university of new mexico **dmt** and **psilocybin** studies

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WE ARE NEARLY ONE-FOURTH through the last of three DMT studies which our current National Institute on Drug Abuse (NIDA) grant is supporting. This study assesses the effects of pre-treatment with cyproheptadine (Periactin) on DMT's biological and psychological responses. Cyproheptadine, in addition to its anti-histamine effects, is a potent serotonin (5-HT)-2 receptor antagonist (blocker). Most animal data support a primary role of the 5-HT-2 site in mediating hallucinogen effects. Thus, a study which attempts to block this site, and then compare DMT responses without cyproheptadine, will elucidate the role of this receptor in humans. We are using our high dose of DMT (0.4 mg/kg intravenously [IV]) in combination with cyproheptadine or placebo-cyproheptadine. The other cells in this four-cell study are placebo-DMT in combination with cyproheptadine or placebo-cyproheptadine. We are measuring psychological responses using the HRS; adrenocorticotrophic hormone (ACTH), prolactin and DMT blood levels; core temperature; and blood pressure and heart rate.

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We began our psilocybin study in the summer of 1994. In a dose-finding study, we began using 0.15 mg/kg of oral psilocybin (free base). One volunteer received this dose, and it seemed relatively low. Three volunteers then received 0.3 mg/kg psilocybin, and a final three volunteers received 0.45 mg/kg psilocybin. The previous data on what a "psychedelic" dose of oral psilocybin is were quite wide-ranging, from 15-90 mg. Hofmann described substantial effects in himself at 15 mg; Hofmann gave Maria Sabina 30 mg, eliciting a "full-blown" psychedelic response; Malitz's group at Columbia University gave over 30 mg; Leary/Alpert/Metzner gave 60 mg at Harvard; and I believe a German group some years ago administered 90 mg, and were still able to obtain psychological test responses from their volunteers!

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We have found that 0.45 mg/kg (about 32 mg in a 70 kg person) elicits a robust response in our volunteers, and this will be our high dose. In fact, one volunteer found it too intense, and requested Valium to "come down." However, this volunteer had had difficulty with high dose DMT sessions in the past, finding the surrender and relaxation into drug effects frightening. Thus, we will be using serious and prolonged difficult or unpleasant responses to a high dose of DMT as an exclusionary criterion for participation in psilocybin sessions.

This is a convenient high dose for the additional reason that an eighth of this dose, about 0.056 mg/kg, or 4-5 mg in a 70 kg person) is traditionally believed to be a sub-active dose. This will be helpful in using a low dose that people have difficulty distinguishing from placebo. This is the identical model we used in our first DMT dose-response study, using 0.05 mg/kg and 0.4 mg/kg as our polar doses; 0.05 mg/kg was often not distinguished from placebo.

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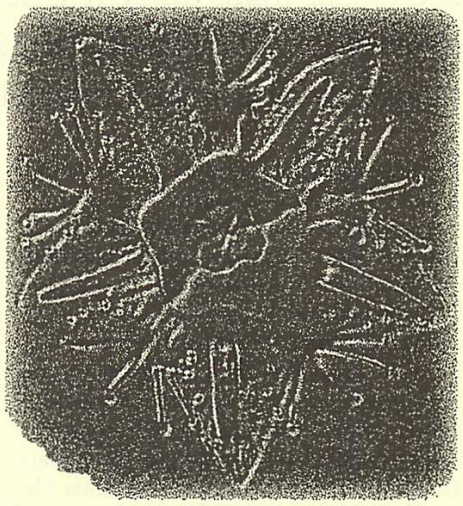
We will now begin our full psilocybin study, with 12 volunteers. People will come in for non-blind low and high doses, to get used to the hospital setting for an eight hour day, and to drop out if it is too intense for them, before we have collected much data. Then, four doses of psilocybin (high, low, and two intermediate doses) and placebo will be administered, each, at 1-2 week intervals for men, and 1 month intervals for women. We will be drawing blood samples hourly for ACTH, prolactin, cortisol, psilocybin, psilocin (the presumably active de-phosphorylated metabolite of psilocybin); assess heart rate and blood pressure; measure temperature (using skin or ear temperature); administer the Hallucinogen Rating Scale (HRS) several times during the day; and provide the opportunity to produce art for interpretation and scoring by our art therapy graduate student, Tamara Allen. We anticipate this protocol will take nearly a year.

Sitting for an eight hour session requires more patience and stamina on the part of our research nurse, Laura Berg, and myself. We attempt to orchestrate silence, music, interviewing and collecting data without too much of a strain on our volunteers, who are in an unusual environment. We anticipate our resources will be stretched in different ways than has been the case with our DMT work. With DMT, no matter how rough a ride it is, effects resolve within 30 minutes. With an all-day session, dealing with anxiety, fear, and other temporarily difficult emotions will provide new opportunities for our psychiatric skills.

The next cycle of grants requires submission to NIDA of a new grant application by February 1, 1995, to hopefully continue this work, whose funding is completed March 1, 1996. We have in mind several additional DMT and psilocybin studies.

Readers may be interested in looking up a chapter I wrote on the human psychopharmacology of psychedelics, which appears in the proceedings of the Swiss Academy of Medical Science's October, 1993, meeting: entitled *50 Years of LSD: Current Status and Perspectives of Hallucinogens* (Parthenon Publishing, New York and London, 1994, pp 145-174). This is a good source of current research here and in Europe, and provides perspectives from some of the original researchers in the field. •



Parnassia palustris. Common Grass-of-Parnassus flower.

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