A Report on FDA-Approved Human Studies with DMT

by Dr. Rick Strassman

I became interested in hallucinogenic tryptamines, such as DMT and 5-methoxy-DMT, some years ago when it became obvious to me that the pineal gland could possibly synthesize these compounds. I had been intrigued by the possible role of the pineal in unusual states of consciousness, and the hypothesis that the pineal could mediate those states biologically had great appeal. I began a thorough study of the biological effects of melatonin. We have published 5 scientific papers in the role of melatonin, and have found only a moderating effect of the hormone on the nighttime temperature rhythm in normal humans. The lack of major effects of melatonin led me to believe that a more direct approach to studying hallucinogenic tryptamines was in order.

I more or less switched fields of interest, and dropped the melatonin work. I decided to focus on DMT (N,N-dimethyltryptamine) as a model hallucinogenic tryptamine for several reasons. It is found in the human body, brain, spinal fluid, urine and blood) and its existence has yet to be properly explained. It is very short acting and could be used in the hospital clinical research setting that seemed necessary for reinstituting any human studies with these drugs at the present time. It is not a well-known compound, advantageous for both the subjects in the study, and the regulatory agencies that would be overseeing such research; that is, subjects would not have major expectations one way or the other as to its effects, and the regulatory agencies would not have to face the intense public scrutiny that would be brought to bear if word emerged that "LSD was being studied again." Finally, it produces an extremely interesting hallucinogenic state: florid visual hallucinations, euphoria and a sense of bodily dissociation subjects find immensely pleasurable.

I decided to take a biological and descriptive approach to studying DMT. That is, what are the effects of DMT, both psychological and as an effector of brain function? As indicators of brain function, I used the "neuroendocrine" approach. This model is built on the fact that the brain is both an organ containing nerve cells (neurons) and also one that regulates the secretion of various hormones (a controller of endocrine function). From the psychological perspective, I believed it important to develop a way of looking at the effects of DMT that focused more on the phenomenology of the drug, rather than how effects might reproduce those seen in certain pathological states. Early rating scales of hallucinogens were based on the theory that these drugs induced a brief schizophrenic episode, and questions were asked that tapped those effects. People, however, do not take hallucinogens to become schizophrenic. So, I interviewed about 20 smokers of DMT and developed a draft of a questionnaire that was revised early in the study, and that we have been spending a great deal of time analyzing the results of.

Experienced hallucinogen users were recruited as subjects for the study. This was for several reasons. Experienced hallucinogen users could report more accurately the effects of the drugs, and particularly could compare effects of DMT with other drugs they had taken over the years. They were more experienced with the unusual states induced by hallucinogens and were less likely to panic at the effects of DMT. Finally, "drug abuse" problems that might be "blamed" on the DMT study would be less sustainable in subjects with an extensive prior history of drug use.

It took 21 months to receive permission to give DMT. The first 18 months was spent finding a source. The last 3 months were spent making certain the drug that was finally made met Food and Drug Administration specifications for pharmaceutical purity. [Ed. note: Dr. Rick Strassman has published the fascinating story of the process he went through to gain permission for his research in the Jan.-Mar., 1991 issue of the *Journal of Psychoactive Drugs* in an article entitled "Human Hallucinogenic Drug Research in the United States: A Present-day Case History and Review of the Process."]

Subjects were carefully screened. They could not be on any medications, have any history of psychotic symptoms (that were not drug or fever induced), and had to be in good health, as determined by a medical history and physical examination, electrocardiogram, thyroid function tests, and blood chemistry and blood counts. Current drug abuse (alcohol or cocaine) also excluded subjects.

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Furthermore, I needed to feel secure with subjects' ability to manage their hallucinogenic drug effects comfortably, even the most extreme states. This last issue was determined by informal interviews with me.

