cathartic emotions and insightful experiences.
- Palhano-Fontes et al (2015) conducted only known double-blind placebo-controlled trial with 29 people with treatment-resistant depression - nearly 70% achieved reduced depressive symptom compared to controls.
- Sanches et al (2016) tested ayahuasca on 17 patients with recurrent depression. They found a single dose had rapid antidepressant effect, patients had significant score decreases in depression-related assessment at all time points.
- Osorio et al. (2015) six patients suffering from treatment-resistant depression were administered with ayahuasca. Results found 82% of people had statistically significant reductions in symptoms.
- Long term ayahuasca users show preserved cognitive functions compared to similar cohorts.
- No addictive properties.

MECHANISMS OF ACTION

- Both neurobiological and psycho-spiritual aspects involved.
- Classical psychedelics are 5-HT_{2A} receptor agonists, which connected to the regulation of complex emotional behaviours and mood.
- Enhanced amygdala inhibition produced positive mood and emotion.
- Decreases connectivity within the Default Mode Network.
- Modulates the glutamatergic neurotransmission process.
- Lowers inflammation in the body.
- Profoundly meaningful and spiritually significant experiences.
- Nearly two thirds of participants in clinical trials have attributed increased life satisfaction or wellbeing to spiritually-profound experience.
- 'Afterglow'.
- Heightened state of consciousness.
- 'Inverse PTSD'.

"The potential significance of LSD and other psychedelics for psychiatry and psychology is comparable to the value the microscope has for biology or the telescope has for astronomy," (Grof, as cited in Stolaroff, 2004, p. 16).

"Psychedelics have the potential to transform the care of cancer patients with psychological and existential distress, but beyond that, it potentially provides a completely new model in psychiatry of a medication that works rapidly as both an antidepressant and anxiolytic and has sustained benefit for months," (Ross, as cited in Anderson, 2016, p1).

"If research is allowed to continue, psilocybin treatment with psychological support will be found to have important areas of superiority over current interventions like SSRI's and CBT," (Carhart-Harris & Goodwin, 2017).