

3, 4-METHYLENEDIOXYMETHAMPHETAMINE (MDMA)-COGNITIVE BEHAVIORAL CONJOINT THERAPY (CBCT) FOR PTSD: PROPOSED RESEARCH TRIAL

DR. BRANDI LUEDTKE
CLINICAL PSYCHOLOGIST
PROGRAM MANAGER, PTSD/MST PROGRAM-PHOENIX VA HEALTHCARE SYSTEM
CBCT FOR PTSD NATIONAL TRAINER AND CONSULTANT
WWW.NELLIEHEALTH.COM



DISCLOSURES & DISCLAIMERS

- I have no conflicts of interest to disclose.
- The views expressed in this presentation are those of the presenter and do not reflect the official policy of the United States Department of Veterans Affairs or the United States Government.
- MDMA is expected to have FDA approval in 2024 until then it is a Schedule 1 Substance and is restricted for use except in clinical trials and expanded access settings.
- I want to thank our future MDMA-CBCT study therapists: Drs. Courtney Baker (Co-I), Veronica High, Chris Ogle, and Michael O'Connor

OBJECTIVES

- History of MDMA usage in clinical settings
- Mechanism of Action
- Non-ordinary States of Consciousness
- FDA Trials
- Couples Treatment for PTSD
- Proposed Trial of MDMA-CBCT for PTSD

The background features a dark blue gradient with a subtle pattern of white stars. On the left side, there are several technical diagrams, including a large circular scale with numerical markings from 40 to 260 in increments of 10. Other diagrams consist of concentric circles, dashed lines, and arrows, suggesting a technical or scientific theme. The word "BACKGROUND" is centered in a bold, white, sans-serif font.

BACKGROUND



- Throughout history non-ordinary states of consciousness have been central to spiritual and healing practices across numerous cultures around the world.
- Rich traditions have existed in Indigenous cultures and lineages of teachings involving visionary substances.
- The Native American Church founded in 1918 uses Peyote as its sacrament.
- In Mexico, the Mazatec use Psilocybin or Salvia for ceremonial practices.

- Synthesized by Merck in 1912.
- Legally used as an adjunct in psychotherapy in the 1970s.
- 1980s: Recreational use increases
- 1985: DEA designates MDMA as Schedule 1 substance.
- 1986: Multidisciplinary Association of Psychedelic Studies (MAPS) is founded by Rick Doblin.



MAPS MDMA Timeline



WHY MDMA?

Empathogen—
generating empathy

Prosocial—helps
establish therapeutic
alliance with
practitioners

Manageable
psychedelic

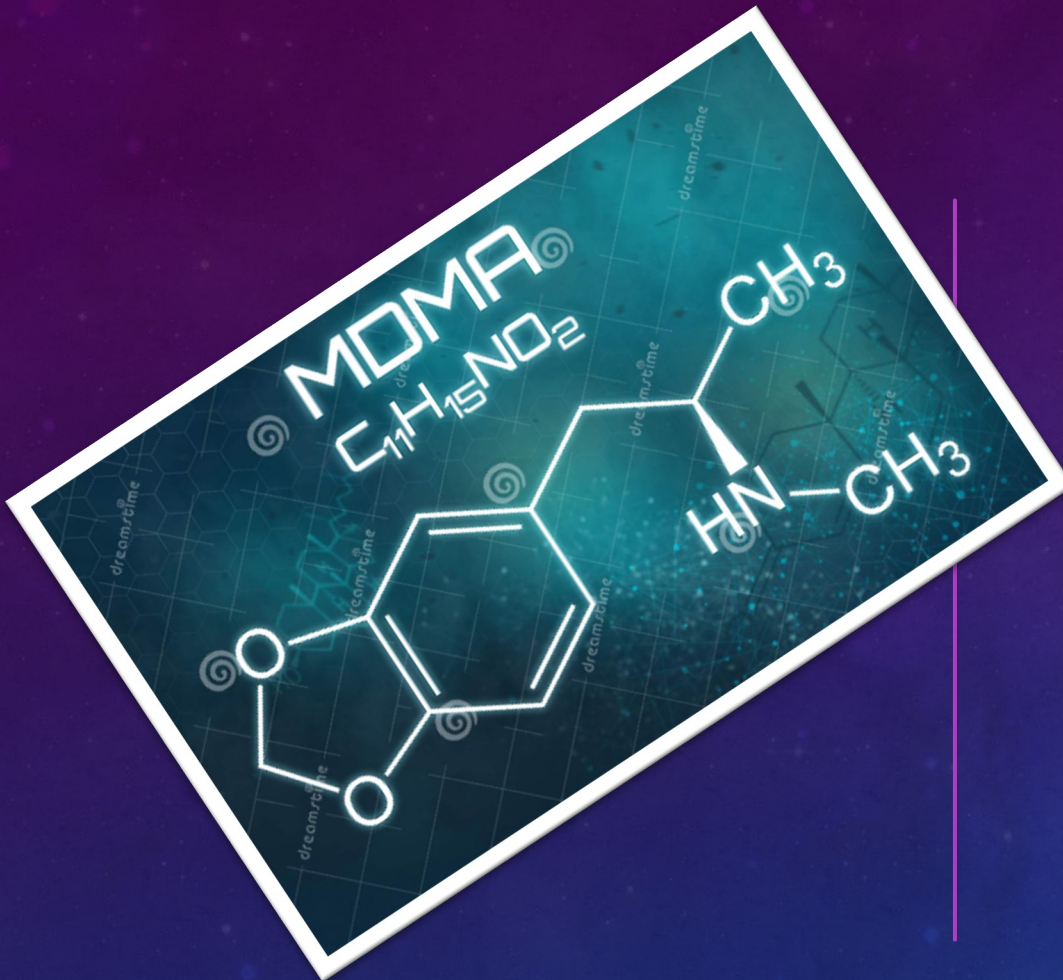
Resource rich —
safety, relaxation,
and the possibility of
felt sense experience

Fear becomes
proportional,
anxiolytic

Love -curiosity,
compassion, and
understanding

Other Benefits of MDMA

- Robust anticancer properties
 - In 2011, research showed slightly modified forms of ecstasy was 100x more potent at destroying cancer cells than the original forms
- Shown to be useful in treating PTSD
 - >\$3 billion for PTSD care a year
 - \$17 billion on service-connection for PTSD
 - Phase 3 studies cost around \$11,537 per patient and for every 1000 patients treated it gives a 30 -year savings to medical system of \$132.9 million



MECHANISM OF ACTION

- MDMA increases the release of a group of neurotransmitters called monoamines: serotonin (5-HT), norepinephrine (NE), and dopamine (DA).
- MDMA exerts its main effects through the release of serotonin.
- Pre-clinical animal models have demonstrated that by activation of the serotonin system, MDMA causes the release of the neurohormone, oxytocin.
- Enhanced blood concentrations of oxytocin have been observed in humans following MDMA consumption.



