Psychedelic-Assisted Therapies for Autistic Adults

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Disclosures

I have the following relevant financial relationships with commercial interests to disclose:

• Employment:
  • Clinical Psychologist and Researcher at The Lundquist Institute (a 501(c)3 independent non-profit biomedical research institution at the Harbor-UCLA Medical Center)
  • Clinical Psychologist providing psychotherapy and psychological services for autistic adults in specialty private practice

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Disclaimer: None of my slides and/or handouts contains any advertising, trade names or product-group messages. Any treatment recommendations I make will be based on clinical evidence or guidelines.
Expanding Treatment Options

Conventional Psychopharmacology:
• Drug administered on daily basis for weeks/months/years
• Ameliorate a presumed “core deficit”/pathological brain state
• Relief not dependent on patient's attitude or insight

Psychedelic Psychopharmacology:
• Drug administered once or several times
• Loosens defenses
• Facilitates insight
• Carefully monitored
• Supportive psychotherapy

AND
Neurodiversity and Disability

“Neurodiversity describes the idea that people experience and interact with the world around them in many different ways; there is no one ‘right’ way of thinking, learning, and behaving, and differences are not viewed as deficits.”

Source: Harvard Health Publishing, Harvard Medical School

https://www.health.harvard.edu/blog/what-is-neurodiversity-202111232645
Neurodiversity and Disability

“Ableism is a set of beliefs or practices that devalue and discriminate against people with physical, intellectual, or psychiatric disabilities and often rests on the assumption that disabled people need to be ‘fixed’ in one form or the other.”

Source: Center for Disability Rights
Disability in Autism

<table>
<thead>
<tr>
<th>Levels of Disability in Autism</th>
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<tbody>
<tr>
<td>Level 3</td>
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<tr>
<td>&quot;Requiring very substantial support&quot;</td>
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<td>Level 2</td>
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<td>&quot;Requiring substantial support&quot;</td>
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<td>Level 1</td>
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<td>&quot;Requiring support&quot;</td>
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Neurodiversity and Disability

Examples of neurodiversity-affirming approaches in clinical research:

- Community-based Participatory Research
- Settings with reasonable accommodations
- Avoid ableist language (Bottema-Beutel, et al., 2021)
- Reduce harmful messages in literature/media
Therapeutic Processes in Psychedelic Therapy

- Re-evaluating relationships (e.g., grief, forgiveness, missed opportunities)
- Profound attachment experiences
- Recovered memories
- Emotional catharsis
- Conviction of insight
Why Autistic Adults?

- Very high risk of mental health problems (Lai et al., 2019)
- Heightened risk of suicide (Hedley and Uljarević, 2018)
- Autism not always readily apparent
- Struggle with social adaptability
- Expectation to understand social norms
- Start with individuals who can consent to treatment
Why Autistic Adults?

- Conventional pharmacotherapy often ineffective (Meyers, 2007)
- Gaps in psychotherapist education and expertise (Lipinski, et al., 2022)
- Qualitative data support experimental studies (Danforth, 2019)
Why Autistic Adults?

Need for more pre-clinical and basic research:

• Atypical inhibitory response
  • (e.g., Oblak, Gibbs, & Blatt, 2011)
• Atypical oxytocin utilization
  • (e.g., Lerer, et al., 2008)
• Atypical serotonergic transmission
  • (e.g., Devlin, et al., 2005)
MDMA-Assisted Therapy for Social Anxiety in Autistic Adults Pilot Study

Objectives:

- Randomized, double-blinded, placebo-controlled Phase 2a exploratory pilot study (Danforth, et al., 2018)
- N = 12
- Assess feasibility and safety of MDMA-assisted therapy in clinical setting
- Estimate placebo-subtracted effect size

Sponsor: Multidisciplinary Association for Psychedelic Studies (MAPS) 2014-2018
MDMA-Assisted Therapy for Social Anxiety in Autistic Adults

- 2 Double-blinded medication sessions (MDMA or inactive placebo)
- 2:1 random allocation favoring MDMA
- Dose-finding study
  - Grp 1: \(75\) mg and \(100\) mg
  - Grp 2: \(100\) mg and \(125\) mg
  - Optional open-label after placebo: \(75\) mg and \(125\) mg (n=4)
- Primary Outcome Measure = Liebowitz Social Anxiety Scale
Participants

