

MDMA-Assisted Psychotherapy for Treatment of Chronic PTSD: Findings from MAPS-Sponsored Phase 2 Clinical Research Trials

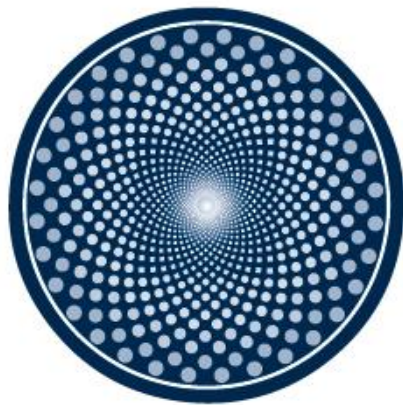


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MAPS Public Benefit Corporation



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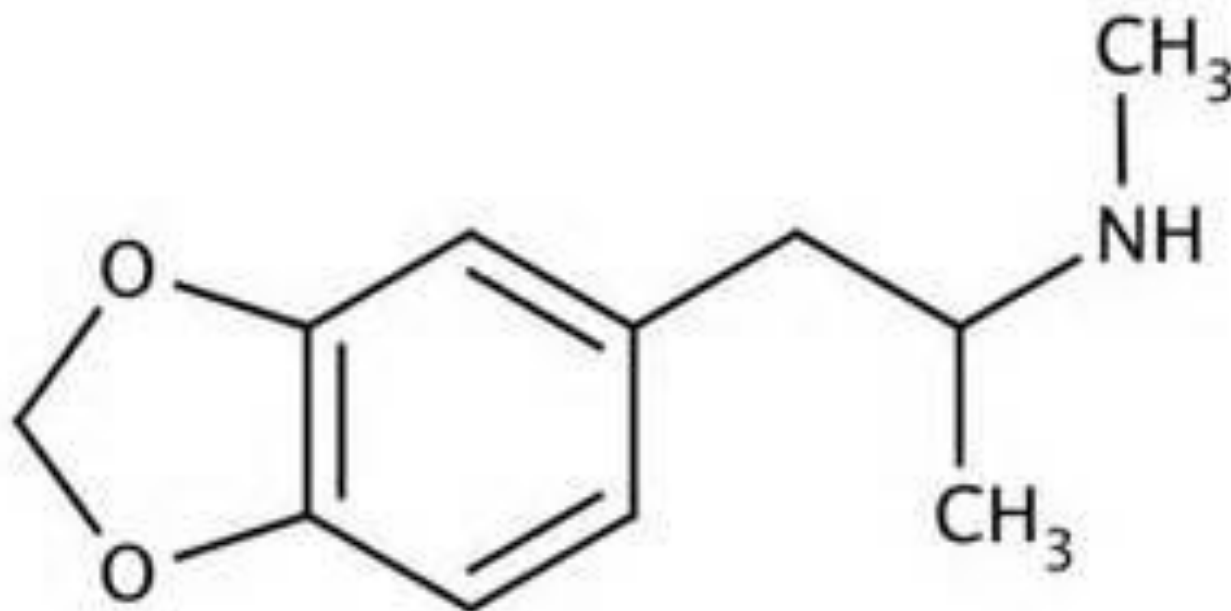
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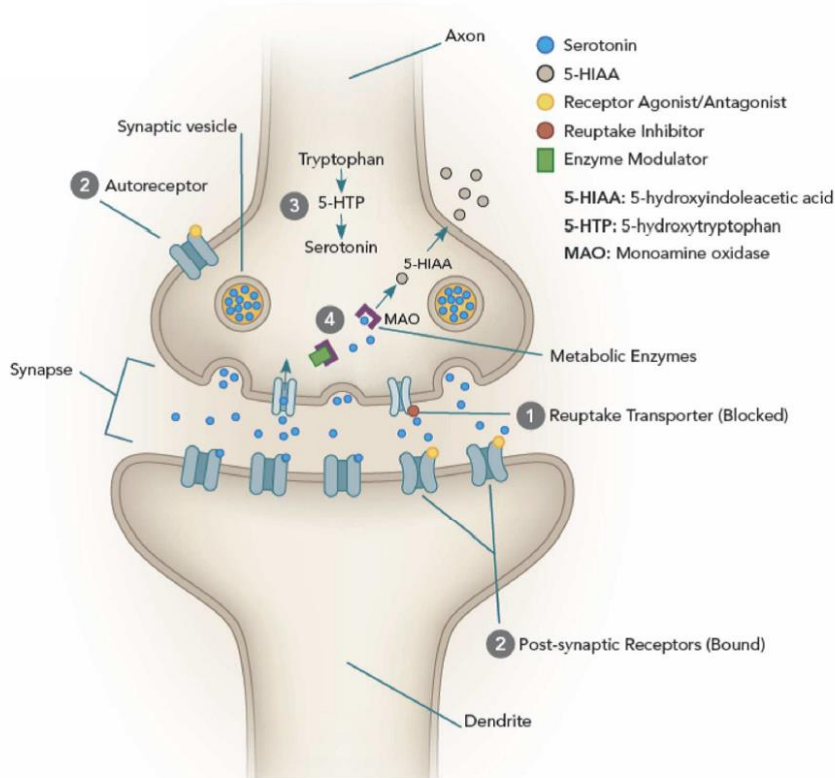
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3,4-methylenedioxyamphetamine (MDMA)



