Postpartum Psychedelic Therapies, Substance Use and Intergenerational Trauma

MA PQUIN Webnar
Larry Leeman MD MPH
Professor of Family and Community Medicine
Medical Director UNM Milagro Perinatal Substance Use Program
Co-Director UNM Research Program for Psychedelic Assisted Therapies

THE UNIVERSITY OF NEW MEXICO

1

Disclosures

- No conflicts of interest
- Lykos Therapeutics (formerly MAPS PBC) has provided the MDMA free of charge for postpartum study of MDMA-AT for Post Traumatic Stress Disorder and Opioid Use Disorder
- MDMA and Psilocybin are schedule one substances that are under investigational use in FDA approved studies and Ketamine is a schedule three drug approved for anesthesia but "off label" for mental health indications

2

Objectives

- Identify the **roles of trauma and Post-Traumatic Stress Disorder (PTSD)** as common root cause of addiction
- Describe the hypothesized **mechanisms of change** involved in the use psychedelic assisted therapies for trauma and addiction including neurochemical and psychological pathways
- Describe research study of MDMA Assisted Therapies for **people 6-12 months after childbirth with PTSD and Opioid Use Disorder** including hypothesized effect on maternal infant bonding and attachment
- Potential use of psilocybin and ketamine or other **Psychedelic Assisted Therapy for postpartum depression and birth trauma**

3

Rapidly Changing Landscape Regarding Acceptance of Psychedelic Therapies

- FDA has granted Breakthrough status to MDMA for PTSD and psilocybin for depression
- 2022 NIH Psychedelics as Therapeutics: Gaps, Challenges and Opportunities: NIDA involved and presentations included :
  - -safety and efficacy of MDMA for the treatment of PTSD
  - -Psilocybin and smoking cessation
  - -Ketamine assisted psychotherapy in the treatment of alcohol use disorder and other addictions

4

Increasing Support for psychedelic therapies from NIH, Congress, and Executive Branch

MAY 2022 LETTER: IN RESPONSE TO CONGRESSIONAL INQUIRIES

SAMHSA AGREES THAT TOO MANY AMERICANS ARE SUFFERING FROM MENTAL HEALTH AND SUBSTANCE USE ISSUES, WHICH HAVE BEEN EXACERBATED BY THE ONGOING COVID-19 PANDEMIC, AND THAT WE MUST EXPLORE THE POTENTIAL OF PSYCHEDELIC-ASSISTED THERAPIES TO ADDRESS THIS CRISIS. SAMHSA ALSO AGREES THAT THE USE OF PSYCHEDELIC MEDICINES WILL REQUIRE A BROAD-SPECTRUM INTERDISCIPLINARY STAKEHOLDER APPROACH TO EFFECTIVELY TACKLE THE COMPLEXITY OF ISSUES THAT STAKEHOLDERS ANTICIPATE WILL ARISE WITH THEIR INTRODUCTION.

MIRIAM E. DELPHIN-RITTMON
ASSISTANT SECRETARY FOR MENTAL HEALTH AND SUBSTANCE USE.

5

Acknowledge Indigenous Use and Knowledge

- Psilocybin (from psilocybin mushrooms), mescaline (from peyote cactus) and DMT (from ayahuasca) have been been used for thousands of years by indigenous cultures
- The indigenous knowledge should be recognized and honored
- Concerns include patenting the use of these medicines, culture appropriation of traditional ceremonies, and potential failure to facilitate access for indigenous people if these become FDA approved medicines

6

Why is a Family Physician trained in Addiction Medicine interested in using psychedelic compounds for trauma and addiction?

- I have cared for pregnant and postpartum women as well as their babies for twenty years at UNM and have been Medical Director UNM Milagro Program since 2011
- Milagro Program cares for about 150 women a year with opioid or other substance use disorders in pregnancy and we have about 200 babies a year with Neonatal Opioid Withdrawal Syndrome at UNM
- Model program with integrated prenatal care and substance abuse counseling/medication assisted treatment (MAT) in family medicine clinics including caring for women during delivery and newborns in in a continuity model where women often have physician of their choice at birth
- Prior to the pandemic a high proportion of women in remission for opioid use disorder at time of birth but many eventually resume use

7

Postpartum Resumption of Use

- We "successfully" treated opioid use disorder in pregnancy with medication assisted treatment (buprenorphine and methadone) and counseling however the underlying trauma remained
- High incidence of childhood sexual and physical abuse and other Adverse Childhood Events (ACES)
- Postpartum period is high risk time for relapse and overdose
- Presence of PTSD and postpartum depression are risk factors for relapse

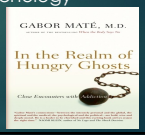
Gopman S. Obstet Gynecol Clin North Am. 2014 Jun;41(2)

8

Links between trauma and addiction

"Not all addictions are rooted in abuse or trauma, but I do believe they can all be traced to painful experience. A hurt is at the centre of all addictive behaviours. It is present in the gambler, the Internet addict, the compulsive shopper and the workaholic. The wound may not be as deep and the ache not as excruciating, and it may even be entirely hidden—but it's there. As we'll see, the effects of early stress or adverse experiences directly shape both the psychology and the neurobiology of addiction in the brain."

