Psychedelic Science and Neurodiversity:

Twelve Autistic Adults Treated in MDMA-Assisted Therapy for Social Anxiety Trial

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By the time this update is published, investigators will have completed the blinded treatment phase of the first pilot study of MDMA-assisted therapy for social anxiety in autistic adults, sponsored by the Multidisciplinary Association for Psychedelic Studies (MAPS). We enrolled and treated 12 participants, with 11 completing all treatments per the study protocol (one participant had to drop out after the first treatment session for a reason unrelated to safety). The last subject treated will remain in follow-up until April 2017, and might be eligible for two open-label MDMA-assisted therapy sessions a month apart if we learn that they received placebo. Currently, the investigators—Charles Grob, M.D. and I—are still blinded to the results from the primary outcome measure, the Liebowitz Social Anxiety Scale (LSAS). We are looking forward to sharing our findings at the Psychedelic Science 2017 conference in Oakland, Calif., this April.

RECRUITMENT DELAYS

If you have been following our periodic progress updates in the MAPS Email Newsletter, you might be wondering why the study took longer than expected. As has been the case with nearly all clinical trials of psychedelic-assisted therapies so far, we encountered challenges with recruitment. Although inquiries have continued to come in from across the country at a steady pace, finding individuals who meet all of the study requirements proved difficult throughout the spring and summer of 2016.

Several key factors contributed to our enrollment challenges. First, with safety as our top priority, MAPS and the investigators set a high bar for screening, with strict inclusion and exclusion criteria. Anxiety and depression are common in autistic adults, so many potential participants were ruled out when we could not advise tapering off their standard psychiatric medications.

Another obstacle to enrollment was making initial contact with the individuals we wanted to reach. Our population—adults on the autism spectrum who have completed two years of college or the equivalent—does not qualify for services available to students and younger adults, and typically has lower levels of disability than would be required for them to access the scarce public services available for adults. They also often do not have the resources to afford private services. As a result, we could not rely on local clinicians, service providers, or regional centers for leads. Many of the adults we sought for the trial were also often unemployed, living in social isolation and less likely to receive information about the study from others. MAPS generated consistent leads through their monthly newsletter and social media, but the majority of inquiries came from outside of the Los Angeles area, or from individuals who had prior experience using MDMA, did not want to stop using medical cannabis to treat their anxiety, or did not have adequate resources (such as reliable transportation) to meet the study requirements.

DEMONSTRATED SAFETY AND FEASIBILITY

Despite the recruitment delays, this study met its primary goal, demonstrating both safety and feasibility. We established feasibility by successfully treating 12 individuals, and the safety data have been encouraging thus far and support future studies of MDMA-assisted therapy. MAPS, as the sponsor for this pilot study, completed an interim analysis for safety at the halfway point, finding no evidence of harm to participants.

There have also been no serious adverse events reported for the duration of the study.

Because we were working with a population with a high incidence of sensory hyperarousal and atypical responses to psychoactive medications, we structured the protocol as a dose-finding study as an extra measure of caution. By using a dose range of 75-125mg MDMA, we wanted to minimize the risk of overstimulation while still providing potentially therapeutic doses. All participants tolerated the lower doses well, and opted to escalate to higher doses for their second session.

POST-SESSION LOW MOOD REPORTED INFREQUENTLY

One question that comes up frequently about clinical MDMA-assisted therapy research is whether participants experience low mood after treatment. We anticipated reports of what is commonly referred to in non-clinical settings as the "blue Mondays" or the "crash" after taking "Ecstasy" or "molly" (which often contain no MDMA at all and cannot be pharmacologically compared with pure MDMA). Therefore, daily phone calls for seven days post-treatment were included in the protocol. Mood and general wellbeing were monitored closely, and all spontaneously reported reactions were recorded and rated as either mild, moderate, or severe. Although some participants processed challenging emotions during the treatment, no participants reported severe low mood during treatment sessions or during the seven-day period following treatment with either placebo or MDMA. Moderate and mild low mood reactions were reported infrequently and resolved quickly (see chart).

