



MDMA-Assisted Psychotherapy for Posttraumatic Stress Disorder



MAPS

MULTIDISCIPLINARY ASSOCIATION FOR PSYCHEDELIC STUDIES

 Fluence



3,4-Methylenedioxy-methamphetamine (MDMA)

Background

MDMA was Patented at Merck in 1912

Mid-1970s MDMA was rediscovered by the biochemist Alexander Shulgin
Patented at Merck in 1912

Passed on MDMA to psychiatrists, psychologists, and therapists



Background

MDMA has been sought after illicitly

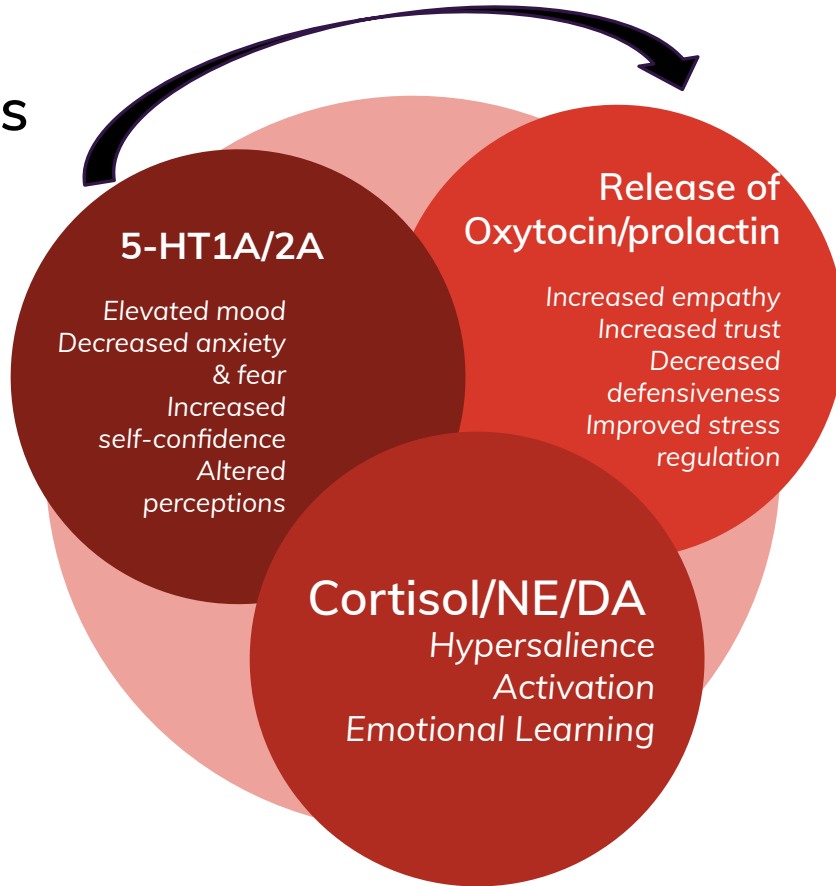
- Stimulant
- Elevate mood
- Induce euphoria
- Feeling of closeness with others (Stevens & Smith, 2009)

- Entactogen/Empathogen - closeness to others, empathy, well being, and insightfulness, with little perceived loss of control (Metzner, 1983)

- Releasing agent: serotonin, dopamine, norepinephrine, and oxytocin



MDMA Effects on Neurotransmitters



Background

Schedule I:

- The drug or other substance has a high potential for abuse.
- The drug or other substance has no currently accepted medical use in treatment in the United States.
- There is a lack of accepted safety for use of the drug or other substance under medical supervision.

(DEA, Office of Diversion Control, 2003)



What is a Drug-Assisted Psychotherapy?

“Hallucinogens have pronounced acute psychoactive effects ... They are also hypothesized to have persisting effects that outlast the acute pharmacologic effects...

The persisting effects may be mediated by the acute psychological effects. Although there are obviously brain correlates of these effects, it cannot be assumed that the therapeutic brain changes could be obtained without the subjective experience. No medications share this property, but psychotherapies do...

In many cases their clinically relevant effects are hypothesized to be dependent on the therapeutic context, so that what is really being measured is the combined effect of the drug-psychosocial treatment combination.”

-Bogenshutz, 2013



The background features a solid blue color. On the right side, there are several thick, flowing, wavy lines that transition through a spectrum of colors including yellow, orange, red, and purple. These lines appear to be moving or flowing downwards and to the left.

Post-Traumatic Stress Disorder

Post-Traumatic Stress Disorder

Experiencing or witnessing “traumatic event” with significant distress and/or impairment

Symptom Clusters

- Arousal & Reactivity
- Intrusion
- Negative Alterations in Cognitions & Mood
- Avoidance

Delayed Expression or Dissociative Subtypes
(American Psychiatric Association, 2013)

Chronic

Single Incident vs. Complex Trauma



Why MDMA for PTSD?