Gabor Mate MD
Canadian Family and Addiction Physician
Author of *In the Realm of Hungry Ghosts: Close Encounters with Addiction*



9

ADVERSE CHILDHOOD EXPERIENCES – ACES

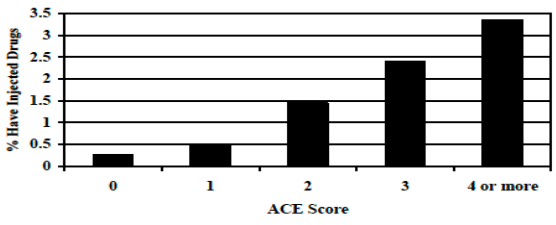
What are Adverse Childhood Experiences (ACEs)?
ACEs are potentially traumatic events that occur in a child's life:

Causing lifelong medical, mental & social suffering

American SPCC
americanspcc.org
The Nation's Voice for Children
*Center for Disease Control

10

ACE Score vs. Injected Drug Use



A male child with an ACE Score of 6, when compared to a male child with an ACE Score of 0, has a 46-fold (4,600%) increase in the likelihood of becoming an injection drug user sometime later in life.

Dube SR, Felitti VJ, et al . Childhood abuse, neglect, and household dysfunction and the risk of illicit drug use: the adverse childhood experiences study. Pediatrics. 2003

11

Mechanisms of Intergenerational Transmission of trauma/substance use

Intrauterine Biological

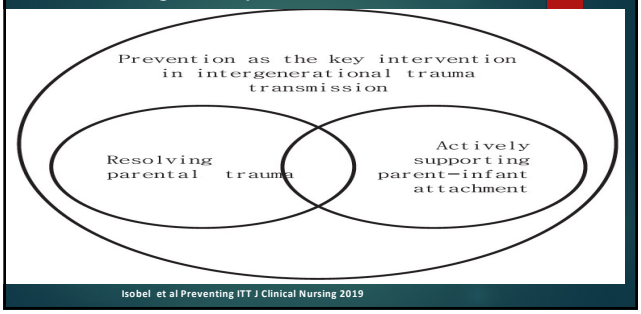
- Disruption of Hypothalamic-Pituitary-Adrenal (HPA) Axis
- Methylation of stress related gene
- Developmental effects on fetus

Parental Trauma

- **Impaired maternal infant bonding/attachment**
- **Maternal PTSD**
- **Maternal substance use disorder**
- Socioeconomic factors associated with illicit substance use

12

Potential Affects of Maternal MDMA Assisted Treatment for Co-occurring PTSD/Opioid Use Disorder



Isobel et al Preventing ITT J Clinical Nursing 2019

13

frontiers | Frontiers in Pharmacology
REVIEW
published: 27 June 2022
doi: 10.3389/fphar.2022.905753

Psychedelic Therapies at the Crossroads of Trauma and Substance Use: Historical Perspectives and Future Directions, Taking a Lead From New Mexico

Snehal R. Bhatt[1], Maya Armstrong[2], Tassy Parker[2,3,4,5,6], Marcello Maviglia[2,5], Rebecca Kass[1], Lawrence Leeman[2], Paul Romo[1] and Douglas Ziedonis[7]*

14

Psychedelic compounds studied for trauma and addiction

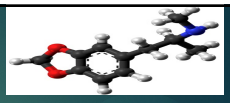
MDMA: PTSD

Classic Psychedelics: Psilocybin is prototype

Ketamine: "Dissociative" used "off label" for Addiction, PTSD, and Depression

15

MDMA



- 3,4-methylenedioxymethamphetamine (*MDMA*): a derivative of amphetamine
- Properties of stimulant and psychedelic but not a "classic" psychedelic
- "Entactogen" or 'empathogen" — a drug that can increase self-awareness and empathy
- Synthesized 1912 and used legally by psychotherapists from 1976 to 1985

16

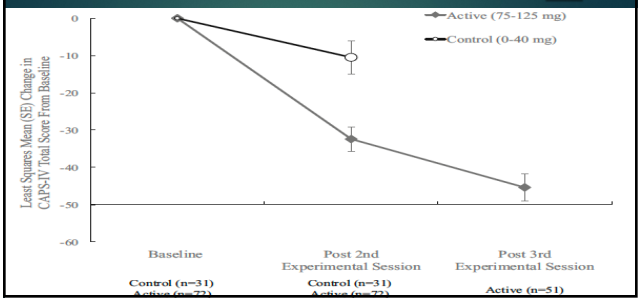
MDMA Assisted Therapy for PTSD

- First PTSD study in 2010.
- Six phase two studies published from 2013 to 2019
- Pooled analysis of six studies of people with moderate to severe PTSD
  - **82% clinically significant symptom improvement** (15 points or more reduction in CAPS-IV total severity scores) with CAPS-IV total severity scores dropping on average – 44.8 points 1-2 months post tx
  - -56% of participants no longer met the criteria for PTSD.
- Long term follow-up (LTFU) at 12 months
- **-Increased to 67% no longer meeting PTSD criteria and 20% had continued improvement from study end to 12-month LTFU**