5-HT1A/2A

*Elevated mood
Decreased anxiety & fear
Increased self-confidence
Altered perceptions*

Release of Oxytocin/prolactin

*Increased empathy
Increased trust
Decreased defensiveness
Improved stress regulation*

NE/DA/Cortisol

*Hypersalience
Activation
Emotional Learning*

Most Common Side Effects of MDMA



MDMA can cause temporary increases in blood pressure and pulse.



muscle
tightness



decreased
appetite



nausea



sweating



feeling cold



pupil
dilation



restlessness

No drug is without risks.

MDMA has been administered to nearly **2000 people in clinical studies** with one serious adverse reaction reported, with no lasting harms.



Safety:

- MDMA has shown to be safe for use in treating PTSD
 - Serious Adverse Events:
 - 0 participants in MDMA group experienced SI and/or SI attempt
 - 2 participants in placebo group
 - Adverse Events of Special Interest:
 - Cardiovascular concerns
 - 0% in MDMA group
 - 2% in placebo group
 - Abuse potential
 - 0% in MDMA group
 - 0% in placebo group

NON-ORDINARY STATES OF CONSCIOUSNESS



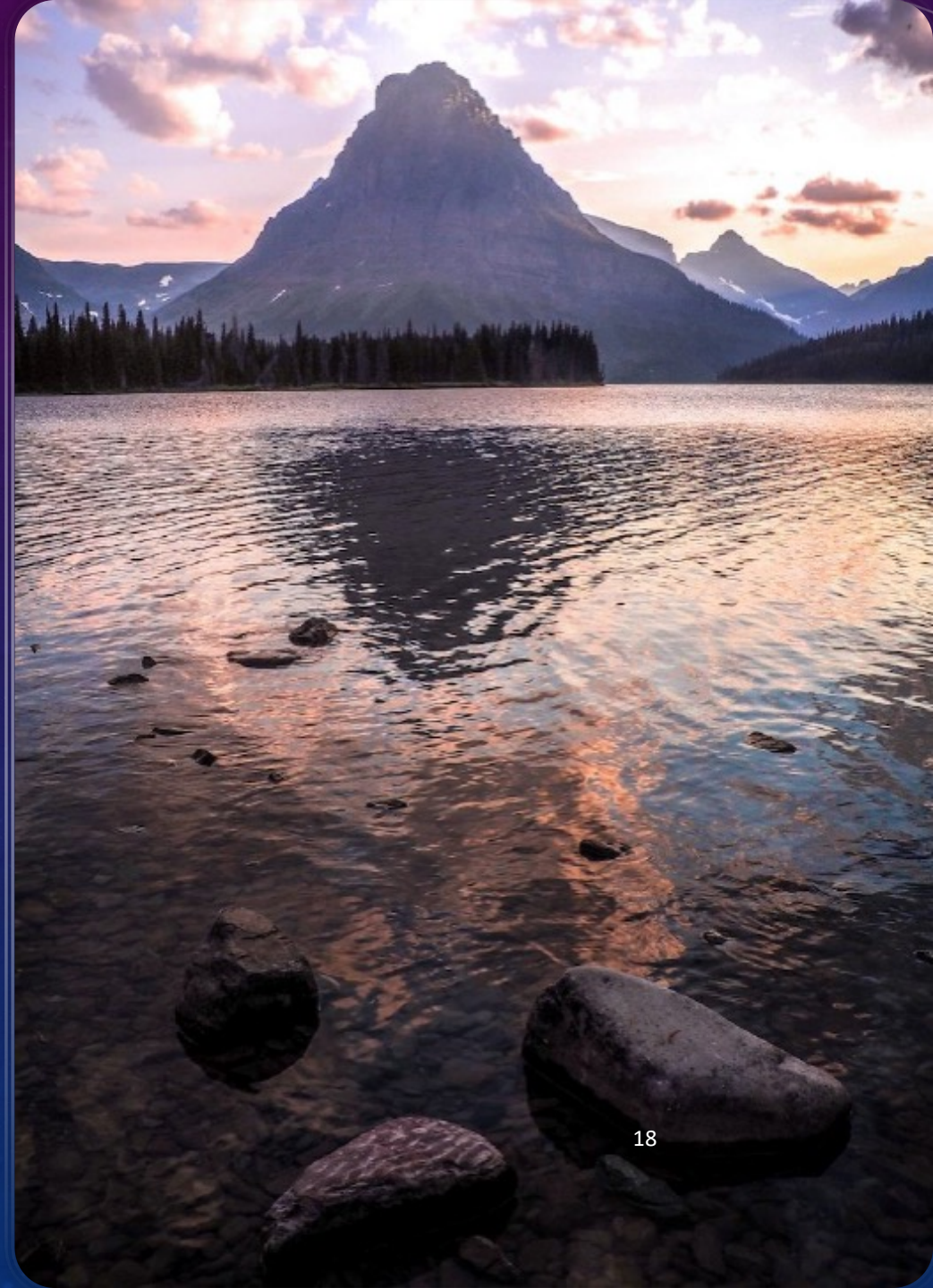
*“MY CONSCIOUSNESS EXPANDED AT AN
INCONCEIVABLE SPEED AND REACHED COSMIC
DIMENSIONS. THERE WERE NO MORE BOUNDARIES OR
DIFFERENCE BETWEEN ME AND THE UNIVERSE. I FELT
THAT MY OLD PERSONALITY WAS EXTINGUISHED AND
THAT I CEASED TO EXIST. AND I FELT THAT BY
BECOMING NOTHING, I BECAME EVERYTHING.”*

