Evaluating the Correlation Between the Efficacy of MM120 (Lysergide) in Generalized Anxiety Disorder and Self-Reported Mystical Experience

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Abstract Introduction: The administration of classic psychedelic drugs has been associated with improvements in overall mental health and psychological disorders such as major depressive disorder (MDD) and generalized anxiety disorder (GAD). In some individuals, these compounds cause transient subjective effects that include qualities described as “mystical.” It has been hypothesized that such experiences have a causal role in producing therapeutic benefits. Some research suggests that these transient subjective effects are related to neurobiological, cognitive, and affective processes involved in recalling, engaging with, and making meaning of the psychedelic experience and might play a critical role in their potential efficacy. Conversely, other literature indicates that such effects are not necessary for efficacy. Notably, many studies examining the association of mystical experience with improvements in mental health have lacked methodological rigor and most involved co-administered psychotherapy or facilitation, thus making the interpretation of their results challenging. MM120 (lysergide D-tartrate), a formulation of LSD, is currently under development as a potential treatment for GAD and MDD. This analysis explored the correlation between mystical experience and subsequent improvement in GAD using data from a phase 2b dose-finding study of MM120.
Methods: The Mystical Experience Questionnaire (MEQ30), measuring self-reported mystical experience, was administered during a phase 2b (NCT05407064) multicenter, randomized, double-blind, placebo-controlled, dose-finding study of MM120 in adults diagnosed with GAD and moderate-to-severe anxiety as defined by a Hamilton Anxiety Scale (HAM-A) of ≥20. The MEQ30 is a 30-question validated instrument used to measure the acute subjective effects of psychedelics, particularly focusing on mystical-type experiences. A score of > 60% suggests a full mystical experience. MEQ30 was completed by participants approximately 24 hours post-MM120 dosing. Correlation between MEQ30 and change in HAM-A at weeks 4 (primary endpoint) and 12 was assessed by calculation of Pearson’s correlation coefficient, r.
Results: MEQ30 score increased with MM120 dosage (25, 50, 100, and 200 µg) compared with placebo. Mean MEQ30 scores were 36.7+26.8, 50.5+29.6, 65.6+25.6, 75.4+23.7, and 11.7+17.4, respectively. Median MEQ30 scores were 32.0, 61.3, 68.7, 82.7, and 4.70, respectively. Correlations between MEQ30 and change in HAM-A at weeks 4 and 12 were weak to moderate across all dosing

groups, and most P values >.05. The strongest correlation was observed among the placebo and 25 µg groups at week 4. Among participants in the 100 and 200 µg groups who met criteria for HAM-A response, there was no correlation between total MEQ30 and change in HAM-A at week 4 (r=-0.03, P=.868). Among participants identified as having achieved remission, a weak correlation was observed at week 4 that was not statistically significant (r=0.23, P=.221).
Conclusion: Results suggest MEQ30 does not strongly predict reductions in HAM-A after a single MM120 treatment. However, for the placebo and 25 µg groups, MEQ30 demonstrated some predictive value for reduction in HAM-A at week 4, suggesting that the degree of mystical experience in these groups may have contributed to a placebo response. Across all groups, the correlation between MEQ30 and HAM-A reductions weakened over time, with no statistically significant associations observed at week 12. Despite the prevailing theory that MEQ30 predicts treatment response, these results suggest that MEQ30 scores do not predict sustained treatment response, or that a mystical experience is needed to achieve a drug effect.

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