MDMA Pharmacology:

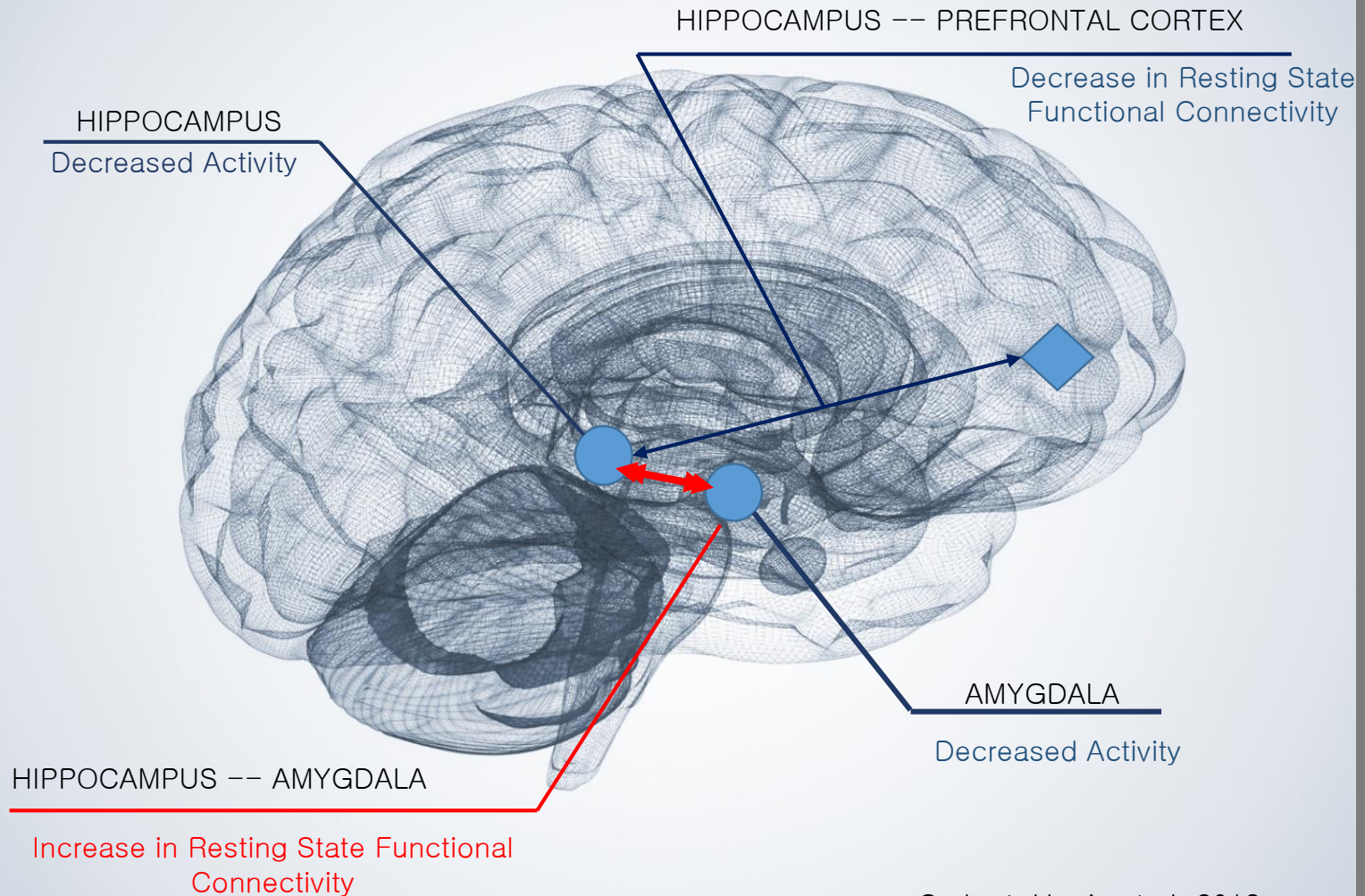
- Increases release of serotonin (5-HT), norepinephrine (NE), and dopamine (DA) into the synapse by reversing transporter proteins
- Enhances release of hormones oxytocin, prolactin, vasopressin, and cortisol