Jerome et al . Psychopharmacology (Berl). 2020 Aug
Mithoefer MC, et al Psychopharmacology (Berl). 2019 Sep

17

MDMA-AT AND CAPS-IV Total Score From Baseline



18

MDMA Phase Three Studies

- MAPP1 published June 2021 Nature Medicine: RCT of 91 participants US and Canada
- The mean change in CAPS-5 scores in participants completing treatment was −24.4 (s.d. 11.6) I in MDMA group and −13.9 (s.d. 11.5) in placebo group.
- At the primary study endpoint(18 weeks after baseline), **28 of 42 (67%) of the participants in the MDMA group no longer met the diagnostic criteria for PTSD**, compared with 12 of 37 (32%) of those in the placebo group after three sessions.
- MDMA did not induce adverse events of abuse potential, suicidality or QT prolongation.

Mitchell JM, Bogenschutz M, et al. MDMA-assisted therapy for severe PTSD: a randomized, double-blind, placebo-controlled phase 3 study. Nat Med. June 2021

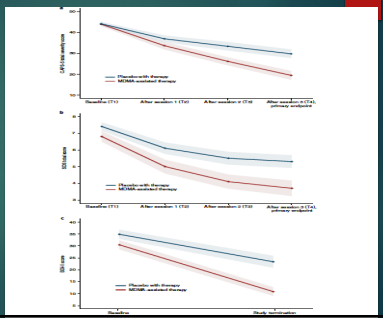
19

Phase 3 2021 Outcomes on multiple scales: Transdiagnostic

CAPS –PTSD

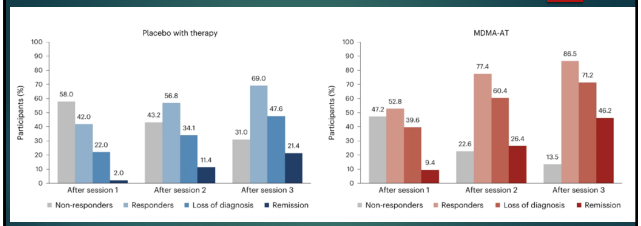
Sheehan Disability Scale

BDI: Depression



20

Phase 3 2023: Treatment and Remission in the MDMA-AT (n=53) and placebo with therapy groups (n=50)



Nat Med **29**, 2473–2480 (2023)

A ≥10-point reduction in CAPS-5 total severity score was considered to be clinically meaningful.
Responders (≥10-point reduction from baseline), loss of diagnosis (≥10-point reduction from baseline and no longer meeting PTSD diagnostic criteria) and remission (loss of diagnosis and CAPS-5 total severity score of 11 or less) were tracked in both groups as a percentage of participants. Non-responders were defined as any CAPS-5 total severity score change <10-point reduction from baseline.

21

22

MDMA Assisted Psychotherapy Sessions

- Two person therapist team usually male and female
- Nondirective; Empathetic Presence and Listening
- Safe environment
- Access patient's "inner healing" ability
- Usually do not need to bring up trauma – it comes up
- Eyeshades
- Common initial dose 125 mg with option of 62.5 supplemental dose 2 hours later
- Blood pressure monitoring before first dose and supplemental dose

23

MDMA Assisted Therapy Manual

- Therapeutic effect is the "interaction between the effects of the medicine, the therapeutic setting and the mindsets of the participant and the therapists"
- MDMA reduced fear allowing staying engaged and not overwhelmed by anxiety and painful emotions while revisiting traumatic experience

24

How does MDMA assisted therapy treat PTSD: Complex Neurochemical and psychological pathways?

- Increase release of serotonin , dopamine, noradrenaline and oxytocin
- Activate 5 –HT1a, and 5-HT1b receptors which decreases anxiety and amygdala related fear response and increases empathy, emotional closeness, and compassion
- Effect on alpha 2 receptor supports psychotherapy by decreasing trauma activation/hypervigilance

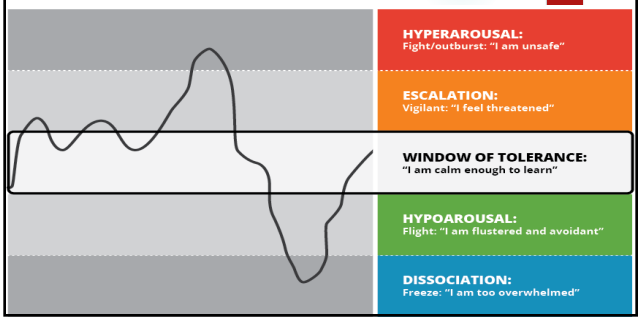
25

How does MDMA assisted therapy treat PTSD: Neurochemical and psychological pathways?