PTSD associated with:

Increased amygdalar activity

Decreased hippocampal activity

Heightened fear response/limited ability to explore trauma in therapy

Experiential avoidance/emotional numbing

Subjective: Lack of trust, hypervigilance

MDMA associated with:

Reduction in amygdalar activity

Increased hippocampal activity

Reduction in fear and defensiveness

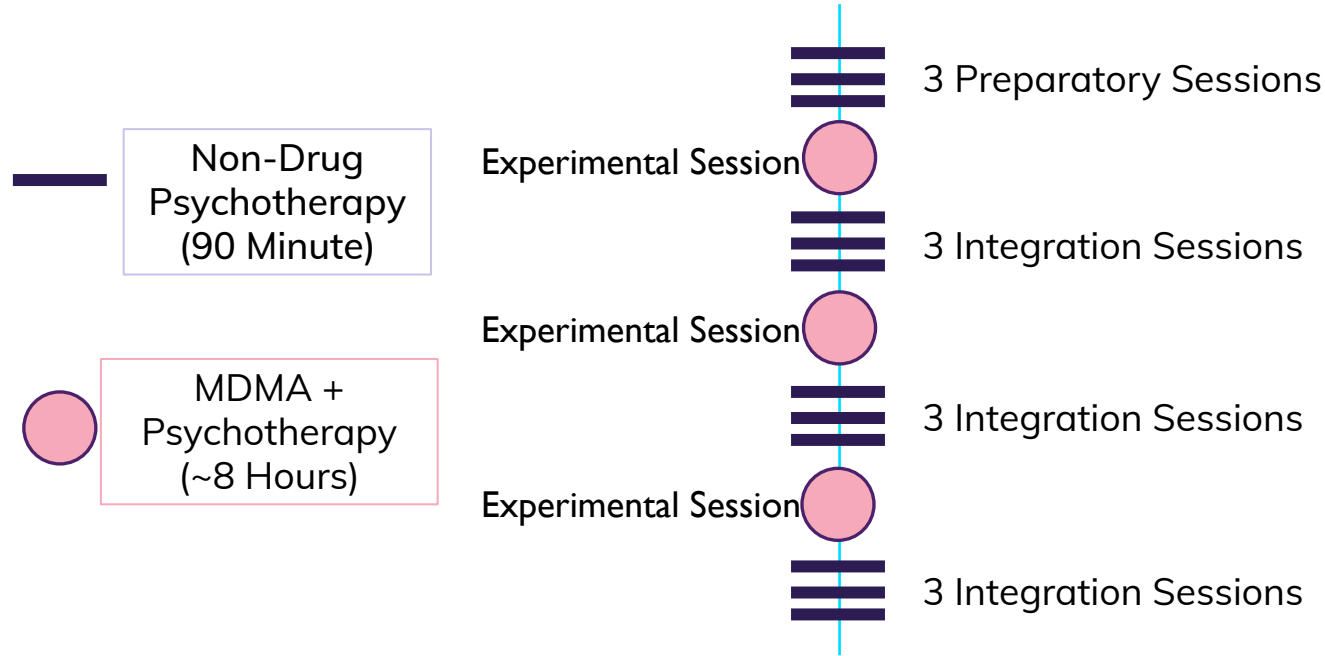
Increased access to traumatic memories without flooding

Subjective: Increased sense of safety and trust



MDMA-assisted Psychotherapy

MAPS-Sponsored Clinical Trials



MDMA-assisted Psychotherapy: Therapeutic Approach

A Manual for MDMA-Assisted Psychotherapy in
the Treatment of Posttraumatic Stress Disorder

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- Controlled clinical setting
- Co-therapy team (male/female)
- Supportive environment;
Nondirective approach
- Trust in innate healing capacity
- Inner focus (music/eyeshades)
communication
- Intention for trauma processing w/o
expectations of how that will occur



MDMA-assisted Psychotherapy includes elements of...

