Pilot study of MDMA-assisted psychotherapy for patients with chronic, treatment-resistant PTSD

November 3, 2018
Whole Human Healing Symposium

Disclosure: The material within this mock slide-set originates from the Multidisciplinary Association for Psychedelic Studies (MAPS) 2011 Final Clinical Study Report for protocol MP-2 (IND 63384) and Oehen P, Traber R, Widmer V, Schnyder U. A randomized, controlled pilot study of MDMA (±3,4-Methylenedioxy-methamphetamine)-assisted psychotherapy for treatment of resistant, chronic Post-Traumatic Stress Disorder (PTSD). *J Psychopharmacology.* 2013;27(1) 40–52. doi:10.1177/0269881112464827.

Background

In the US general population, lifetime prevalence of PTSD ~10%[1] high risk of psychiatric and medical comorbidity and suicidality

Cognitive Behavior Therapy (CBT) standard first-line treatment has limited effect and meets with 20% drop-out rate.[2]

Selective serotonin and norpinepherine re-uptake inhibitors (SSRI and SNRR) show modest effects

Phase 2 study 3,4-methylenedioxymethamphetamine (MDMA)-assisted psychotherapy in patients with treatment-resistant posttraumatic stress disorder (PTSD)

Background

- Early clinical practice before classification as drug of abuse in 1985, MDMA reported to improve PTSD symptoms
- While initial clinical trials established safe use, effectiveness remained unmeasured

Objectives

Primary

To evaluate changes in PTSD symptoms measured using Clinician-Administered PTSD Scale (CAPS) [3]

- At baseline
- At 3 weeks after 2nd experimental session
- At 3 weeks after 3rd experimental session

Objectives
Secondary

- CAPS and Posttraumatic Diagnostic Scale (PDS)[4] self-report measure using varied frequency of time points
- Optional open-label continuation cohort for non-responders (CAPS)
- CAPS and PDS long term follow-up (2, 6, 12 months after the 3rd experimental session

Methods

Population selection

- Adults in stable health who met DSM IV criteria for current PTSD within the past 6 months referred from outpatient clinics and private psychiatrists and psychotherapists.
- Diagnostic cut-off ≥ 50 CAPS score (moderate to severe symptoms) to enroll
- At least 1 unsuccessful prior attempt at treatment (include SSRI, CBT, anxiety management, etc.)
- Participants with psychotic, bipolar-affective, dissociative identity, severe eating, or substance abuse disorders or who would present serious risk for suicide were excluded

Method
Participant characteristics

Characteristic		Full-dose group	Placebo group
		n = 8	*n* = 4
Gender	Female	7 (87%)	3 (75%)
	Male	1 (12%)	1 (25%)
Mean age (SD)	Range 23–67 yrs	42.1 (12.8)	40.0 (6.2)
Country of origin	Study completers	CH: 7, F: 1	CH: 4
	Drop-outs	TR: 1	ZA: 1
Marital status	Single	3 (37%)	2 (50%)
	Married/living with partner	2 (25%)	2 (50%)
	Divorced/separated	3 (37%)	0 (0%)
Work status	On disability	4 (50%)	1 (25%)
	Fit for limited employment	2 (25%)	1 (25%)
	Working full-time	1 (13%)	2 (50%)
	Retired	1 (13%)	0 (0%)

Methods
Study design

Single-center, active placebo-controlled, double-blind, partial crossover study

Randomization weighted toward full-dose (2:1) to better assess safety and to enhance recruitment efforts.

- *Full dose:* 125 mg MDMA followed by supplemental half-dose (62.5 mg) administered 2 to 2.5 hours later
- *Active placebo:* 25 mg followed by supplemental half-dose (12.5 mg) MDMA 2 to 2.5 hours later

Methods
Study design

Stage 1 (double-blind)

- Full-dose and cohorts have 3 experimental sessions (3-5 weeks apart with weekly non-drug session in intervening weeks)
- Symptoms assessed once prior to experimental sessions, then 3 weeks after the second and third experimental sessions
- Follow-up at 2, 6, and 12 months

Stage 2 (open-label)

Optional enrollment for Stage 1 active-placebo cohort to use full-dose MDMA with the same schedule as Stage 1