- Oxytocin release hypothesized to promote empathy and "closeness"
- Reducing activation in amygdala and insula (seen on functional MRI) there is less fear and anxiety as memories are processed and the memories can be "reconsolidated"

26

Window of Tolerance



27

Is MDMA Assisted therapy (MAP) for PTSD Cost Effective?

Decision Analysis of MDMA-AT vs standard care for chronic, severe or extreme treatment resistant PTSD

- **COST:** $7,543 per patient who initiated the protocol.
- Therapists' compensation 91.2%.
- Cost of MDMA 4.7%;
- Test kits for pregnancy and urine toxicology 3.7%;
- Nuclear stress tests and carotid ultrasound for patients who require them 0.4%

Marseille E, Kahn JG, Yazar-Klosinski B, Doblin R. The cost-effectiveness of MDMA-assisted psychotherapy for the treatment of chronic, treatment-resistant PTSD. PLoS One. 2020 Oct

28

Might MDMA-AT be useful to treat addictions?

- Can this occur by treating PTSD?
- Potentially by same mechanisms as classic psychedelics such as psilocybin? What are these mechanisms?
- Lets talk briefly about psilocybin and then we will circle back to MDMA

29

Psilocybin and addiction

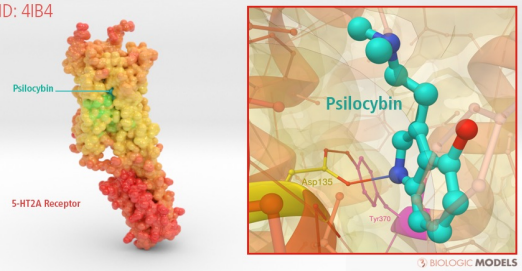
- Active ingredient in psilocybin containing mushrooms
- Metabolized to Psilocin inside human body
- Traditionally used by Mazatecs in Mexico's Sierra Mazateca
- Stimulates *serotonin* 2A *receptors* (5-HT2ARs)
- Addiction: tobacco, alcohol. cocaine and opioids in studies

Maria Sabina
Mazatec Curandera

30

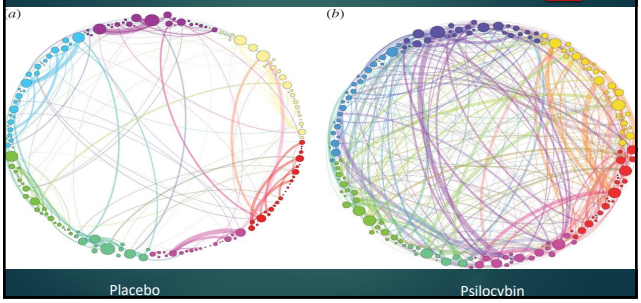
Psilocybin bound to Serotonin (5-HT2A) Receptor

PDB ID: 4IB4



31

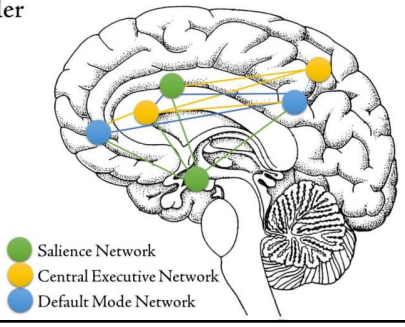
How psilocybin affects brain: increased connectivity



32

Functioning under psychedelics

- Network regions interact more fluidly and flexibly
- Representations of the self become weaker
- The Default Mode Network in particular has been shown to exert less top-down influence over the brain; but other networks may see the same effect



33

Potential Effects of Decreasing Activity in the Default Mode Network (DMN)

Psilocybin and LSD have been shown to decrease blood flow to the DMN which allows for increased connections throughout the brain

- Decrease rumination, obsessive thoughts and focus on autobiographical content that are common in severe depression
- Can explain the effects diminishing anxiety of patients with terminal cancer
- More awareness in the present moment
- Increased connectivity internally between neural networks and externally toward natural environment

34

Psilocybin and tobacco cessation

- 15 PSYCHIATRICALLY HEALTHY NICOTINE-DEPENDENT SMOKERS (AVERAGE AGE 51 YEARS), WITH A AVERAGE OF 6 PREVIOUS LIFETIME QUIT ATTEMPTS, AND SMOKING AVERAGE OF 19 CIGARETTES PER DAY FOR 31 YEARS ON AVERAGE
- OPEN LABEL WITHOUT A CONTROL GROUP. 2-3 MEDIUM TO HIGH DOSE PSILOCYBIN SESSIONS IN CONJUNCTION WITH COGNITIVE BEHAVIORAL THERAPY
- 6 MONTH FOLLOW : 12 OF 15 TO BE HAVE BEEN ABSTINENT FROM TOBACCO FOR AT LEAST 7 DAYS
- 12-MONTH FOLLOW-UP, 10 PARTICIPANTS (67%) WERE BIOLOGICALLY CONFIRMED AS SMOKING ABSTINENT BY URINARY COTININE AND BREATH CARBON MONOXIDE. 13 PARTICIPANTS (86.7%) RATED THEIR PSILOCYBIN EXPERIENCES AMONG THE FIVE MOST PERSONALLY MEANINGFUL AND SPIRITUALLY SIGNIFICANT EXPERIENCES OF THEIR LIVES.