STAN GROF



- **Non-ordinary states of consciousness** are characterized by dramatic perceptual changes, intense and often unusual emotions, profound alterations in the thought processes and behavior, and by a variety of psychosomatic manifestations.
- **Common experiences:**
 - Transpersonal experiences
 - Perceptual changes
 - Extreme states
 - Common Fears
 - Potentially Beneficial Qualities

- **Transpersonal experiences may include:**
- Loss of ego/ego death
- Rebirthing experience
- Mystical experience
- Spiritual quest, hero's journey
- Communicating with those beyond (deceased, ancestors, archetypes, past lives)
- Communicating with Spirit, God, Allah, other god figures and deities
- Identification with deities and the realms in which they live
- Identification with/as an animal, real or mystical creature
- Unity experiences



Potential Benefits to Using MDMA in Psychotherapy

Access to unconscious material

Access to parts of self and past

Expression of emotion, suppressed parts of self

Increased sense of connection with oneself, others, nature, spirit

Increased access to/development of internal resources, sources of wisdom

Ability to take space from “normal mind,” less rigid thinking

Ability to reevaluate sense of self, character, identity

Ability to reevaluate beliefs and thought patterns

Enhanced or renewed sense of purpose, meaning, and belonging

Exploration of existence, one’s own and the very nature of existence

Ways to Induce Non-Ordinary States of Consciousness

Spontaneous
Day-dreaming,
near death
experience

Physical and
Physiological
Fasting, sex

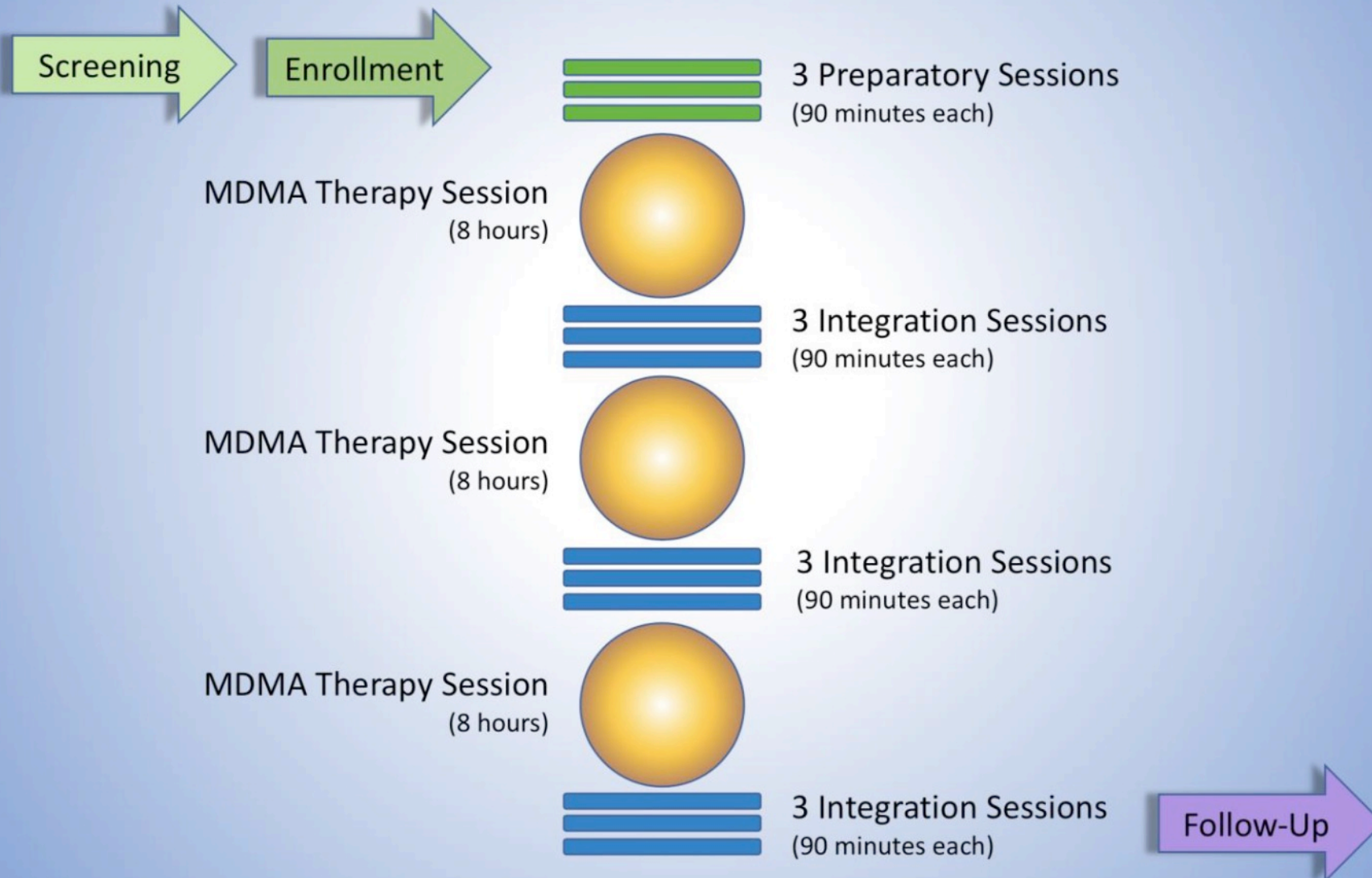
Psychological
Music, meditation,
hypnosis, sensory
deprivation

Pathological
Epilepsy, psychosis,
brain damage

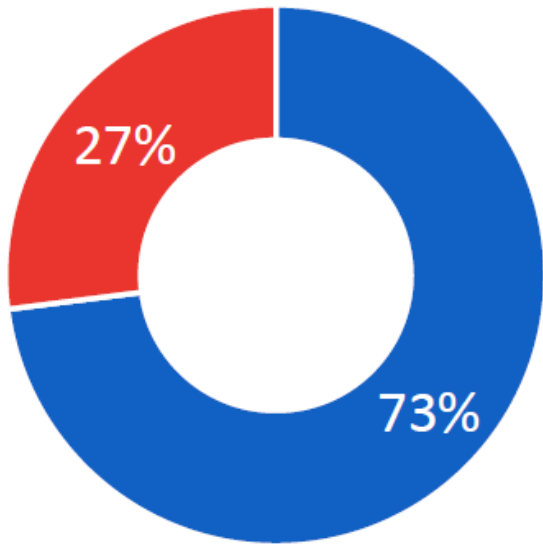
Pharmacological
Psychoactive
substances-**MDMA**