Psychoactive Effects in a Therapeutic Context




- enhance feelings of empathy, such as love, connectedness, and compassion for self and others
- increase feelings of acceptance
- reduce feelings of fear and defensiveness
- increase interpersonal trust
- heighten state of consciousness that allows for insight into self and situations

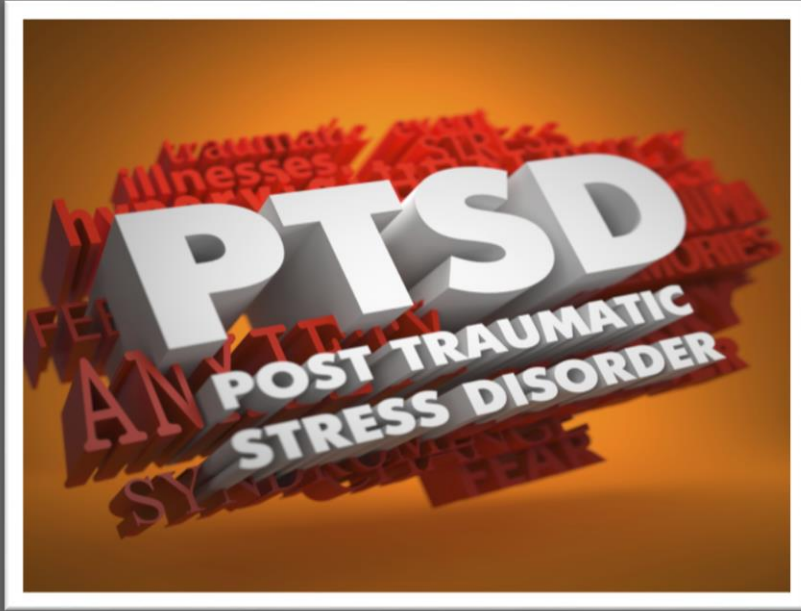
After 100 mg MDMA: changes in cerebral blood flow and resting state functional connectivity