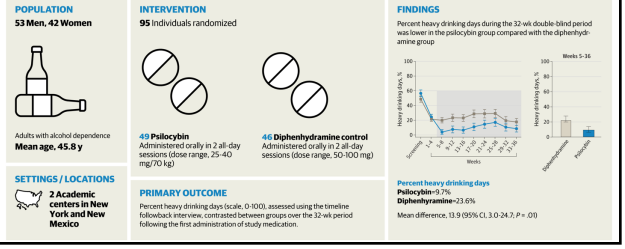
October 2021 NIDA funds three-year Multicenter RCT study of psilocybin for tobacco use disorder @ Hopkins/Alabama/NYU

Johnson MW, J Psychopharmacology. 2014

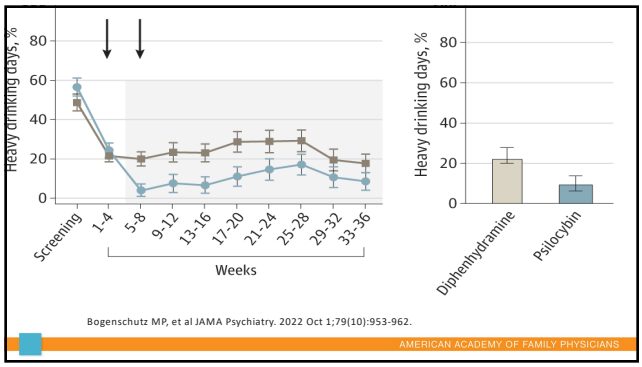
35

JAMA Psychiatry

RCT: Psilocybin-Assisted Treatment of Alcohol Use Disorder



36



Bogenschutz MP, et al JAMA Psychiatry. 2022 Oct 1;79(10):953-962.

AMERICAN ACADEMY OF FAMILY PHYSICIANS

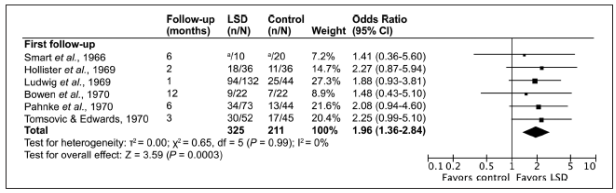
37

Psilocybin and Alcohol Dependence

AMERICAN ACADEMY OF FAMILY PHYSICIANS

38

LSD and alcoholism – Meta-analysis of six randomized controlled trials from 1960-70s



	Follow-up (months)	LSD (n/N)	Control (n/N)	Weight	Odds Ratio (95% CI)
First follow-up					
Smart *et al.*, 1966	6	[a]/10	[a]/20	7.2%	1.41 (0.36-5.60)
Hollister *et al.*, 1969	2	18/36	11/36	14.7%	2.27 (0.87-5.94)
Ludwig *et al.*, 1969	1	94/132	25/44	27.3%	1.88 (0.93-3.81)
Bowen *et al.*, 1970	12	9/22	7/22	8.9%	1.48 (0.43-5.10)
Pahnke *et al.*, 1970	6	34/73	13/44	21.6%	2.08 (0.94-4.60)
Tomsovic & Edwards, 1970	3	30/52	17/45	20.4%	2.25 (0.99-5.10)
Total		**325**	**211**	**100%**	**1.96 (1.36-2.84)**

Test for heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 0.65$, df = 5 ($P = 0.99$); $I^2 = 0\%$
Test for overall effect: $Z = 3.59$ ($P = 0.0003$)

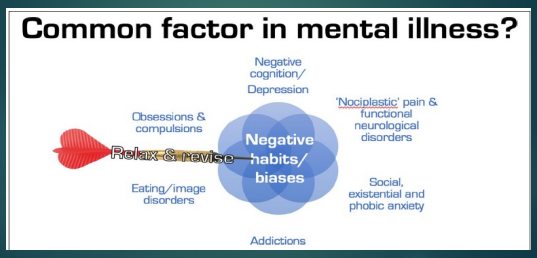
0.1 0.2 0.5 1 2 5 10
Favors control Favors LSD

Figure 2. Improvement on alcohol misuse at the first available follow-up after LSD versus control treatments.
[a]Continuous outcome data.

Krebs TS, Johansen PØ. Lysergic acid diethylamide (LSD) for alcoholism: meta-analysis of randomized controlled trials. J Psychopharmacol. 2012 Jul;26(7):994-1002

39

How can psychedelic assisted therapies treat wide range of illness?