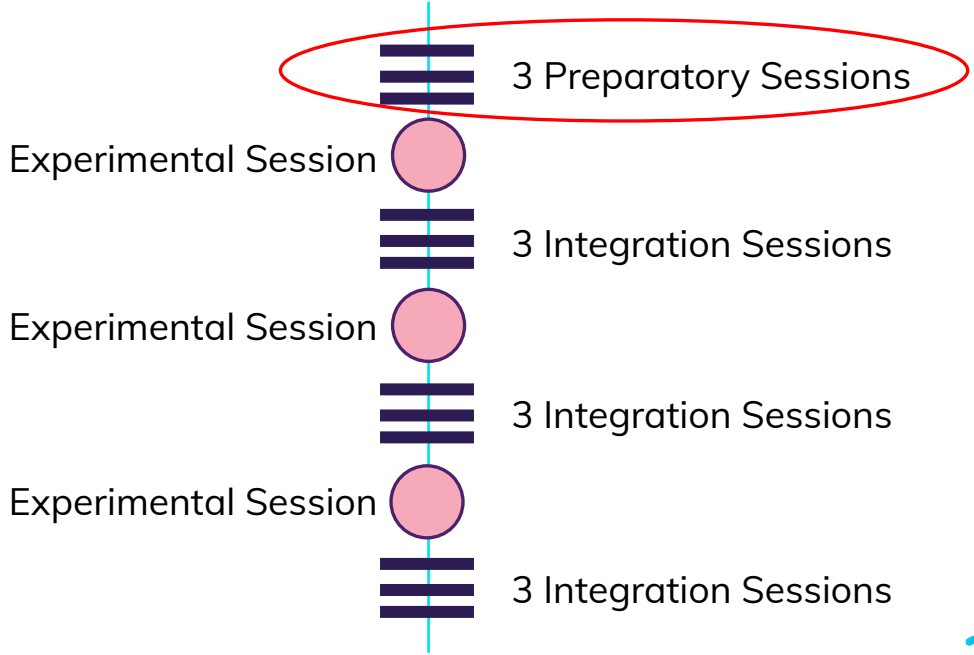
- Establishing a safe and supportive therapeutic setting and a mindset conducive to healing
- Anxiety Management Training/Stress Inoculation Training
- Exposure Therapy
- Cognitive Restructuring
- Transference and Countertransference
- Working with Multiplicity of the Psyche
- Somatic Manifestations of Trauma

MDMA-Assisted Psychotherapy: How Different is it from Other Psychotherapy?
Michael Mithoefer, MAPS Bulletin 2013



Preparation Sessions

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Therapeutic Approach

Preparation

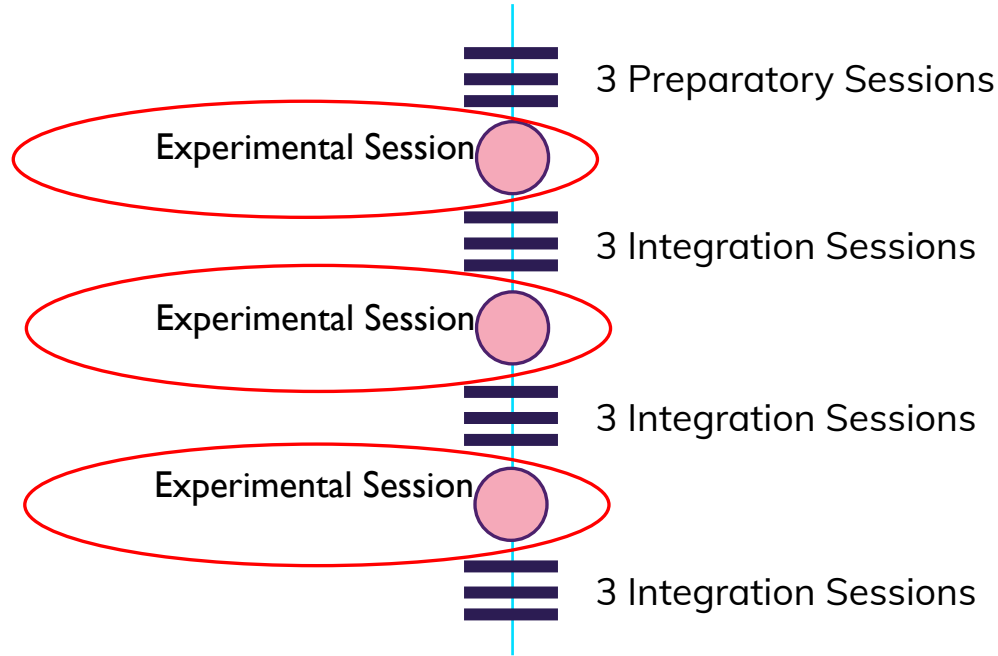
- Building rapport
- Eliciting trauma related history
- Describing what experimental session might be like
- Safety
 - Preventing falls
 - Negotiating Touch
- Anything said is a recommendation, not a command.
- Assess & Provide self-regulation tools





Experimental Sessions (a.k.a “Dosing” or “Overnight”)

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Therapeutic Approach

Experimental Session


- Letting go of an agenda that has to be done
- Non Linear Process
- Inner-Directed
- Not get ahead of the medicine

First 90 minutes:

- Working with anxiety while effects of MDMA are beginning (breath, music, relax)

After 90 minutes:

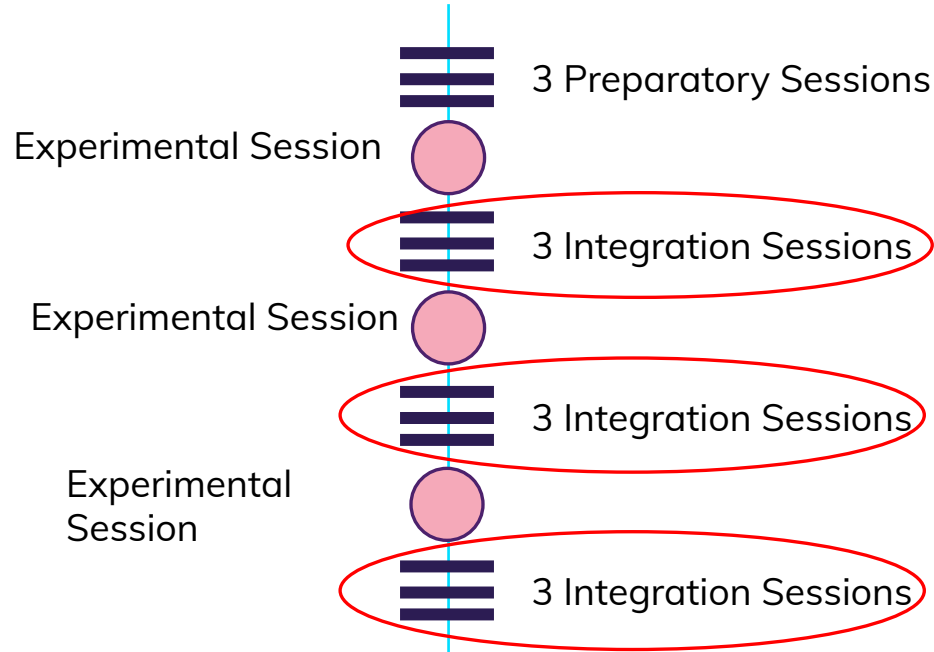
- Feel into feelings/anxiety when main effect of MDMA has come on. Breath into feeling, rather than breathing to relax.

Identifying resistance rather than "pushing through"  Fluence



Integration Sessions

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Therapeutic Approach

Integration Sessions

- Emotional and Cognitive Response to MDMA Session
- Validate affirming experiences or insights
- Explore challenges participant might be experiencing
- Therapists remind participant that the experience will continue to unfold
- Discourage strenuous activities on days after MDMA session
- Connect to support system (family & friends)





Mechanisms of Action

Psychological Domains of Action

- **Psychedelic (Mystical-like Experience)**

- MDMA & Psilocybin

VS.

- **Interpersonal (within a relationship)**

VS.

- **Intrapsychic (within oneself)**

Psychedelic (mystical-like) vs. Psycholytic (biographic)



Possible Mechanisms of Action of MDMA for PTSD

Therapeutic Alliance

- Oxytocin: Affiliation, trust, perception of emotion

Imaginary Exposure (Prolonged Exposure; Habituation)

Memory Reconsolidation Hypothesis (Cognition)

- Recall, recontextualization, and reconsolidation of long-term memory.

Personality Change (Openness)

- Change in openness moderated relationship between reduced PTSD symptoms and MDMA treatment (Wagner et al., 2017)



Possible Mechanisms underlying Therapeutic Effects

- MDMA promotes fear extinction in mice [Young et al. (2015) *Translational Psychiatry*]
- MDMA may allow for memory reconsolidation [Feduccia et al. (2018) *Progress in Neuropharmacology*]
- MDMA and other psychedelics (LSD, DMT, psilocybin) all converge on a pathway important for neuroplasticity (BDNF – mTOR – structural and functional neural plasticity) [Ly et al. (2018) *Cell Reports*]
- MDMA makes adult mice brains more like during adolescence, with greater reward from being social. The effect was due to oxytocin in the nucleus accumbens [Nardou et al. (2019) *Nature*]



SLC6A4 binding site and acute prosocial effects of (+/-)-3,4-methylenedioxy methamphetamine (MDMA) are evolutionarily conserved in *Octopus bimaculoides*.

Eric Edsinger and Gül Dölen
Current Biology (2018)



Does MDMA reduce anxiety?

MDMA is often discussed as a substance that reduces anxiety

Effects of 3,4-methylenedioxymethamphetamine on socioemotional feelings, authenticity, and autobiographical disclosure in healthy volunteers in a controlled setting.

(Baggott, Coyle, Siegrist, Garrison, Galloway, Mendelson, 2016)



I don't think I would have survived another year. It's like night and day for me compared to other methods of therapy. Without MDMA I didn't even know where I needed to go. Maybe one of the things the drug does is let your mind relax and get out of the way because the mind is so protective about the injury.

- **Charleston**
Subject X (MAPS
Website)

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