DMT Research: Latest Findings

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WE HAVE ALMOST completed the first of four projects that our National Institute on Drug Abuse grant will be supporting. This is an attempt to develop tolerance to repeated administrations of intravenous (IV) DMT, in 12 volunteers. Longer acting hallucinogens, such as LSD or psilocybin, if administered at the same dose daily for four days, produce almost complete tolerance to both their biological and psychological effects. That is, no effects are seen on the fourth day, in response to a dose that produces a full response the first day. Why might this be important?

First, DMT's presence in human body fluids may have some relationship to "spontaneous" psychedelic states: e.g., schizophrenia, near-death experiences, and the like. Thus, if tolerance developed to DMT's effects, these unusual states would only last as long as tolerance did not develop, say, an hour or two. Certainly, the hallucinations and altered thinking processes seen in naturally-occurring "psychoses" last longer than this. In addition, "field reports," many of which came in response to my request for information regarding tolerance in a recent MAPS newsletter, were quite inconsistent regarding whether or not tolerance to repeatedly smoked DMT free base occurred. Ayahuasca, with orally activated DMT, is taken frequently during the week, and no tolerance seems to develop either. Therefore, validation or refutation of reports of variable, some, or no tolerance needed to take place in the controlled setting of a clinical research environment.

As four daily doses produced tolerance to LSD and psilocybin, we decided four doses of DMT should be attempted, too. Determination of dose of DMT and interval were worked out in some pilot studies with 4 people. Based on a comparison of the time it takes to metabolize DMT versus LSD, we thought 30-60 minute intervals for DMT would be comparable to every day with LSD. In addition, animal brain cells show tolerance to serotonin-active drugs, which hallucinogens also are, within 30 minutes. So, we did not think 30-60 minute intervals were too short.

Calibrating the dose

We began with our lowest dose, 0.05 mg/kg every hour, four times. We started with this lowest dose because previous animal work with DMT and 5-methoxy-DMT showed the opposite effect of tolerance, that is "sensitization," or an enhanced response, to these drugs depending on the interval of administration. The variables in this animal research were EEG changes and prolactin blood level responses. Thus, we did not want to give volunteers repeated injections of our highest dose, if sensitization occurred and they were over-dosed. We saw no change in response to hourly injections of this lowest dose, and then, a week later, shortened the interval to every 30 minutes. We repeated this procedure, on a weekly basis, with our volunteers, until we tried our largest dose, 0.4 mg/kg, every hour, in one person. After the third dose of 0.4 mg/kg in this volunteer, we needed to stop. This was because she did not feel able to receive a fourth dose, due to physical and emotional malaise, fatigue and an "ill-at-ease" feeling, from which she completely recovered within an hour. We had already tried 0.3 mg/kg every 30 minutes in two other volunteers, and saw this was safe and practical from the perspective of people being able to answer questionnaires and →

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give a detailed account of their experiences. We settled on 0.3 mg/kg every half hour.

The full study involved two separate admissions, in which people received, double-blind, either repeated injections of saline placebo, or repeated injections of 0.3 mg/kg DMT. We drew blood samples for ACTH (adreno-corticotrophic hormone), a pituitary hormone, that stimulates the adrenal gland to release cortisone; and prolactin, another pituitary hormone that seems regulated differently than ACTH. We already had much normative dose-response data for these hormones' responses to DMT from our first study. We also abbreviated the Hallucinogen Rating Scale (HRS), to a 3-page version, which could be filled out in less than 5 minutes. This version of the HRS consisted almost entirely of questions that demonstrated a significant effect of DMT in our original dose-response study. Our longer "new" version, contains questions that did not show a significant DMT effect, but which we wanted to keep in case other drugs showed effects on these items. Finally, we monitored temperature, blood pressure, and heart rate in the usual manner.

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Preliminary findings

As of today, 11 people (3 women, 8 men) have completed the study. We will most likely finish the entire study before July is over. There seems to be relatively robust tolerance developing to the blood pressure and heart rate responses to DMT. HRS data, although not analyzed very thoroughly yet, does not show clear-cut tolerance to the subjective effects. And, we have only started analyzing the blood data. The DMT blood level data we have to date, however, show that there is only a small amount of DMT remaining right before subsequent injections, and peak levels at 2 minutes after each administration are quite similar across all 4 doses.

The pattern of responses to these 4 doses is quite interesting. People all "brace" themselves for a 0.4 mg/kg experience, because they had never received 0.3 mg/kg before. This was the case even though they "knew" that the 0.3 mg/kg dose is 25% less. They are primarily relieved that they are not completely swept away with this dose. Then, they seem to settle into a progression of effects throughout the morning. For most, the third session is the hardest, with many wondering if anyone had dropped out at that point. I would always say, "Not yet," and they would continue for the fourth dose. It is as if resistances and defenses are being progressively "worn away" by the repeated process of intoxication-sobriety-processing-intoxication-sobriety-processing cycle. Nearly all volunteers find that the "work" they could do during 2 hours of on-again, off-again DMT intoxication is much deeper and thorough than that possible with the 0.4 mg/kg single dose. For example, one young woman, raped 6 years before, who since had suffered from chronic upper left abdominal pain, found "I can finally breathe into that pain. It's finally gone." Although the pain returned later, it was much less intense and frequent, and she could "breathe into it" and "dissolve it" when she was practicing meditation. Thus, there may be some potential therapeutic utility in doing this type of repeated DMT administration in one sitting. Of course, this anecdotal data can only provide the basis for additional, more rigorous studies.

We are now beginning work on additional psychopharmacological investigations of DMT's effects. Three "pre-treatment" studies are being developed. There will involve using oral medications an hour or two before DMT administration, that may modify DMT's biological and psychological effects, by interacting with relevant brain receptors, including two types of serotonin receptors, and one endorphin receptor. We also will begin some preliminary work looking at magnetic resonance (MR) spectroscopy of living brain metabolism effects, by scanning individuals before and after DMT administration. This is as precise as PET scans, but spares people the danger of the high doses of radiation involved in PET work (the equivalent of 100 chest x-rays to the bladder). And finally, we hope to begin the dose-response study of oral psilocybin early next year. •••