Brouwer A, Carhart-Harris RL. Pivotal mental states. J Psychopharmacol. 2020 Nov

40

Pivotal Mental States

- Leaving a long-standing state of addiction, depression, PTSD, anxiety, or obsession can occur from a transformative experience that produces a pivotal state
- The classic psychedelic acting at the serotonin 5 $HT2_a$ receptor can produce a challenging experience, a mystical state, or other pivotal experience

Brouwer A, Carhart-Harris RL. Pivotal mental states. J Psychopharmacol. 2020 Nov

41

42

Integration of psychedelic assisted therapy

- How does one reach the pivotal state ?
- How does one choose which stream to follow?
- With a poor set and setting or a lack of preparation one can head to down the "wrong stream"
- Not always clear at the point when one is in the middle of the "river"

Brouwer A, Carhart-Harris RL. Pivotal mental states. J Psychopharmacol. 2020 Nov

43

44

Bill Wilson's HALLUCINOGENIC VISION

- In 1933 and 1934, Wilson was hospitalized for his alcoholism four times. After his third admission, he got the "belladonna cure " made from a compound extracted from the berries of the *Atropa belladonna* bush aka "deadly nightshade," an extremely toxic hallucinogenic.
- Wilson had a **vision of a "chain of drunks"** all around the world, helping each other recover. This was foundation of his sobriety, his belief that a spiritual experience is essential to getting sober, and the genesis of Alcoholics Anonymous.

45

Bill Wilson AA Founder and LSD

- In 1956 Bill Wilson took LSD in VA Hospital under medical supervision due to the positive results from studies of LSD and alcoholism
- He was sober at the time but still suffered from lifelong depression
- He felt that LSD could be beneficial for alcoholics; however, this was strongly opposed by AA leadership and in 1958 he resigned from AA leadership over this issue.

Stephen Ross, Director of NYU Langone's Health Psychedelic Medicine Research and Training Program, explains: "[In A.A.] you certainly can't be on morphine or methadone. There's this attitude that all drugs are bad, except you can have as many cigarettes and as much caffeine and as many doughnuts as you want."

46

Psychedelics in Recovery is a fellowship of people in 12-step programs who also have an interest in psychedelics and/or plant medicines as an aid to our recovery

https://www.psychedelicsinrecovery.org/

47

Integration of psychedelic assisted therapy or other psychedelic experiences

- Challenging experiences are not "bad" but may leave us at the bifurcated pivotal states
- Most individuals with a challenging psychedelic experience eventually follow the stream to positive transformation
- In survey of 2000 with adverse psilocybin experience outside of a clinical trial 1/3 reported as one of most challenging life experiences
- Eventually 84% reported long term positive gains

Gorman Psychedelic Harm Reduction and Integration Front. Psychol.15 March 2021
Carbonaro TM,. J Psychopharmacol. 2016

48

UNM –MAPS PBC Investigator Initiated Study of Postpartum Women with PTSD and Opioid Use Disorder

- Open label feasibility study
- Postpartum women 6-12 months after birth
- Women with opioid use disorder on buprenorphine or methadone and diagnosis of moderate or severe PTSD based on CAPS-5
- MAPS PTSD protocol of 12 weeks of psychotherapy including three MDMA medication sessions, preparation and integration

49

UNM –MAPS PBC Investigator Initiated Study of People with PTSD and Opioid Use Disorder 6-12 months after Childbirth: Primary and Secondary Outcomes

- Primary: PTSD based on CAPS-5 total score 4 weeks after the final experimental session
- Secondary: Opioid Use disorder: TLFB comparing the 30 days prior to enrollment to monthly TLFB assessment for 6 months after 3rd MDMA session. Urine drugs screens that are performed monthly for six months after the third experimental session.

50

UNM –MAPS PBC Study of People with PTSD and Opioid Use Disorder 6-12 months after Childbirth: Primary and Secondary Outcomes: Exploratory Outcome of Psychological Processes of Behavioral Change

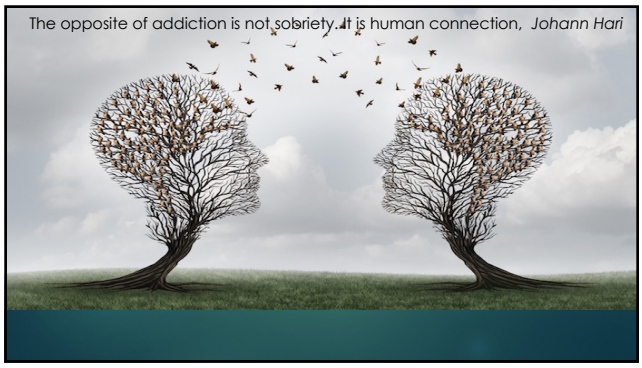
- **Mystical Experience Questionnaire (MEQ)**: used to assess the experimental session with regards to the dimensions of a classical mystical experience
- **Emotional Breakthrough Inventory (EBI):** designed to assess emotional processing associated with the experimental session
- **Challenging Experience Questionnaire (CEQ):** Seven factors associated with the challenging experiences encountered during the experimental session.