FDA TRIALS

Course of Treatment

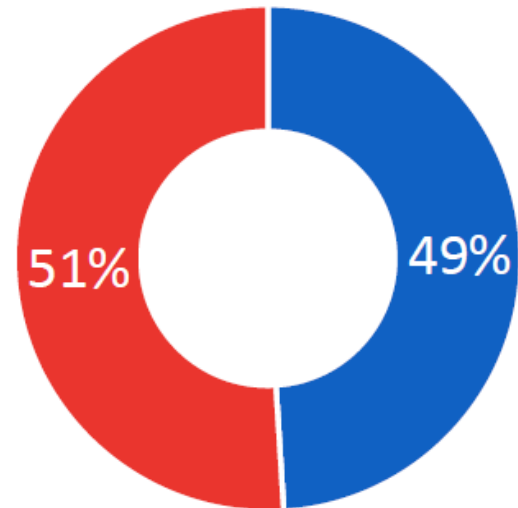




**MAPP 1 Enrolled- White Compared to POC
(including Hispanic)**



-  White (excl. Hispanic)
-  People of Color (incl. Hispanic)

**MAPP 2 Enrolled-
White Compared to POC (including Hispanic)**

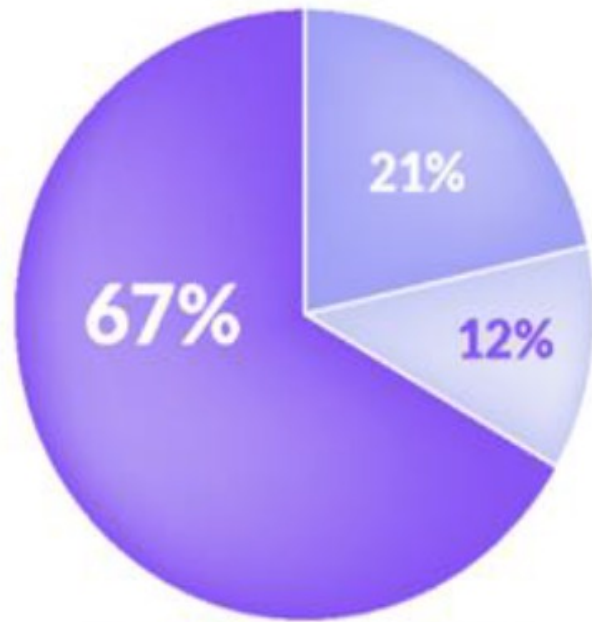


-  White (excl. Hispanic)
-  People of Color (incl. Hispanic)

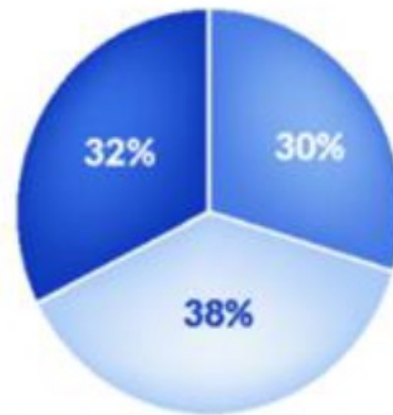


Treating PTSD with MDMA-Assisted Therapy

Phase 3 Trial Results Published in *Nature Medicine*, May 2021



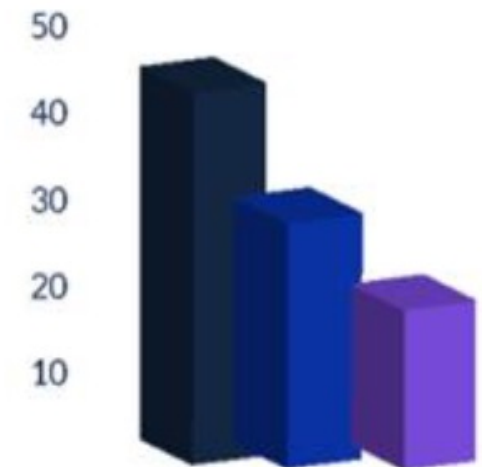
MDMA-ASSISTED THERAPY



PLACEBO WITH THERAPY

- Lost PTSD diagnosis
- Clinically meaningful response
- No response

Average Severity of PTSD Symptoms (CAPS-5 Score)



- Before treatment
- Placebo with therapy
- MDMA-assisted therapy



TREATMENT OF PTSD

The
Economist

**MDMA: A CURE
FOR PTSD?**



- The body initiates a remarkably complex and sophisticated healing process and always spontaneously attempts to move toward healing.
- The psyche too exhibits an innate healing intelligence and capacity.
- Various paradigms of thought and faith would articulate these concepts in different ways:
 - Spirit
 - Truth
 - Inner champion
 - Inner healer
 - Deep knowing
 - Innate wisdom



Therapist Role

- **Active Non-Doing**
- Practitioners do not push for a particular experience, outcome, or resolution
- Emphasis is on remaining curious about what arises in the moment and trusting that what emerges does so in service of healing

Inner Directed Approach

- A philosophical stance, an attitude; not a "technique"
- Based on the belief that participants have the capacity for self-direction and understanding of their own process
- Builds relationship with inner healing intelligence
- Brings the participant's process into **awareness** rather than making something happen
- Supports participants to work where they are

“WE ENCOURAGE YOU TO APPROACH WHATEVER COMES UP AS SOMETHING THAT’S COMING UP AS PART OF YOUR HEALING PROCESS. WE TRUST THAT YOUR INNER HEALING INTELLIGENCE WILL BRING YOU WHAT YOU NEED FOR HEALING AND THAT’S MUCH MORE RELIABLE THAN ANYTHING YOU OR WE COULD FIGURE OUT AHEAD OF TIME WITH OUR RATIONAL MIND.”