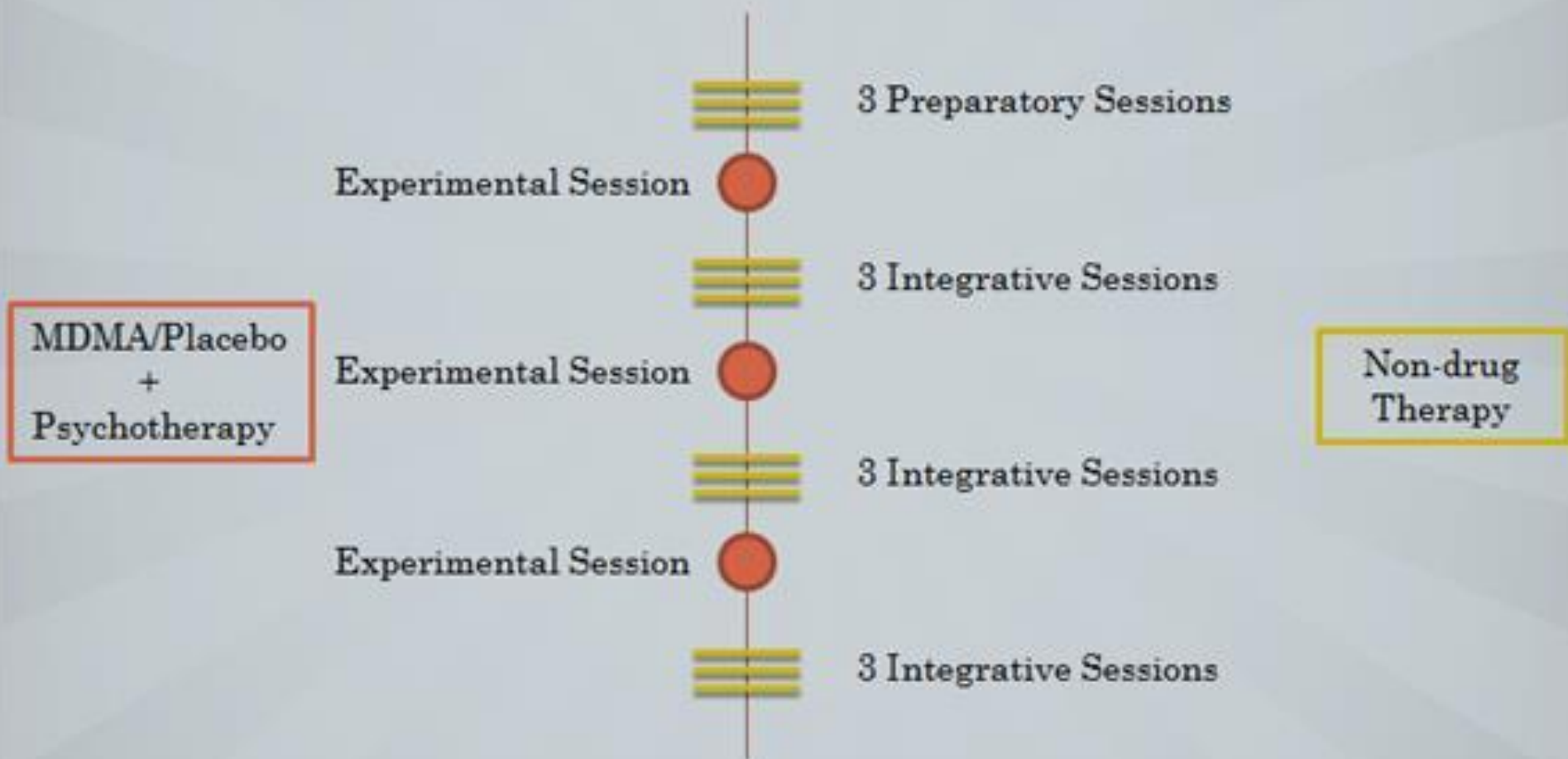
MAPS-sponsored MDMA-assisted Therapy Trials



-  Anxiety related to a life-threatening illness
-  Social anxiety in adults on autism spectrum
-  Posttraumatic stress disorder



MAPS-sponsored Clinical Trials



Therapeutic Approach

Non-directive, supporting emerging experience.

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

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Controlled Clinical Setting in a supportive environment with 2 therapists, male and female.

MAPS-sponsored PTSD Clinical Trial Publications

The safety and efficacy of {+/-}3,4-methylenedioxymethamphetamine-assisted psychotherapy in subjects with chronic, treatment-resistant posttraumatic stress disorder: the first randomized controlled pilot study.

Mithoefer MC, Wagner MT, Mithoefer AT, Jerome L, Doblin R.