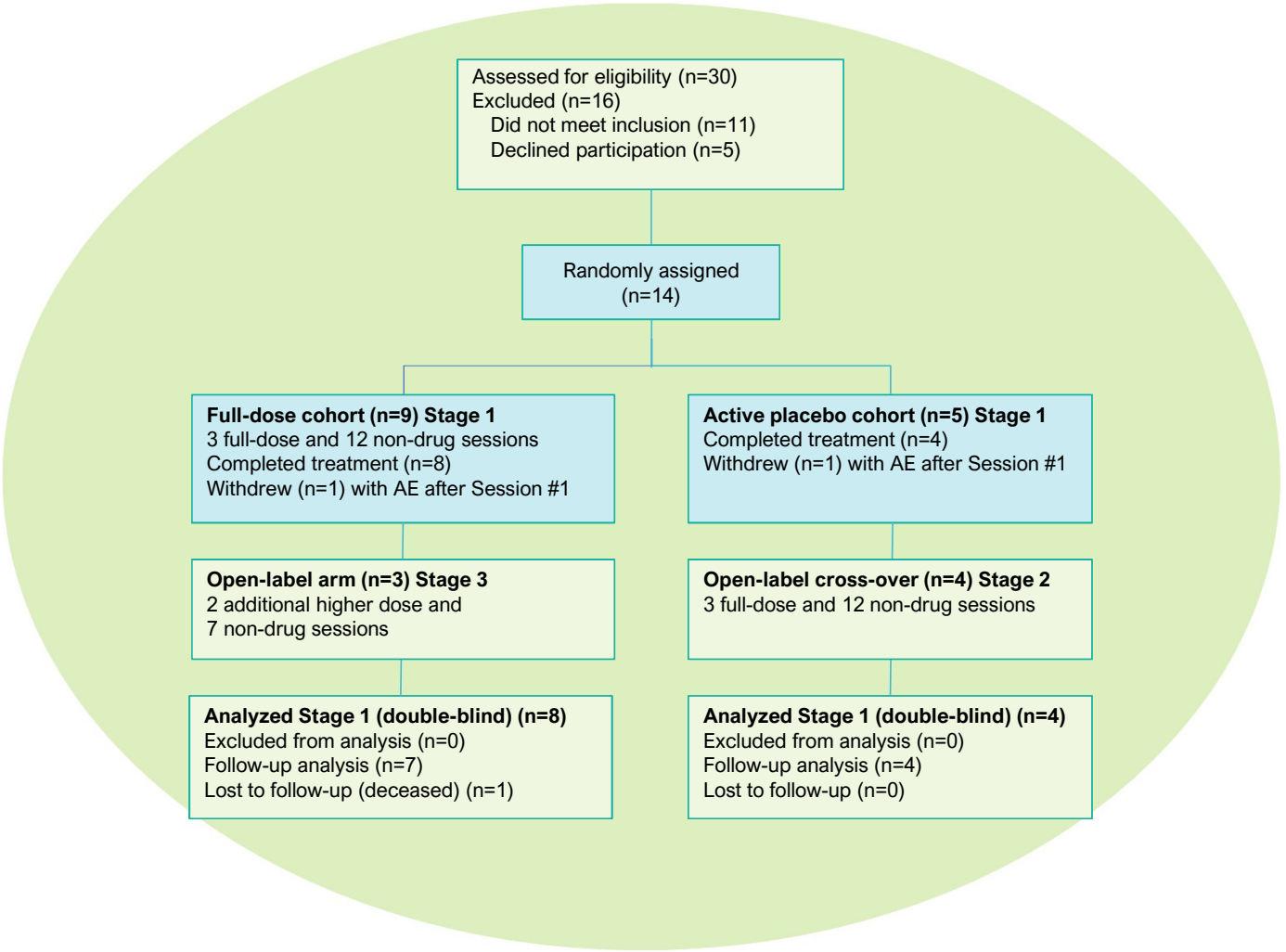
Stage 3 (open-label)

For a limited time for full-dose MDMA to increase dose (150 mg and 75 mg dose 2.5 hour later)