51

UNM MAPS PBC Investigator Initiated Study of Postpartum Women with PTSD and Opioid Use Disorder: Exploratory Outcome of "Connectedness"

- **Identification With All Humanity (IWAH):** Assesses a person's subjective experience of connection to society and humanity
- **Social Connectedness Scale (SCS):** Measures the self-perceived emotional distance or connectedness between the self and other people
- **WCS: Watts Connectedness Scale (WCS)** Developed to assess has three subscales (i) ***"connection to self"*** which includes connection to senses, emotions, values and life meaning; (ii) ***"connection to others"*** which includes feeling part of the surrounding environment and empathy for others (iii) ***"connection to world/universe'\"*** which includes connection with nature, the 'bigger picture' and feeling that everything is interconnected.

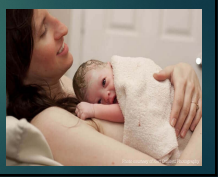
52



53

UNM –MAPS Investigator Initiated Study of People with PTSD and Opioid Use Disorder 6-12 months after Childbirth: Exploratory Outcome of Maternal Infant Bonding /Attachment

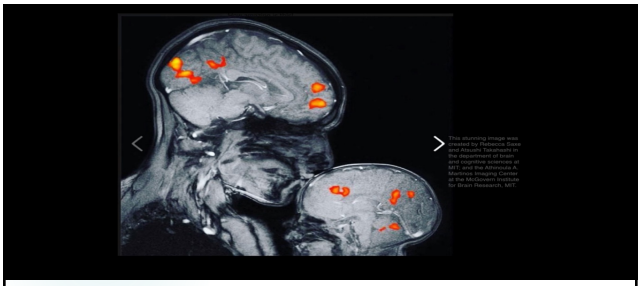
- **Maternal Infant Bonding Scale (MIB)**
- **Parenting Sense of Competence (PSOC)**
- **Qualitative semi-structured interviews**



54

Healthy and secure attachment and bonding are crucial protective factors to mediate the effects of trauma

55



Coregulation as seen by functional MRI

AMERICAN ACADEMY OF FAMILY PHYSICIANS

56

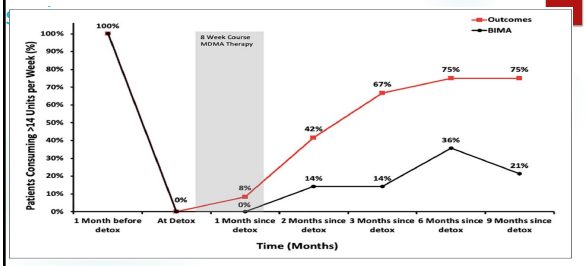
Will MDMA assisted Therapy treat Complex PTSD with early childhood developmental trauma?

- In MDMA PTSD Phase III Study 84.4% (76/90) had histories of developmental trauma, and 87.8% (79/90) had suffered multiple traumas
- In Secondary study led by Bessel A. van der Kolk ("The Body Keeps the Score") benefit was shown in psychological measures of outcomes common to PTSD with developmental origins and associated with poor outcome
  - -Alexithymia : Difficulties recognizing and verbalizing emotions
  - -Self-compassion:
  - -Inventory of Altered Self Capacities (IASC) factors:

van der Kolk BA, Wang JB, Yehuda R,Bedrosian L, Coker AR, Harrison C, et al. (2024) Effects of MDMA-assisted therapy for PTSD on self-experience. PLoS ONE 1

57

Bristol Imperial MDMA in Alcoholism (BIMA)



3,4-methylenedioxymethamphetamine-assisted psychotherapy

AMERICAN ACADEMY OF FAMILY PHYSICIANS

58

Is there a role for Psychedelic Assisted Therapy for postpartum depression, anxiety, and birth trauma?

59

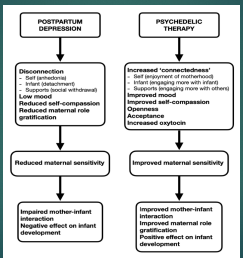
Could psychedelic assisted therapy be used in the postpartum period for treatment of depression, anxiety or PTSD?

