SAFETY, PHARMACOKINETICS, AND PHARMACODYNAMICS OF MSD-001 AFTER SINGLE DOSING IN HEALTHY ADULTS: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY

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1. Background

Recent clinical trials have shown that psychedelics such as psilocybin, LSD and DMT have therapeutic potential for mental health disorders. However, their subjective effects may limit suitability for some patients.

MSD-001 (5-MeO-MiPT) is an oral 5-HT_{1A}, 5-HT_{2A}, 5-HT_{2C}, 5-HT_{6}, and 5-HT_{2B} receptor agonist selected to produce mild psychoactive effects without strongly disorienting effects.

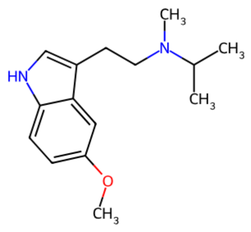


Figure 1. MSD-001

2. Methods

In study, healthy participants received MSD-001 to assess safety, tolerability, pharmacokinetics (PK), and pharmacodynamics (PD).

- **Part 1** (N=40) included CYP2D6 Intermediate and Extensive Metabolizers (IM/EM; gene activity score 1-2.5), and was randomized, placebo-controlled, and double-blind.
- **Part 2** (N=7) included CYP2D6 Poor Metabolizers (PMs), was open-label.

Figure 2. Study Cohorts

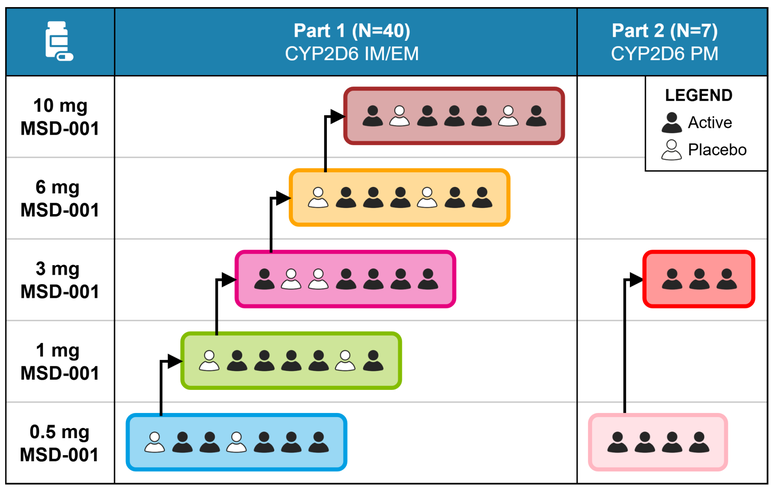


Figure 3. Study periods

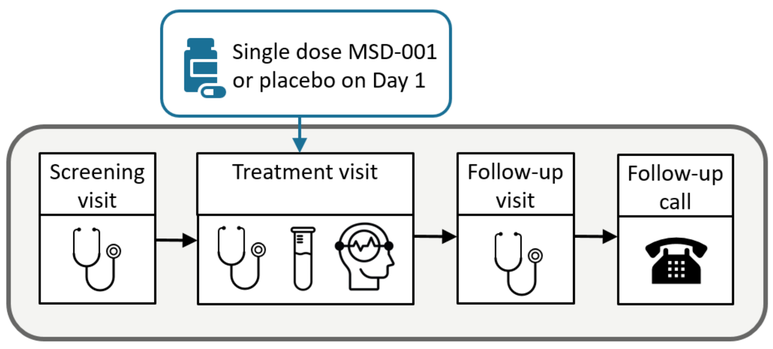


Figure 4. Assessments

Safety
ECG and vital signs, laboratory assessments, and psychiatric and physical examinations, up to 48 hours post-dose.

PK
Urine and plasma PK sampling

PD
Resting-state EEG (rs-EEG)

NeuroCart test battery
- Saccadic Peak Velocity (alertness)
- Adaptive tracking (oculomotor)
- Body sway (postural stability)
- Smooth Pursuit (attention)

Subjective effect measures:
- Real-Time Intensity scores
- 5D-ASC questionnaire.