Participant's State During MDMA Session

*Time points are averages, expect variation



0 - 2 Hours	Focus: Inward, present moment experience, engage right brain
	Music: Slower, spacious, welcoming, inquiring, curious
2 - 5.5 Hours	Focus: Balance between inner and relational work (non-linear following participant)
	Music: Tempo & energy increase to match participant. Have spacious music to match waves. Open-hearted, deep, powerful
5.5 - 8.5 Hours	Focus: Tends to relational, curious, surrender, release, struggle, insight, "AHA" moments
	Music: Relaxing, slower tempo, integrating, connecting, spacious, thoughtful, considerate
9+ Hours	Focus: Everyday life concerns return

Hours	0	1	2	3	4	5	6	7	8	9	
Phases	Onset			Active (Main Working Phase)			Tapering of Effects			Approaching New Baseline	New Baseline
	<ul style="list-style-type: none"> Not about process, but MDMA effects. Tracking somatic sensations (cold, heavy, nausea, loss of control, anxiety). Practitioner's response is different here than later in the session. 			<ul style="list-style-type: none"> Inner directed Inner Healing Intelligence Following Pace Curiosity Set agenda aside Safety Self titration Present moment 			<ul style="list-style-type: none"> Encourage participant to return to their inner process (when waves slow, participant often thinks "working time" is over). Self-Consciousness returns 				

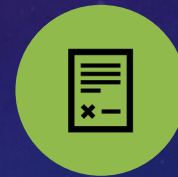
Clinical Considerations



Appropriateness



Cultural Humility



Termination

Cognitive-Behavioral Conjoint Therapy for PTSD



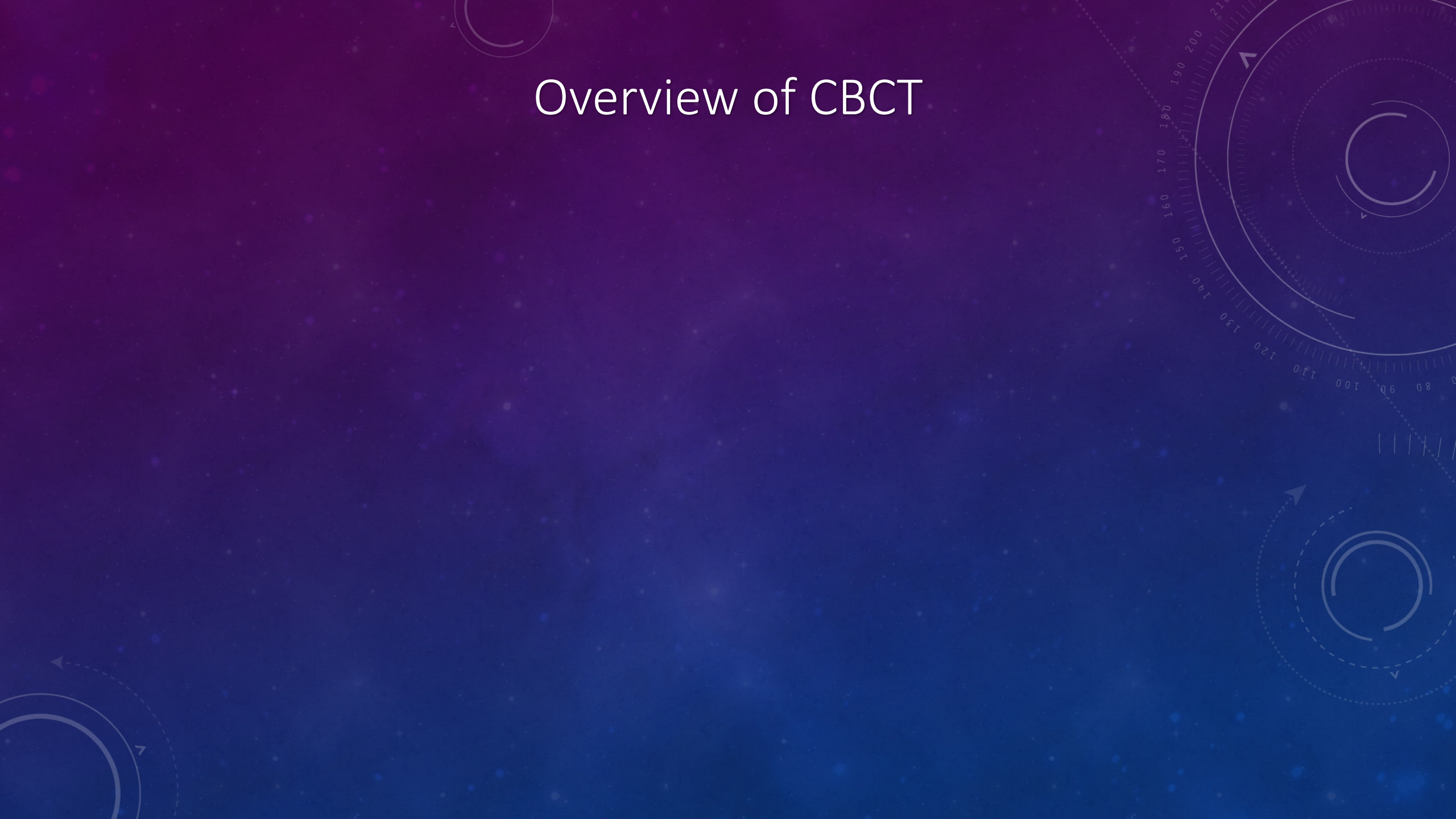
Harnessing
the Healing Power
of Relationships

Candice M. Monson and Steffany J. Fredman

What is CBCT for PTSD?

- Trauma-focused, exposure-based, but **not** imaginal
 - 15 sessions, manualized therapy
 - 75 minute sessions
 - Stand-alone treatment
- The goals of therapy are to:
 - Reduce PTSD symptoms and distress related to traumatic memories, along with frequently co-occurring symptoms (i.e. depression)
 - Improve the relationship and functioning between person with PTSD and their significant other

Overview of CBCT



The background is a dark blue gradient with a starry or particle-like texture. It features several abstract white line graphics: a set of concentric circles in the top-left corner, a circular scale with numerical markings (90, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, 200) and arrows in the top-right corner, and another set of concentric circles in the bottom-right corner. There are also some faint, dashed circular lines and arrows scattered throughout the background.