• Moderate to severe social anxiety
• Autism Spectrum
  • Independent Assessor (ADOS-2 module 4)
• Age 21+ [enrolled mean,(SD): 31.3 (8.8)]
• MDMA-naïve
• 2 yrs college or comparable
• Speaking
Set & Setting: Reasonable Accommodations

**Autism-friendly Setting:**
- Minimal noise
- Soft lighting and colors
- Elements of nature
- Private, all-genders restroom nearby
- Room for movement
- Study Support Partner (consented)
- **Adult** space/decor
- Private/Calm
- Soft, automatic recliner (sense of control)
- Stim objects
Set & Setting: Reasonable Accommodations
Method

- Preparatory psychotherapy
- Follow-up evaluation and integration
- 6-month follow-up
- Placebo group (n=4): optional open-label MDMA
- Hourly BP, HR, and temp
Preparatory Psychotherapy

• Dialectical Behavioral Therapy (DBT)-based (Linehan, 1993)
• Core mindfulness skills module
• Later feasibility studies of DBT for autistic adults (e.g., Ritschel, Guy, & Maddox, 2022)
• Individualized instead of group
• Vocabulary for sharing ineffable states of mind
• Somatic awareness (5 senses + proprioception)
Drug Treatment Sessions

- Two full-day treatment sessions
- 4 – 6 weeks apart
- Female/Male therapist dyad
- Music/Eyeshades model (inward)
- Social interaction (outward)
- Video assessment of social inference
Integrative Psychotherapy

- 7 daily phone calls post-treatment
- 3 office visits (processing/reflection)
- Journaling (optional)
- Multisensory Memory aids
  - e.g., CD of session music; art; transitional object, taste/smell foods
  - Reinforce state-dependent memories
Q: “If you don't mind me asking, what was the procedure like, and would it [be] replicable in a non-clinical setting?”
A: “Replicated outside of clinic... Hard for me to tell. Therapist was most helpful as an integrator/facilitator, and just to have a nice person with me while I did it. Doing it alone would likely resulted in markedly less positive impact. The MDMA was very much just an aid to the general process of therapy. Yes, without a therapist I'd still have felt good, pleasant, calm... But I'd have no one to go to help me integrate, make sense of, construct a narrative, etc. afterwards.”
Safety Data

• Study drug tolerated well:
  • No Serious Adverse Events (SAEs)
  • All subjects able to escalate dose
  • No evidence of harm
Primary Outcome Measure

- Liebowitz Social Anxiety Scale (LSAS)
- Single, blinded independent rater
- Clinician-Administered at:
  - Baseline
  - Post Session 1
  - Post Session 2
  - Primary Endpoint
  - 6-month follow-up
Liebowitz Social Anxiety Scale (LSAS)
(by treatment group - N=12 with data)

- Cohen’s D Placebo-subtracted effect size at Primary Endpoint: $d=1.4$
- Values expressed as mean LSAS Total Scores (+/- SD)
- Cut-off for study entry was 60
- Reductions were significant at End of Treatment based on Mean change from Baseline to End of Treatment via independent-samples t-test ($P = 0.037$)
- Significant reductions maintained at blinded 6-Month Follow-up ($P = 0.036$)
Classic Psychedelics and Autism

- Anecdotal accounts, social media, podcasts
- Peer-support communities
- Early research with minors:
  - Late 1950s – Early 1970s
  - Flawed methodology by today’s standards
  - Did not restore speech
  - No indication altered course of autism
  - No data re long-term outcomes
- New research proposed/recruiting
Regarding new research with minors

• Autism highly heritable (Bai et al., 2019; Yasuda et al., 2023)
• No data from early studies with LSD, psilocybin, UML in minors suggested change in course of autism (Danforth, 2019)
• Lack of informed consent/assent
• History of iatrogenic interventions for autism
• Developmentally inappropriate?
• Higher risk of incoherent or late-emerging sense of agency (SoA)
• Recommendations:
  • Skills-based pre-work in childhood and early adolescence
  • Supportive work with parents
Future Directions

• Improve screening for likely non-responders
• Train autism-informed clinicians
• Fund neurodiversity-affirming settings
• Safety and feasibility protocols for non-speaking participants
• Strengthen ethical standards and guardrails
References