J Psychopharmacol. 2011 Apr;25(4):439-52. doi: 10.1177/0269881110378371

<http://jop.sagepub.com/content/25/4/439.long>

Durability of improvement in post-traumatic stress disorder symptoms and absence of harmful effects or drug dependency after 3,4-methylenedioxymethamphetamine-assisted psychotherapy: a prospective long-term follow-up study.

Mithoefer MC, Wagner MT, Mithoefer AT, Jerome L, Martin SF, Yazar-Klosinski B, Michel Y, Brewerton TD, Doblin R.

J Psychopharmacol. 2013 Jan;27(1):28-39. doi: 10.1177/0269881112456611. Epub 2012 Nov 20

<http://jop.sagepub.com/content/27/1/28.long>

A randomized, controlled pilot study of MDMA (\pm 3,4-Methylenedioxymethamphetamine)-assisted psychotherapy for treatment of resistant, chronic Post-Traumatic Stress Disorder (PTSD).

J Psychopharmacol. 2013 Jan;27(1):40-52. doi: 10.1177/0269881112464827. Epub 2012 Oct 31.

Oehen P1, Traber R, Widmer V, Schnyder U.

<http://jop.sagepub.com/content/27/1/40.long>

A Randomized Triple-Blind, Phase 2 Pilot Study Comparing 3 Different Doses of MDMA in Conjunction with Manualized Psychotherapy in 26 Veterans, Firefighters, and Police Officers with Chronic Posttraumatic Stress Disorder



PI: Michael Mithoefer, M.D.
Co-therapist: Annie Mithoefer, B.S.N.
Charleston, South Carolina

Unpublished Data Slides Removed

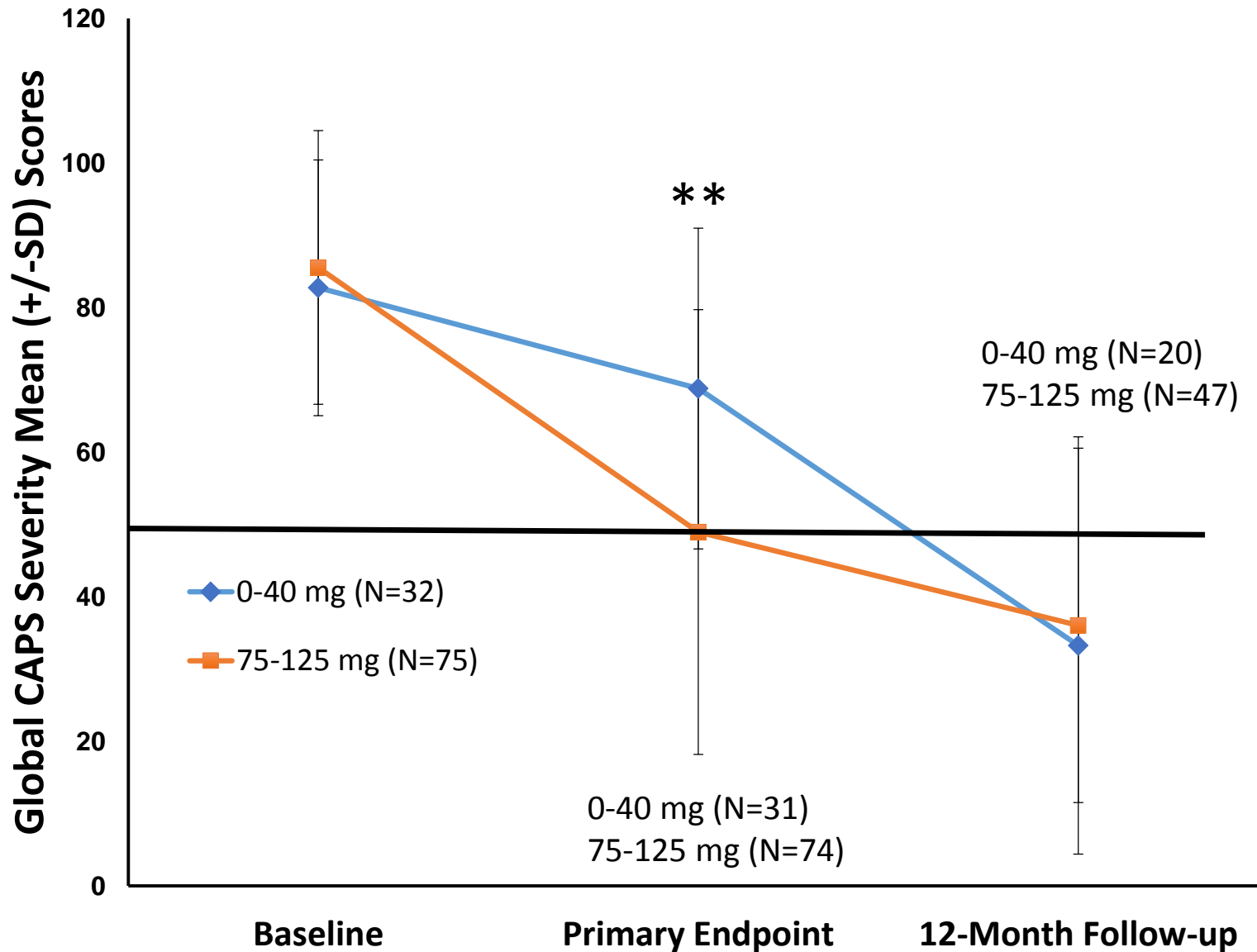
I don't think I would have survived another year. It's like night and day for me compared to other methods of therapy. Without MDMA I didn't even know where I needed to go. Maybe one of the things the drug does is let your mind relax and get out of the way because the mind is so protective about the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