OUTCOMES OF CBCT FOR PTSD

CBCT FOR PTSD FINDINGS


- 7 case studies (Fedynich et al., 2020; Brown-Bowers et al., 2012; Blount et al., 2015, 2016; Fredman et al., 2011; Luedtke et al., 2015; Monson et al., 2008)
- 6 uncontrolled studies
 - Male Vietnam veterans and their wives (Monson et al., 2004)
 - Mixed (Monson et al., 2011)
 - Male OIF/OEF veterans and their wives (Schumm et al., 2013)
 - Retreat format with US veterans and service members and partners (Fredman et al., 2020)
 - Mixed MDMA-facilitated (Monson et al., 2020)
 - Mixed era veterans and their partners (Pukay-Martin et al., 2015)

4 controlled studies

- Mixed waiting list comparison (Monson et al., 2012)
- US active-duty service members compared with PE (Monson et al., 2017)
- Retreat format with US veterans and partners (Davis et al., 2021)
- Abbreviated format in person or via telehealth with US veterans and partners (Morland et al., 2023)

Improvements in:

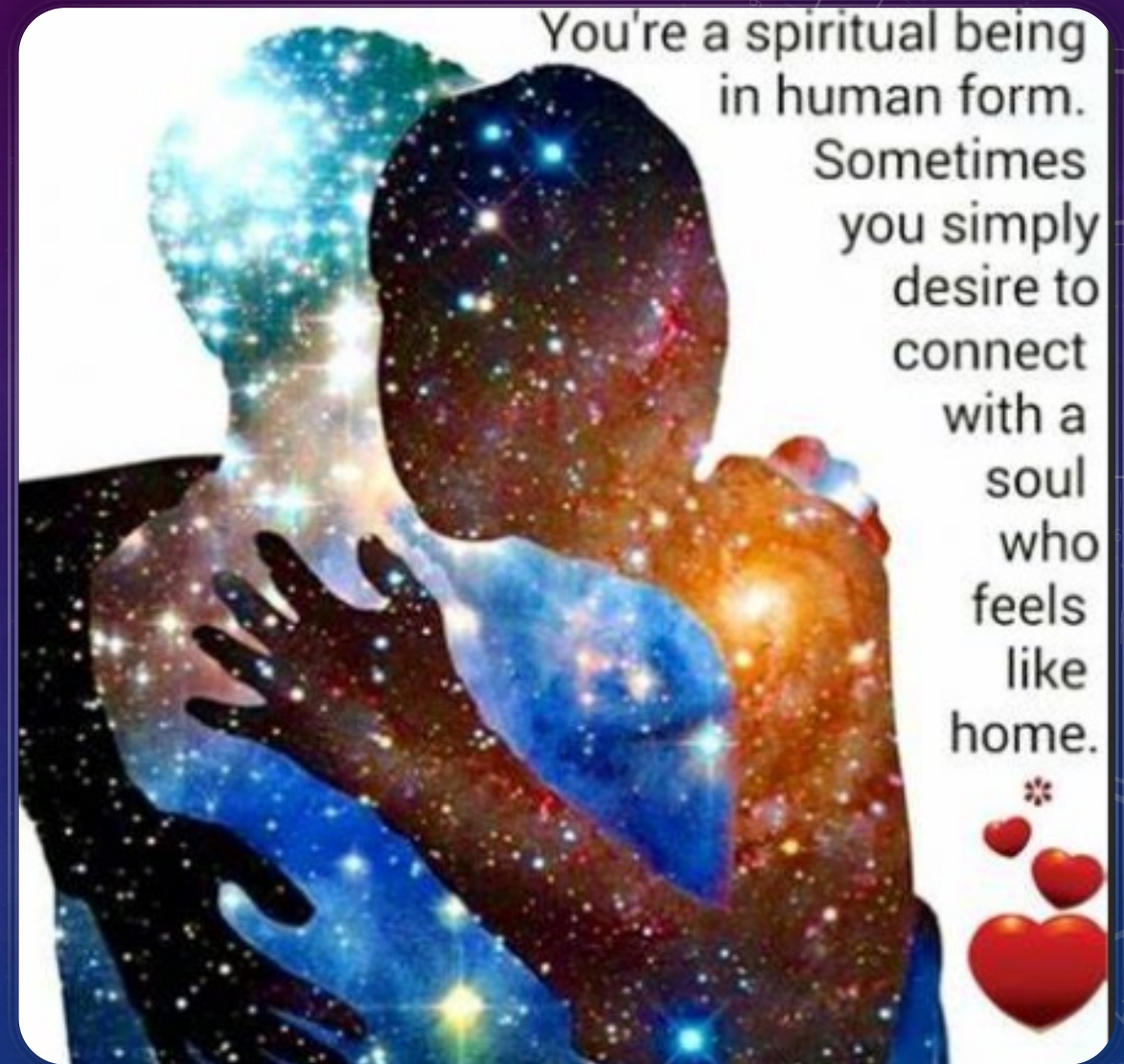
- PTSD and comorbid conditions (on par with individual EBTs)
- Partners' well-being
- Relational functioning



