Group presentation Script

Slide 2 (Intro to PTSD)

PTSD is a common psychological disorder. Lifetime prevalence in the United States is somewhere between 6 and 10 percent in the U.S and the prevalence for U.S. soldiers returning from Afghanistan and Iraq was as high as 18%. Diagnosis of PTSD occurs after a traumatic event and since many us will be exposed to a traumatic event one day, this indicates that many of us will be at some level of risk for acquiring PTSD.

PTSD is a type of anxiety disorder characterized by symptoms of hyperarousal (so an elevated fight or flight response), negative emotions, avoidance, intrusive re-experiencing of the traumatic event, as well as cognitive and mood disturbances

Slide 3 Currently available treatments

Current FDA approved drug treatments for PTSD include SSRI and benzodiazepines (Bahji et al., 2019). A problem with these medications in general is that the patients must take them every day or multiple times a day. SSRI can carry side effects such as sexual dysfunction (high as 75%), nausea, and GI disturbances (Ferguson, 2001). Benzodiazepines carry an even greater risk of side effects such as cognitive and motor skills impairment as well as the added risk of dependence and withdrawal (Stewart, 2005).

Psychotherapies are talk based therapies in which the clinician aims to create a therapeutic alliance with the patient in order to induce a positive change in the patients way of thinking (*What Is Psychotherapy?*, n.d.). Current psychotherapies used to treat PTSD include exposure based therapies, cognitive processing therapy, and cognitive behavioral therapy (CBT). These treatments are effective for many but are ineffective for a large proportion of individuals and can be difficult for some to access, moreover, some individuals can find it difficult to engage themselves in CBT. Current treatments are ineffective for 25-50% of individuals who start this treatment

With the high prevalence of PTSD and the various drawbacks of current treatments, this creates a need for the development of new treatments

Slide 4 and 5 (lit review)

MDMA-assisted psychotherapy is a new form of treatment that combines existing psychotherapies with the effects of MDMA. Due to the subjective effects of MDMA such as feelings of euphoria, increased self-confidence, sociability, well-being, empathy, and most notably in this context, a decreased fear response, MDMA was theorized to enhance the therapeutic connection and processing of traumatic experiences through its subjective effects. In other words, based on learning theory, cognitive processing theory, and social cognitive theory, for psychotherapies to work there must be this emotional balance between being overwhelmed and underwhelmed. And MDMA is thought to widen this window.

Moreover, in PTSD there are exaggerated and uncontrolled responses of the amygdala to cues specific to the trauma that the given individual went through as well as limited activity in the ventromedial prefrontal cortex (vmPFC) to inhibit the amygdala (Frewen, 2006). MDMA decreases the responsiveness of the amygdala and increases the activity of the ventromedial PFC, and thus might help treat PTSD in this manner (Gamma et al., 2000).

Outside of theory, MDMA assisted psychotherapy was used in case reports in the 1970s in which its therapeutic effects were reported. However, no clinical trials were conducted at this time and due to the fact that in the 1980s, MDMA became popular for its recreational use, it became a schedule 1 controlled substance and was made illegal to use. This has created gaps in the literature as government control over this substance has made research difficult. However, the Multidisciplinary Association for Psychedelic Studies (MAPS) filed a drug master file application in order to investigate the safety of MDMA for use in clinical trials. Currently phase 1 clinical trials have demonstrated that MDMA is safe to use.

Slide 6: hypothesis

The next logical step in the investigation of MDMA-assisted psychotherapy is to investigate its effectiveness in individuals with PTSD relative to control groups in the form of a phase 2 drug trial. Our proposal is based upon 5 empirical research reports that all took the form of a phase 2, randomized, double-blind, crossover studies (I'll go over what these mean in the methods section)

Our hypothesis is the following: MDMA can be administered in conjunction with psychotherapy in order to significantly reduce the symptoms of patients with treatment-resistant PTSD when compared to the same psychotherapy combined with an inactive placebo.

We also hypothesize that MDMA-assisted psychotherapy can produce clinical significance through the reduction of symptoms of PTSD.

Explain clinical significance: refers to practical relevance through a treatment effect

Slide 7 (participants)

We aim to choose a sample of 30 participants from the age of 20 to 40, with around 3 years of post secondary completed as the mean level of education. Our main method of recruitment will be through referrals from health professionals but also social media advertisements. Participants were included on the basis that they…

had treatment resistant PTSD (meaning they already tried at least one form of psychotherapy and one form of pharmacotherapy in which there was inadequate improvement), had CAPS-IV scores of greater than or equal to 50 (we will go over what CAPS is in the next slide), had no medical contraindications to MDMA (pregnancy, low body weight, CVD), and also no other psychiatric comorbidities

Slide 8

In terms of our primary measure we plan to use the clinician administered ptsd scale (CAPS-IV). This takes the form of semi-structured interview that is conducted by the clinician. It includes 6 components: exposure to a traumatic event, re-experiencing of a traumatic event, avoidance, negative mood, and increased arousal. The clinician scores the frequency and intensity of each criterion, in which higher scores are indicative of more frequent and severe symptoms of PTSD. The primary outcome measure we will be using will be mean scores of the MDMA and inactive placebo group.

Our secondary testing instrument for symptoms of PTSD is the measuring of heart rate reactivity since this is a hallmark predictor of PTSD (difference in resting heart rate and heart rate after presentation of an external stressor). In this case we would be looking for decreased heart rate reactivity following exposure to treatment

We will also be monitoring blood pressure, heart rate, and body temperature during the experimental sessions. We included secondary measures to improve concurrent validity.

Slide 9

*Overview*

* 2-8 hour MDMA assisted psychotherapy sessions spaced one month apart
* No compensation was made to participants

*Step-by-step*

* Participants were randomized via a web-based system into either the experimental group or control group
  + Experimental group
  + Control group: Received inactive placebo
* Neither participants nor the researchers knew what groups the participants were in (double blind)
* Doses administered at two-8 hr psychotherapy sessions spaced one month apart
* Following the conclusion of the last 8 hour psychotherapy session, participants who were in the placebo group had the option of completing a non-blinded MDMA session as part of the crossover segment and those who were in the active group had the option to complete a third session of MDMA that was non-blinded (this crossover segment will not be included in our data analysis)
* Follow up will occur at 2 months following the final experimental session

Slide 10-11-12

Because our hypothesis is centred around whether MDMA can result in a significant reduction in CAPS-IV scores, no correlation (r = 0) or a positive correlation of any given strength between CAPS-IV scores and time after exposure to 2-8 hour MDMA-assisted psychotherapy would not be in concordance with our expectations. In addition, a small-moderate negative correlation of up to r = -.49 would not align with our expectations. Again we are looking for clinical relevance.

In this study we would expect there to be a strong negative correlation (p < 0.05) between CAPS-IV scores and time after exposure to MDMA-assisted psychotherapy.

An example of this is on the next slide.

In this graph by Wagner et al, we see scores for CAPS on the y-axis and time following treatment on the left, going up to two months following treatment.

In this example, the correlation between time after exposure to 2-8 hour sessions of MDMA-assisted psychotherapy and CAPS-IV scores is significant (*p* < 0.05) indicating that CAPS-IV scores decrease as time after exposure to 2-8 hour MDMA-assisted psychotherapy sessions increases.

In addition, in order to assess clinical significance, we will use Cohen's d to compare the mean CAPS-IV score of the experimental group and control group. Any Cohen's d score below a 0.8 would not align with our expectations as we are looking for a large treatment effect.