- **Charleston**
Subject X

It feels almost like the inner healer or the MDMA is like a maid doing spring cleaning. It's as if you thought you were cleaning before but when you got to things you didn't really want to deal with you'd just stick them in the attic. If you're going to clean the house you can't skip the stuff in the attic.

- Charleston
Subject X

Preliminary PTSD Outcome Analysis of All MAPS' MDMA/PTSD Studies at 12-Month Follow-up all Subjects had Full Dose MDMA in Stage 1 or Stage 2



Preliminary Effect Size Estimates Across 6 Studies

| Dose Comparison | Effect Size – 2 experimental sessions | Effect Size – 3 experimental sessions | Effect Size |
|--------------------------|---|---|--------------|
| 75-125 mg vs. 0-40 mg | 0.8 N=72:31 | 1.24 N=51:31 | Large |

Small Effect = 0.3 Medium Effect = 0.5 Large Effect = 0.8 or greater

Effect Size Cohen's $d = \frac{\text{difference in group means pre-treatment} - \text{post-treatment}}{\text{pooled pre-post raw SD}}$

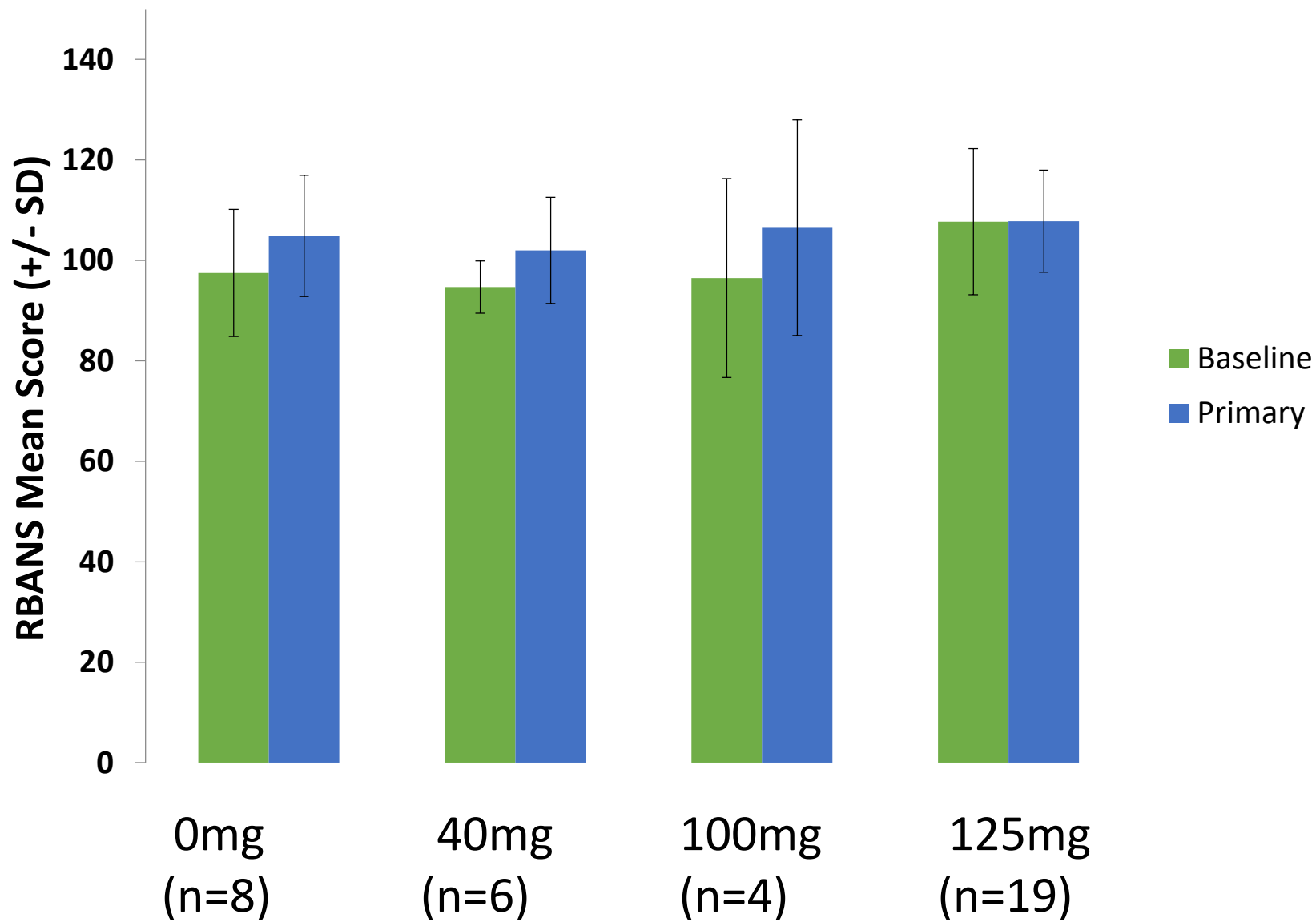
Common Adverse Reactions to MDMA at Any Severity during Experimental Sessions

| | Dose | 100-125 mg | Placebo 0 mg |
|--------------------|----------|------------|--------------|
| | Subjects | 100 | 12 |
| | Sessions | 255 | 24 |
| Jaw Clenching | | 55% | 21% |
| Anxiety | | 58% | 48% |
| Decreased appetite | | 42% | 8% |
| Headache | | 37% | 50% |
| Fatigue | | 34% | 42% |
| Muscle Tension | | 27% | 13% |
| Nausea | | 27% | 13% |
| Feeling Cold | | 27% | 13% |

Common Adverse Reactions at Any Severity 7 Days after Experimental Sessions

| | Dose | 100-125 mg | Placebo 0mg |
|--------------------------|----------|------------|-------------|
| | Subjects | 100 | 12 |
| | Sessions | 255 | 24 |
| Anxiety | | 24% | 38% |
| Fatigue | | 24% | 30% |
| Insomnia | | 14% | 29% |
| Depressed Mood | | 13% | 13% |
| Need More Sleep | | 12% | 14% |
| Difficulty Concentrating | | 10% | 13% |
| Decreased Appetite | | 9% | 0% |
| Dizziness | | 8% | 3% |