- There are no studies supporting this. Our UNM MDMA-AT study is the first looking at women after childbirth
- FDA will not support studies in breastfeeding postpartum women even with prolonged "pump and discard " strategies without lactation studies which are challenging to conduct and expensive
- FDA had concerns about our study using MDMA prior to 6 months however it was a higher risk population based on OUD and PTSD
- Highest incidence of postpartum psychosis as sequelae of PPD is in first 30 days and that is likely barrier to study of psilocybin or other classic psychedelics in first month

Jairaj and Rucker Psychopharmacology 36 (8) 2022

60

Therapeutic rational for use of psychedelic assisted therapy for postpartum depression



Jairaj and Rucker Psychopharmacology 36 (8) 2022

61

Potential Use of Ketamine Assisted Therapy for Postpartum depression or Birth Trauma

62

Proposed Model for Ketamine Assisted Therapy for Postpartum Depression or birth trauma

- Ketamine Assisted Psychotherapy
- Individual vs. group models: Group may improve "connectedness"
- Initial sessions "psycholytic" therapy using lower doses for trauma processing followed higher doses for "psychedelic" therapy

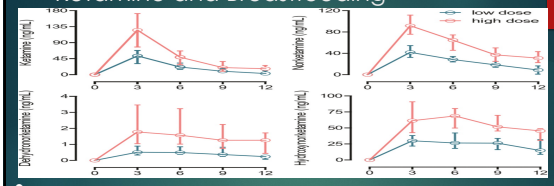
63

Potential Postpartum Uses of Ketamine Assisted Therapy

- **Postpartum Depression**: Works much quicker than SSRI- suicidality may resolve within hours of initial session providing help in critical time for new parent and newborn help as soon possible.
- **Birth Trauma:** Theoretical potential to support trauma processing before trauma pathways are "etched" into body and prevent PTSD- research needed

64

Ketamine and Breastfeeding



- Pharmacokinetic analysis of the presence of ketamine and several of its major metabolites in four women receiving two different intramuscular doses of ketamine – 0.5 mg/kg and 1.0 mg/kg.
- Low and rapidly declining levels of ketamine and metabolites in breast milk during the 12-hour post-dosing period.

Philp Wolfson et al The Pharmacokinetics of Ketamine in the Breast Milk of Lactating Women: Quantification of Ketamine and Metabolites, Journal of Psychoactive Drugs 2022

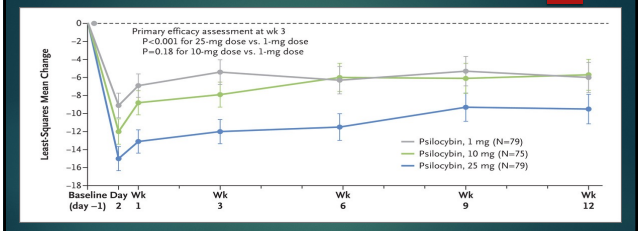
65

Postpartum PTSD/birth trauma

- Can represent continuation of PTSD present before and during pregnancy
- PTSD can develop in the setting of birth trauma and likely highest risk is people with preexisting childhood or other trauma significant trauma
- Once MDMA-AT is approved for PTSD then treatment of postpartum PTSD in non breastfeeding women will be an option
- Treatment of birth trauma with MDMA-AT could potentially need a shorter tine frame of treatment than 12-week therapy with 3 medicine sessions

66

Single-Dose Psilocybin for a Treatment-Resistant Episode of Major Depression

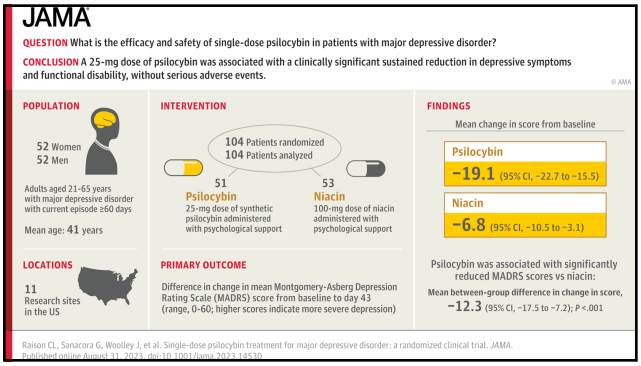


Change from Baseline in MADRS Total Score

Goodwin,NEJM 2022

The NEW ENGLAND JOURNAL of MEDICINE

67



68

Is there potential to use psilocybin for postpartum depression?

- **Mental Health Risk**: Concern regarding postpartum psychosis in this scenario will limit use in the immediate postpartum time (i.e first month)

- **Breastfeeding and Psilocybin**
  - No lactation studies assessing breast milk concentration of psilocin
  - Psilocin has 3 -hour half life and plasma peak is at 105 +/-37 minutes
  - Based on half life by 48 hours all but 0.0016% of psilocin is eliminated from blood stream
  - Psilocin binds to albumin and is acidic both should decease diffusion into breast milk
  - Psilocin has low molecular weight and is more lipid soluble than psilocybin which may increase transfer into breast milk

Jairaj and Rucker Psychopharmacology 2022 36 (8) 2022

69

There are two studies of psychedelic assisted therapy for postpartum depression in development stage using shorter acting compounds

- 5 MeO DMT: 20 minute experience
- 4-OH-DPT: 2 to 3 hour experience

70

Questions and Discussion

For more information on MDMA see Netflix Michael Pollan series episode on MDMA:

71