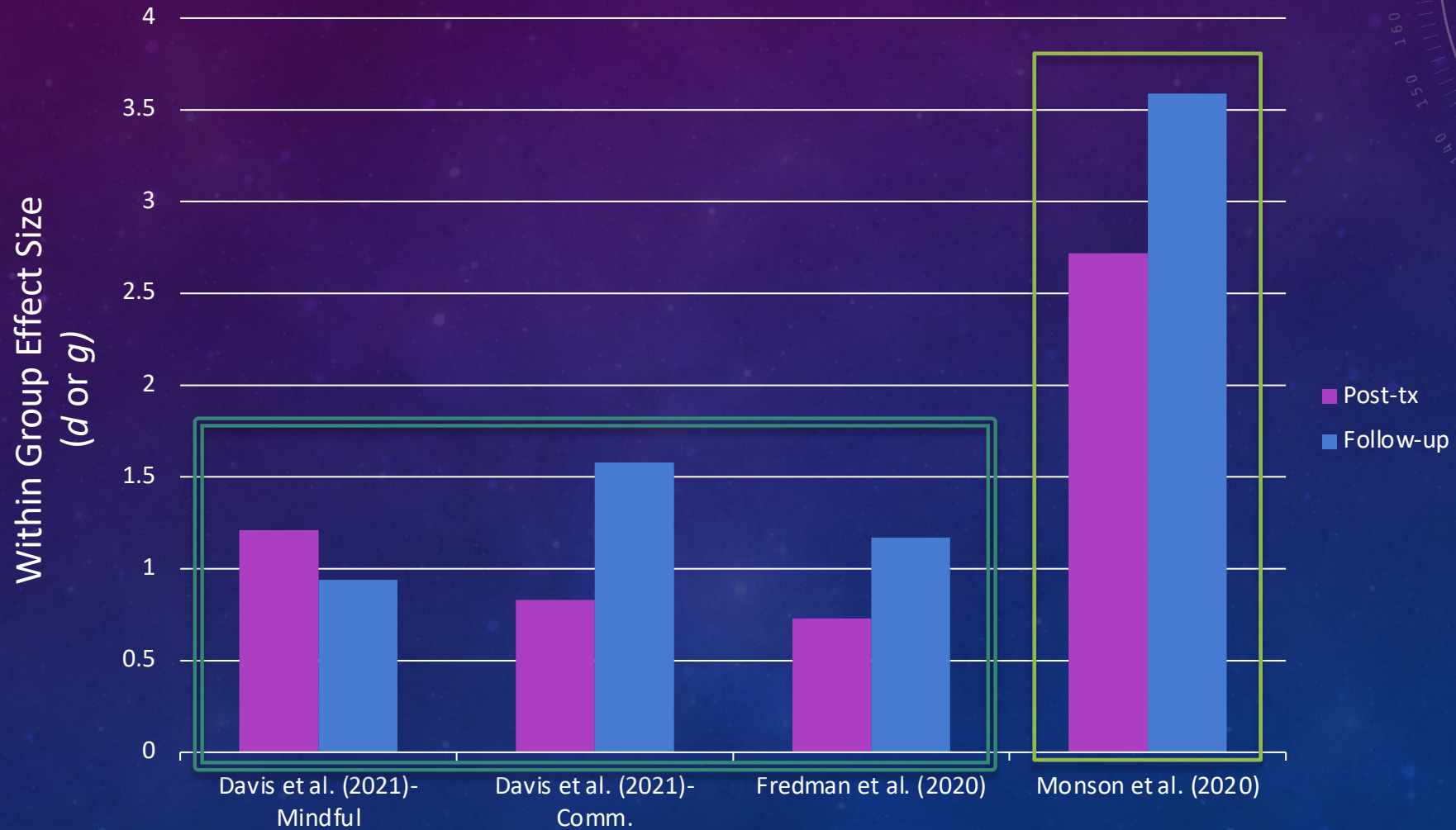
MDMA AND CBCT FOR PTSD

MDMA AND RELATIONSHIPS

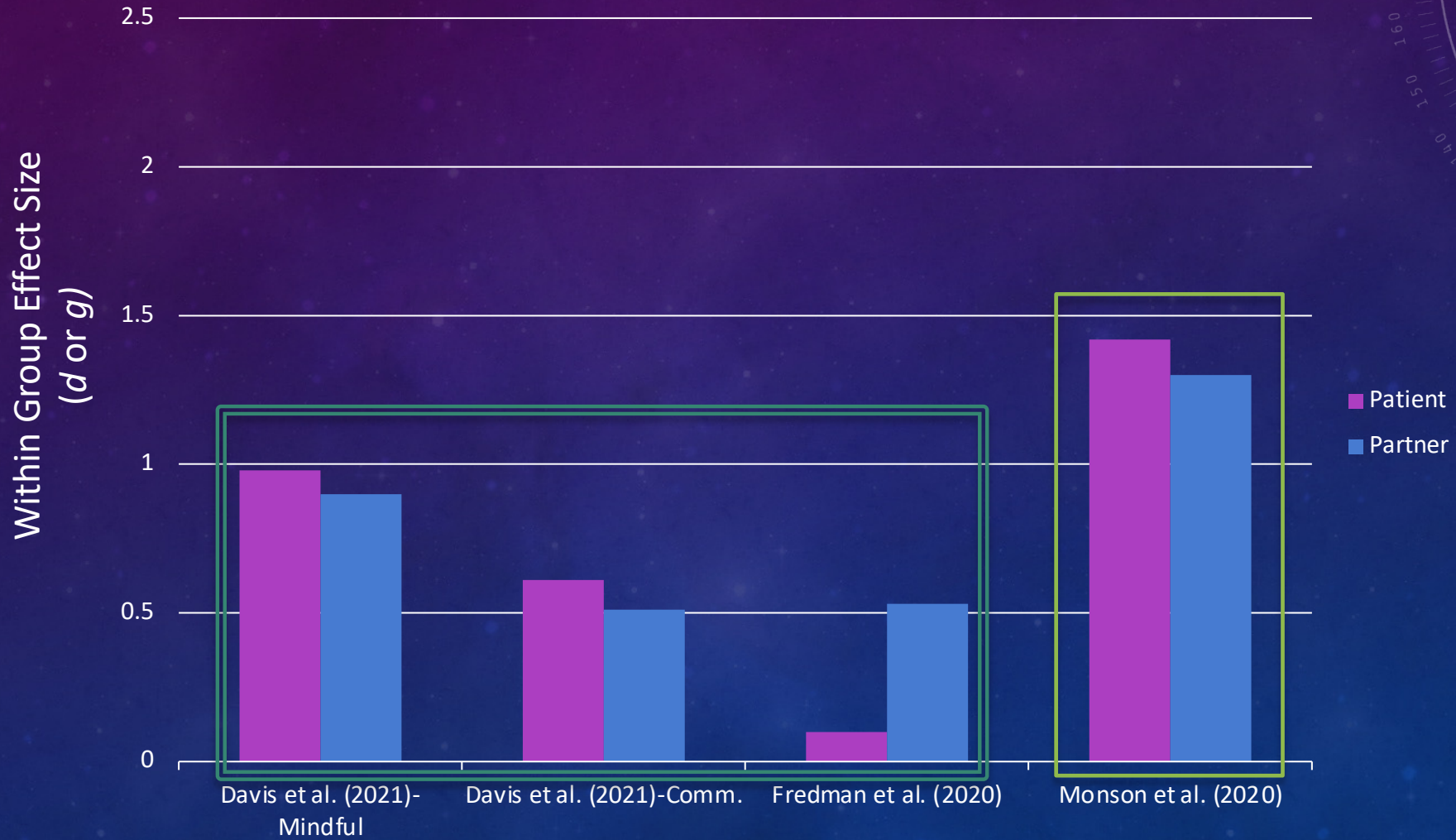
- MDMA has been shown to reduce defenses and fear of emotional injury, enhance communication, and increase empathy.
- MDMA may enhance fear extinction learning in humans. These subjective effects of MDMA create a productive psychological state that enhances the therapeutic process for the treatment of PTSD and other anxiety disorders.
- MDMA helps patients get in touch with their **Inner Healing Intelligence**