3. Results

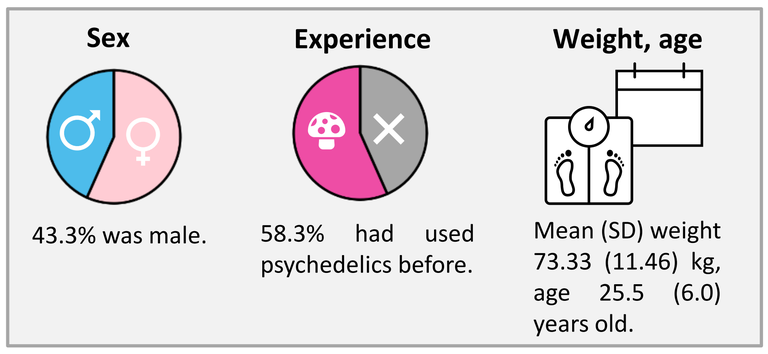
3.1. Safety

MSD-001 was safe and generally well-tolerated. No serious adverse events (SAEs) were reported, and most (98%) AEs were of mild intensity. The AEs reported in the highest proportion of participants dosed with MSD-001 were:

- Sensory processing disorder (e.g., visual effects; 49%)
- Feeling of relaxation (35%)
- Euphoric mood (32%)

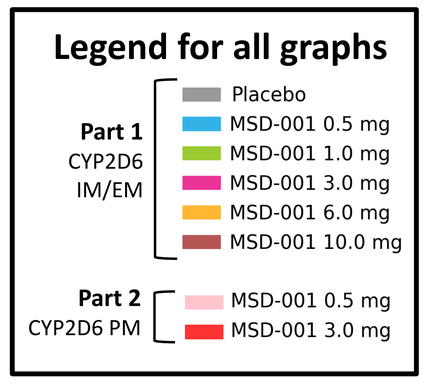
No clinically meaningful cardiovascular, laboratory, physical, or psychiatric abnormalities were observed.

Figure 5. Demographics



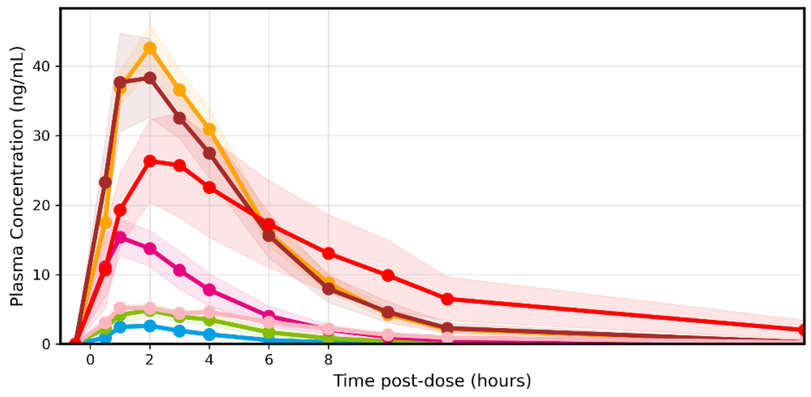
3.2. PK

In **Part 1** (CYP2D6 IM/EMs), MSD-001 was rapidly absorbed (median T_{max} 1–2 h; median t½ ~2–3 h) with dose-related exposure, except for a plateau between 6-10 mg MSD-001.



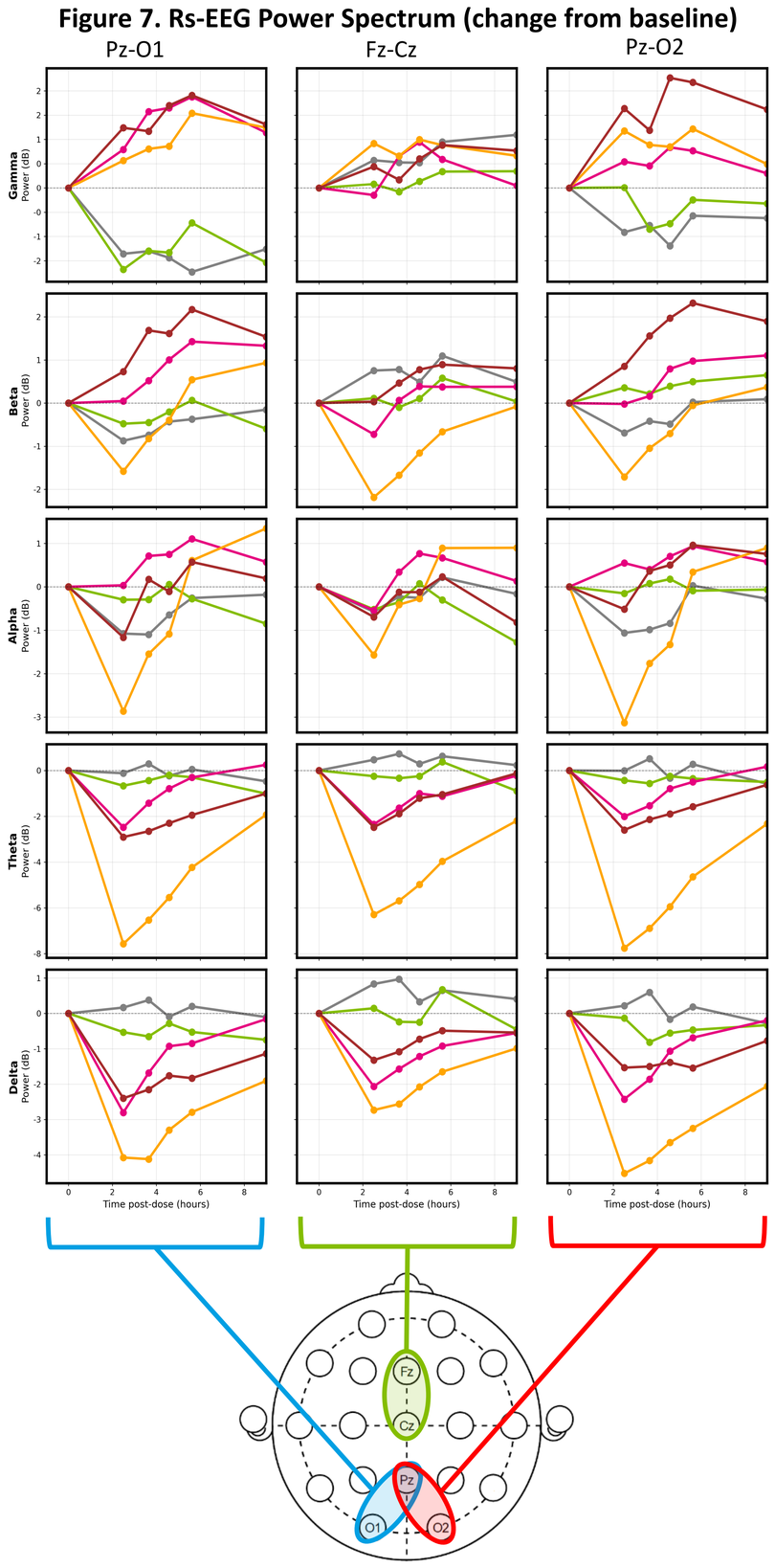
In **Part 2** (CYP2D6 PMs), median C_{max} increased ~1.6–1.8-fold and t½ ~2-fold relative to IM/EMs.