No Change in Neurocognitive Function after 2 MDMA Sessions

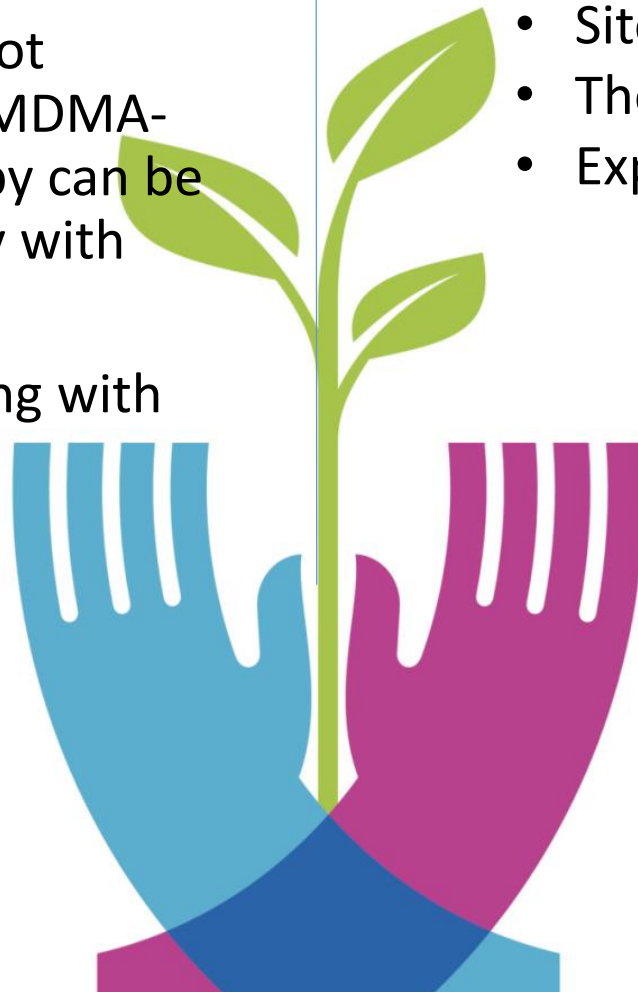


Phase 2 Trials

- Established Safety in controlled clinical settings
- Efficacy has Large Effect Size
- Cause of PTSD does not influence outcomes, MDMA-assisted psychotherapy can be used to treat anybody with chronic PTSD
- End of Phase 2 meeting with FDA in Fall 2016

Phase 3 Trials

- Two Phase 3 studies (approx 450 subjects)
- Phase 3 study design
- Site selection (7-10 sites)
- Therapist Training
- Expanded Access



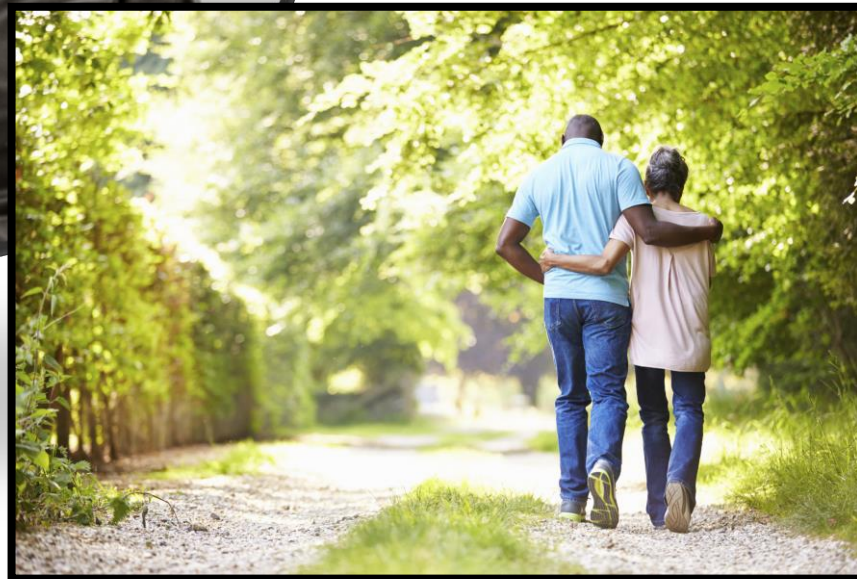
2021



MDMA-assisted Psychotherapy for PTSD (Cognitive Behavioral Conjoint Therapy)



- Dyad MDMA therapy, with one person having PTSD
- Principal Investigator: Michael Mithoefer, M.D.
- Sub-Investigator: Candice Monson, Ph.D.



Acknowledgements



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