CREATING AN AUTISM-FRIENDLY SETTING

Working with neurodivergent individuals on the autism spectrum made it necessary for us to create an autism-friendly treatment space that would be flexible enough to support a wide variety of sensory preferences and sensory integration challenges. Below are a few setting tips for future research teams:

- Spend time in the treatment room at different times of day, and evaluate the setting based on how it affects each of the five senses. Also, when working with autistic individuals, remember that attention to proprioception is important, so having items such as bolsters or weighted blankets might be indicated.
- Pay careful attention to lighting. If possible, avoid fluorescent lights and add elements of soft, diffused light instead. Be extra aware of how to control natural light coming in through window blinds at different times of the day.
- Go above and beyond ordinary measures to minimize noise. For some populations, even the soft whirring of a fan can be a distraction or uncomfortable. Be aware of the potential impact of intermittent external sounds such as heating and air-conditioning equipment, plumbing, and traffic. We had to prepare our participants in advance for the possibility of medevac helicopters landing at the nearby emergency room.

	Treatment Day	Post Day 1	Post Day 2	Post Day 3	Post Day 4	Post Day 5	Post Day 6	Post Day 7
* Subjects Reporting Mild Intensity Low Mood								
Session 1 (n=12)			3					
Session 2 (n=11)	1		1				1	
* Subjects Reporting Moderate Intensity Low Mood								
Session 1 (n=12)	1		2		1		1	1
Session 2 (n=11)								

** Includes combined reports for blinded placebo and MDMA sessions*

During treatment sessions, study participants are invited to explore a variety of ways to express emotions. Pulling cards from the Mixed Emotions™ therapy cards deck can be effective when putting words to feelings is difficult.

- Select a location with a private restroom adjacent to the treatment room. Socially anxious individuals often appreciate the option of stepping into the temporary seclusion of a restroom to regain composure. In other MAPS-sponsored studies, 27% of participants who receive 100-125mg MDMA in clinical settings have reported nausea. Only one subject reported momentary, mild nausea in this study, but we were glad that a restroom was a few steps away just in case.
- Design the treatment room with an adjustable furniture configuration with extra room for stretching and movement. Facilitators should be able to easily adjust their sitting distance from the participants as needed.
- The focus of autism services has been on children for so long that adults often encounter spaces that resemble pediatrician offices when seeking professional support. We received feedback that our study participants appreciated a space designed for adults.
- If your budget allows, invest in a motorized, overstuffed recliner chair that the participant can control. This simple element can go a long way toward reinforcing the participant's sense of agency in the process, as well as their comfort.
- Many autistic individuals use repetitive motions or stimming to self-soothe. One of our participants recommended a website (stimtastic.co) that provides a wide assortment of stim toys and fidget objects that can also be an effective way to address the stimulating effects of MDMA.
- If providing meals or snacks, always confirm food and beverage preferences in advance. Be prepared to inquire in more detail than usual about likes and dislikes.
- Using elements of nature as the primary decorating theme was universally well-received from our neuro-, gender-, age-, ethnically, and spiritually diverse participant group. Relying on design elements from nature also helped to minimize potential expectancy bias that may result from the presence of images and objects from specific cultural and religious traditions.
- Autistic adults frequently require additional time to compose spoken statements and appreciate alternative methods for communication. Be prepared to expand the time required for office visits to accommodate a slower than typical pace of verbal as well as non-verbal conversation, when appropriate.

An analysis of how to establish and maintain elements in support of an effective set for facilitators and study participants will be addressed in future publications.

NEXT STEPS

Based on subjective reports during treatment and at six-month follow-up visits, as well as initial preliminary analysis of secondary measures, we anticipate that outcomes from the final data analysis will support larger, future studies of MDMA-assisted therapy for social anxiety. One of the most challenging aspects of the screening process was hearing so many reports from autistic adults who had already endured years of misdiagnosis and treatments with multiple, costly pharmaceutical interventions which were either minimally effective or not effective at all. Due to the scarcity of proven effective drug or non-drug treatment options for social anxiety, our hope is that future research teams will be inspired to explore the potential of MDMA-assisted therapy to reduce the fear and avoidance of social opportunities which can improve our quality of life as human beings.

Alicia Danforth, Ph.D., *is the co-investigator for a current MAPS-sponsored phase 2 pilot study looking at the effect of MDMA-assisted therapy on social anxiety in autistic adults. She began her work in clinical research with psychedelic medicines with Dr. Charles Grob at the Los Angeles Biomedical Research Institute, Harbor-UCLA Medical Center in 2004. In 2013, Danforth graduated from the Institute of Transpersonal Psychology (ITP) with a Ph.D. in clinical psychology, with a specialization in Transpersonal Research and Education.*