Figure 6. MSD-001 Plasma Concentration



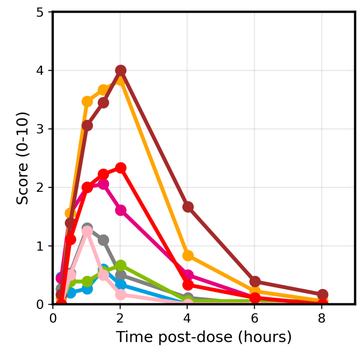
3.3. PD

Figure 7. Rs-EEG Power Spectrum (change from baseline)



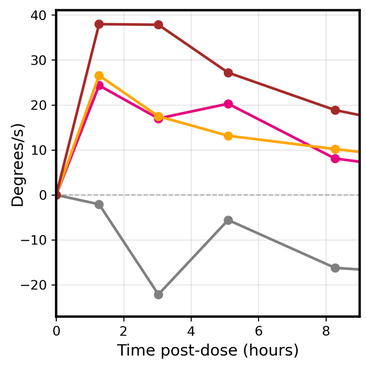
MSD-001 produced eyes-closed resting state EEG changes across frontal (Fz–Cz) and parietal–occipital (Pz–O1, Pz–O2) channels, most pronounced at 6 and 10 mg.

Figure 8. Total Intensity (change from baseline)



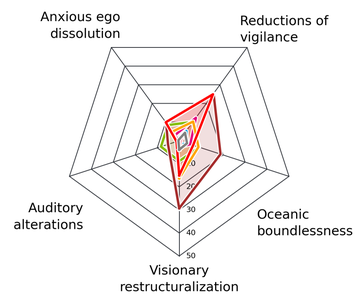
The total intensity score of the Real-Time Intensity scale increased in an exposure-related manner, showing a temporal pattern that closely matched MSD-001 plasma concentration.

Figure 9. Saccadic Peak Velocity (change from baseline)



This test was only performed in Part 1 at doses ≥3 mg. MSD-001 demonstrated an increase in saccadic peak velocity, suggesting heightened arousal. No effects were seen on other parameters, indicating a lack of attention- or psychomotor impairment.

Figure 10. 5D-ASC Questionnaire



Exposure-related increases in 5D-ASC outcomes were observed at doses of ≥3 mg, most prominently in *Reductions of Vigilance* and *Visionary Restructuralization.* No effect was observed for *Anxious Ego Dissolution* and *Auditory Alterations.*

4. Conclusion

This first-in human study demonstrates single oral doses of MSD 001 up to 10 mg in healthy participants to be safe and generally well tolerated. The impact of CYP2D6 activity on its PK profile suggests the potential need for genotype-informed dosing in future clinical trials. MSD-001 elicited mild alterations in subjective experience with no concomitant changes observed for attentional or psychomotor impairment.

Based on these findings, a dose range of 6–10 mg is supported for future clinical investigations of MSD-001.