RESEARCH UPDATE

the **hoasca** project: current status

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REGULAR READERS of the MAPS Newsletter are already aware of the Hoasca Project, a multidisciplinary effort to investigate the human pharmacology of Hoasca, a botanically-derived psychedelic beverage which is utilized as a sacrament in ritual practices of the União do Vegetal (UDV), a Brazilian syncretic religious movement. The background and rationale for the proposed research was reported in the MAPS newsletter for Summer 1992 (Vol. III no. 3), and an update on the status of the research as of the end of 1993 was presented in the MAPS newsletter for Spring 1994 (Vol. IV, no. 4).

. . . we have engaged Dr. Debra Mash and her colleagues at the University of Miami Medical Center to complete the pharmacokinetic arm of the study

As of this writing (May 1995) several of the original objectives of the proposed research have been met. The assessment of the possible long-term effects of hoasca teas in platelet serotonin receptors in members of the UDV has been completed by Dr. Jace Callaway and his colleagues at the University of Kuopio, Finland. The results, which have been published recently (Platelet serotonin uptake sites increased in drinkers of ayahuasca; J. C. Callaway, et al., Psychopharmacology 116:385-387, 1994) were unexpected, and hence, worthy of further investigation. The anomalous increase in the density of platelet serotonin uptake sites in long-term users was a surprising finding. While numerous psychotropic agents, as well as other treatments such as electroconvulsive therapy, are known to downregulate platelet serotonin receptors, no other pharmacological model, other than ayahuasca, has been demonstrated to increase uptake site density in platelets. The possible implications of this long-term effect, as well as the question of whether it reflects a similar effect occurring in the central nervous system, remains unclear. Dr. Callaway's investigations on the long-term effects of ayahuasca on other serotonin receptor sites in platelets are still in progress.

Dr. Callaway and his colleagues are also working on the quantitative phytochemical analyses of the alkaloids present in various samples of hoasca teas and the source plants utilized in the making of hoasca. These studies, apart from their intrinsic interest, are also essential for the projected pharmacokinetic studies, as they will provide the baseline data needed to correlate the volume of tea administered to the volunteers, to the amount of active alkaloids in the test samples. Publication of their results is anticipated shortly.

neuropsychological parameters

In addition to the biochemical measurements, an additional, major component of the study was the assessment of various neuropsychological parameters in long-time UDV members in comparison to non-users with a similar age and cultural background. This was accomplished using various standardized questionnaires such as the TPQ (Tridimensional Personality Questionnaire) and the WHO/UCLA Auditory Verbal Learning Test, as well as the Hallucinogen Rating Scale developed by Dr. Rick Strassman at the

University of New Mexico. The questionnaire-based screening was coupled with extensive, in-depth psychiatric interviews of the 15 UDV members and the control subjects. The interviews and administration of the psychological screening instruments took place under the supervision of Dr. Charles Grob, of the Psychiatry Department, Harbor UCLA Medical Center. The data from the psychological investigations has now been analyzed and the results have been submitted to the Journal of Nervous and Mental Disease.

pharmacokinetic measurements

A major component of the biochemical measurements planned for the study has not been completed: the pharmacokinetic measurement of the levels of DMT and ß-carbolines in the plasma of UDV volunteers who ingested the tea. Plasma samples were obtained from test subjects prior to ingestion of the tea and at known time-intervals during and after the acute intoxication phase of the hoasca tea experience. In addition, urine samples were obtained at 12 and 24 hours after ingestion. The objectives of this portion of the study were to obtain a time-course profile for two of the major components, DMT and harmine (harmine is the major ß-carboline present in hoasca, and the most potent MAO inhibitor of the three major ß-carbolines in the tea). The pharmacokinetic measurements are important for several reasons:

1. They will provide a measurement of the metabolism of DMT when ingested orally in the presence of peripheral MAO inhibitors. This will supplement the data on human metabolism of parenterally-administered DMT which was previously reported by Rick Strassman (Strassman, et al., Dose-response study of N,N-dimethyltryptamine in humans: I. Neuroendocrine, autonomic, and cardiovascular effects. Archives of General Psychiatry 51:85-97, 1994). We anticipate that the pharmacokinetic profile of orally-ingested DMT in the hoasca teas will reflect a less rapid plasma uptake and clearance, consistent with the more prolonged time-course of the hoasca subjective experience.

2. They will provide a measurement of the simultaneous metabolism of DMT and harmine, the MAOI which primarily potentiates oral activity of DMT. One question is, "what levels of harmine must be achieved in plasma in order to manifest the effects of orally ingested DMT?" An obvious corollary question of interest here is the relationship between plasma levels of DMT and harmine and the amounts of alkaloid ingested in the tea; in other words, how much alkaloid must be taken in the tea in order to elicit a perceptible subjective response.

3. A third question of interest is the relationship, if any, between the subjective intensity of the experience and the pharmacokinetic characteristics of the active constituents. Does the most "intense" part of the hoasca experience correlate with the highest plasma levels of DMT? These are obvious questions which can be addressed experimentally via the analysis of the time-course plasma samples.

MAPS funded study

Originally we had engaged Dr. Kym Faull, of the UCLA Neuropsychiatric Institute, to develop the analytical methods for the pharmacokinetic study. Unfortunately, due to other pressing priorities, Dr. Faull has been unable to fulfill this commitment and so we have engaged Dr. Debra Mash and her colleagues at the University of Miami Medical Center to complete this aspect of the study. Dr. Mash's group is eminently qualified to carry out this work as they have been conducting similar studies of ibogaine metabolism in connection with a NIDA project to investigate the potential of this compound as an anti-addictive agent. As a result, many of the methodological challenges which are sure to be present in the hoasca pharmacokinetic study have already been addressed and solved. We are grateful to Dr. Mash for kindly agreeing to collaborate on this project and are looking forward to her results.

One of the few problems that cannot be addressed or adequately resolved in the laboratory for a study of this type is that of continued funding; we have been extremely fortunate in this regard as well. Rick Doblin, the president of MAPS, has generously provided a $5,000 grant to Dr. Mash which has been earmarked for the completion of these pharmacokinetic measurements. We want to express our extreme appreciation to Rick, to MAPS, and to the entire MAPS community for recognizing the significance of this work and for providing the funds that will allow it to go to completion. With Dr. Mash's help and unstinting effort, we are hoping that this final and important phase of the study can be completed in the near future. Further updates on the progress of the study will be reported in future issues of the MAPS newsletter, as will the development of our plans for additional investigations. •

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