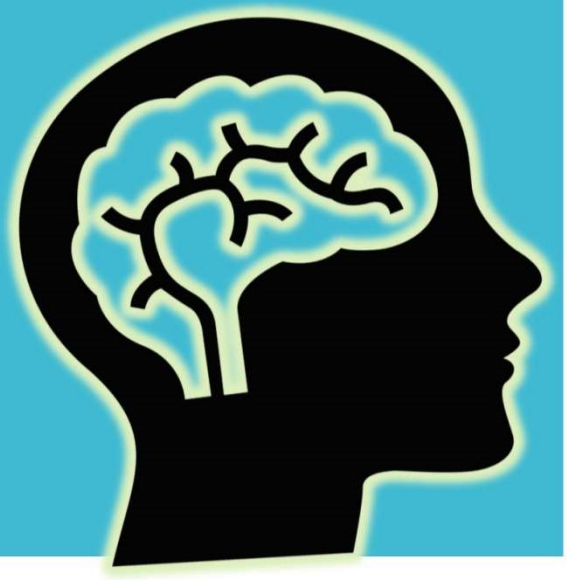
Methods
Safety assessments

- Blood pressure (BP), pulse, and temperature every 30 min at 4 hrs & hourly after up to 8 hrs, or as needed.
- Lab values after completion of each treatment
- AEs collected throughout study & spontaneously reported for 8 days after each experimental session
- Psychological distress during experimental sessions every 60 min to 90 min using Subjective Units of Distress scale

Results
Patient disposition



Results
Efficacy



- For full-dose MDMA participants 23.5% improvement in average CAPS score, a distinct decrease but narrowly missed significance (p=0.066) (5.2% for active placebo cohort)
- CAPS Change Score (standard deviation)
  T0-T1: placebo -3.3 (9.9), full-dose -3.4 (12.0)
  T1-T2: placebo 6.5 (10.3), full-dose -12.2 (8.1)
  T0-T2: placebo -3.2 (15.3), full-dose -15.6 (18.1)
- Efficacy of 3 experimental sessions was greater than the efficacy of 2 sessions

Results
Safety

Most common spontaneously reported reactions (transient):

- *Full-dose:* Insomnia (125 mg: 43%; 150 mg: 50%), loss of appetite, and restlessness with 2 severe anxiety-related AEs
- *Placebo:* Headache, moderate insomnia (31%) and loss of appetite

- No drug-related SAEs (1 death due to brain metastasis)
- Five full-dose participants had systolic BP > 160 mm/Hg
- Two full-dose participants had diastolic BP >110 mm/Hg

Discussion

- Administering full-dose or active placebo to patients with chronic PTSD did not produce deleterious effects and appears to have acceptable safety.
- For full-dose cohort, CAPS dropped to 50.7 ±19.7 on average, a 15.6 point decrease (15 point decrease used in other studies and cited in CAPS Interviewer's Guide as evidence of clinical drug response)

Conclusions

Small pilot study suggests clinically of MDMA-assisted psychotherapy for treatment-resistant PTSD meaningful results warrant larger efficacy studies

Crossover response rate was twice (100%) that for Stage 1 full-dose cohort (50%). Attributed to the establishment of therapeutic relationship prior to MDMA administration. Future studies should increase preparatory non-drug sessions before experimental sessions begin.

References

1 Ozer EJ, Best SR, Lipsey TL, Weiss DS. *Predictors of posttraumatic stress disorder and symptoms in adults: a meta-analysis*. Ann Meet Int Soc Traumatic Stress Studies: 14 Nov 1998, Wash DC, US.

2 Foa EB, Keane TM, Friedman MJ, et al. (2009) *Effective Treatments for PTSD, Practice Guidelines From the International Society for Traumatic Stress Studies*. New York: Guilford Press.

3 Weathers FW, Keane TM, Davidson JR. Clinician-administered PTSD scale: review of the first 10 years of research. Depress Anxiety. 2001;13(3):132–56

4 Foa EB, et al. The validation of a self-report measure of posttraumatic stress disorder: The Posttraumatic Diagnostic Scale. *Psych Assess*.1997;9:445–451.

Questions / Comments?

vivid@lizkuney.com