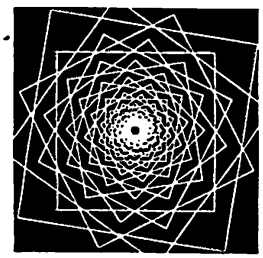
We gave the drug intravenously (IV), rather than intramuscularly (IM), as had been the case with older studies in which DMT was given to humans. This was because our early pilot work with DMT smokers demonstrated that the IM route gave an effect that was slower in onset and less intense than the smoked route. And the smoked route was impossible because of uncertainty as to how much DMT was actually being absorbed, plus the questions about what the burnt DMT products were that people might be inhaling. So, the IV route seemed the most reasonable.

We gave the drug in a double-blind placebo-controlled, dose-response manner. That is, subjects received either 0.05, 0.1, 0.2, or 0.4 milligrams per kilogram of DMT, or salt water placebo in a randomized order, with neither myself nor the subject knowing what they would get any particular day. The pharmacist preparing the injection for the day knew, however, and could be contacted immediately if necessary. Subjects had received, before starting the double-blind study, the low and high doses on consecutive days. This was for them to become familiar with the most and least intense effects to expect in the hospital setting. It was also for the research nurse and me to assess subjects' psychological and blood pressure responses to the drug. One subject had to be dropped because his blood pressure rose too high on the low dose, and we did not want to risk a dose ten times that high.

If anyone is interested in helping support Dr. Strassman's DMT book project, donations can be specifically earmarked for this purpose. MAPS will forward to Dr. Strassman 100% of all funds (in excess of membership dues) specifically donated to the DMT project. In return, Dr. Strassman has agreed to write periodic reports on his research for the MAPS newsletter.

Eleven subjects went through the entire study, for a total of about 85 drug sessions. We have had no adverse effects, and several subjects are volunteering for follow-up studies. We have seen that most of the variables we measured have risen as expected, and that there is a clear relationship between dose and effect. For example, beta-endorphin, prolactin, cortisol, and adrenocorticotrophic hormone (stimulating the adrenal gland) rise dose-dependently. Body temperature, blood pressure, heart rate, and pupil diameter all increase. Our rating is capable of distinguishing between the very lowest dose of the drug and salt water placebo.

These "normative" and descriptive data now suggest follow-up studies that will assess more carefully the mechanisms of action of DMT. For example, we have written a protocol looking at the effects of blocking endorphins, and then treating with DMT. Animal data suggest that endorphins actually inhibit the effects of DMT, and endorphin blockade enhances the effect. Seeing if the same holds true for humans would be of great interest. We have written a protocol that will investigate the electroencephalogram (EEG) effects of DMT, using new computerized technology, that will allow us to focus very carefully on selected brain areas to determine where in the brain DMT is acting. We are now writing a study looking at menstrual phase effects of DMT. That is, are the effects of DMT different depending on different phases of the menstrual cycle? Animal data suggest that it is. Human data also indicate that drugs effecting serotonin (which DMT also does) are more potent if given pre-menstrually rather than at ovulation or early in the cycle. We will also submit a protocol investigating the development of tolerance to the acute effects of DMT. This had never been demonstrated in humans, as opposed to clear tolerance developing to LSD, mescaline, or psilocybin with repeated doses. Perhaps older studies looking at DMT tolerance development in humans did not use frequent enough administrations. Other future studies will look at types of serotonin receptors that might be mediating DMT's effects. Clearly, much more research can, and should be done regarding this more interesting compound.



The funding that I would like to request from MAPS would go to allowing me the time to write up the results of the study in book form, during part of my sabbatical next year. The scientific literature, where most of the scientific data will be presented, is not the place for me to describe subjects' reports in the detail that would be of most interest to the psychedelic community. Also, a book would be more the forum in which to speculate about our findings from several points of view. Finally, the personal approach that a book could offer has advantages that are not available in scientific writing. I think between $8,000 and $10,000 will provide the funds necessary to take the time to complete a book in timely fashion. Of course, any help MAPS could provide would be greatly appreciated. ■