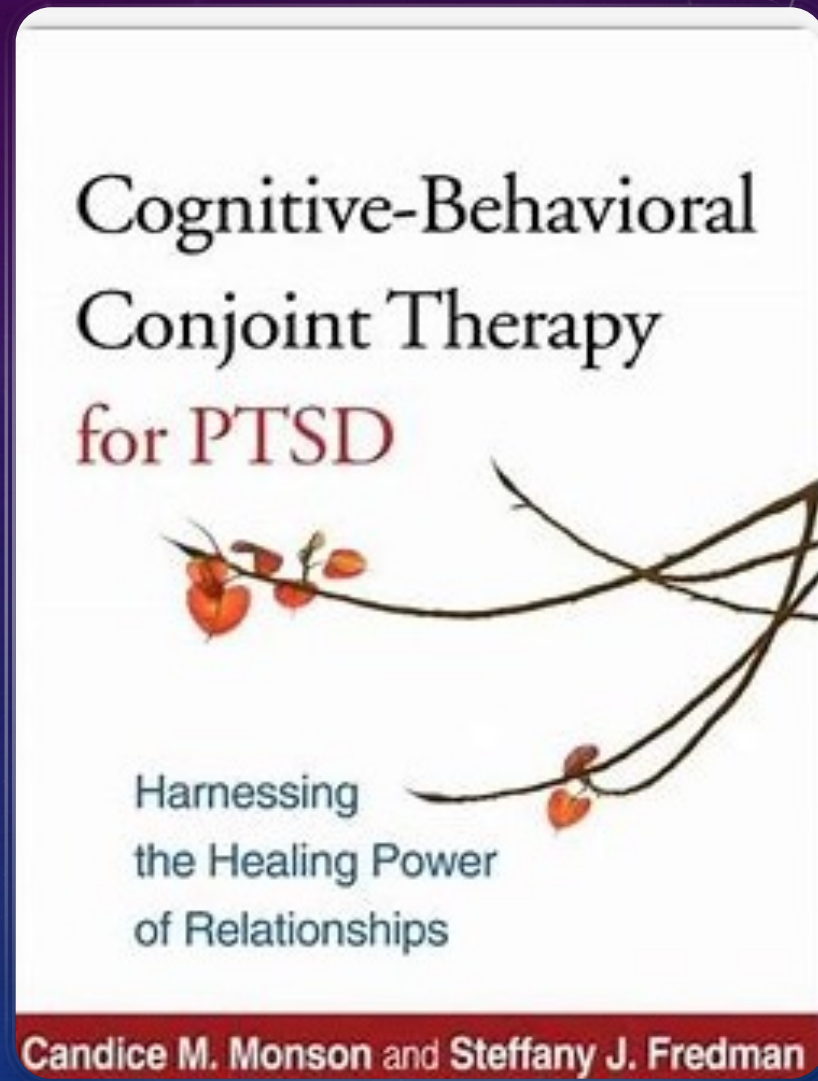
PATIENT-RATED PTSD SCALE



RELATIONSHIP ADJUSTMENT



- **MDMA & Cognitive-Behavioral Conjoint Therapy (CBCT) Research**
- When: Coming soon(ish) to Phoenix VA PTSD Clinical Team
- What: CBCT 15-week protocol with 2 experiential sessions of MDMA
- Who: Veterans and their partner will both be dosed with MDMA



Screening

Enrollment

- Session 1
- Session 2
- Session 3
- Session 4
- Session 5

MDMA Therapy Session
(8 Hours)



Integration

- Session 6
- Session 7
- Session 8
- Session 9
- Session 10
- Session 11

MDMA Therapy Session
(8 Hours)



Integration

- Session 12
- Session 13
- Session 14
- Session 15

Follow-Up

AIMS

- **Aim 1:** Examine the effect of MDMA-assisted CBCT on the primary outcome of PTSD symptoms.
 - Hypothesis 1: Veterans will demonstrate statistically significant improvement in PTSD symptoms on the total severity score on the Clinician-Administered PTSD Scale for DSM-5 (CAPS-5) at mid-treatment, post-treatment, 3-month follow-up, and 6-month follow-up.
- **Aim 2:** Examine the effects of MDMA-assisted CBCT on relationship functioning.
 - Hypothesis 2: Both Veterans and their partners will report statistically significant improvements in relationship satisfaction (Couples Satisfaction Index; CSI), intimacy (Intimate Safety Questionnaire; ISQ), communication (Communication Skills Test; CST), and emotion regulation (Emotion Regulation Questionnaire; ERQ) at mid-treatment, post-treatment, 3-month follow-up, and 6-month follow-up.
- **Aim 3:** Evaluate safety, tolerability, and feasibility of including MDMA administrations with current CBCT protocol.
 - Safety (Columbia Suicide Severity Rating Scale; C-SSRS) and adverse events will be monitored and tracked for the duration of study participation.



THANK YOU

BRANDI.LUEDTKE1@VA.GOV

BLUEDTKE@NELLIEHEALTH.COM