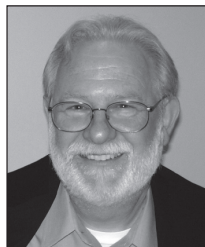


## Heffter Research Institute: Update January 2005 (www.heffter.org)



By David Nichols, PhD  
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As readers of the *MAPS Bulletin* know by now, the Heffter Research Institute has objectives and goals that overlap to a certain degree with those of MAPS. Our central mission is to encourage and support research on consciousness, but in particular to use hallucinogens as tools in that undertaking. Ultimately, we hope to identify medical indications for these substances that will allow them to be used to treat psychiatric disorders that today are addressed only with palliatives. Thus, a long-term goal is to develop these substances so they can be used as prescription medications.

Many readers will know from recent media stories that, along with MAPS, the Heffter Institute supported the study at the University of Arizona on the use of psilocybin in obsessive-compulsive disorder. The first phase of that study has been completed and generated sufficient promise to warrant its further continuation and expansion. In addition, we presently have an ongoing program at UCLA Harbor Medical School to study the value of psilocybin in the treatment of anxiety in terminal advanced-stage cancer patients. That study is completed, and we presently have an ongoing program at Harbor-UCLA Medical School to study the value of psilocybin in the treatment of anxiety in terminal cancer patients. Under the direction of Board member Dr. Charles Grob, we are attempting to replicate the significant results of this form of therapy that were obtained more than three decades ago by Drs. Al Kurland and Stan Grof and their colleagues. Those earlier studies employed LSD, but our objective is to determine whether treatment with psilocybin can provide similar efficacy.

We have now studied three subjects in a double-blind, placebo-controlled design. In addition to examining the response of anxiety to the experimental treatment, effects on mood regulation, pain, and quality of life are also being assessed. All three subjects were women in their late fifties who had had personal experience with psychedelics in the 1960s and 1970s. Notably, all three tolerated the procedure well, and reported improved psychological status subsequent to treatment. Two of the three subjects experienced mild blood pressure elevation, which gradually returned to normal.

Recruitment of new subjects has been very challenging, largely because we are adhering to very tight inclusion/exclusion criteria. Of course, as readers of the *Bulletin* will also appreciate, the controversial nature of this study adds an additional burden when convincing oncologists to refer patients to us. The setting for the research is the Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center. If you know of persons who might qualify for this study, they can obtain further information concerning protocol design and subject selection criteria at: [www.canceranxiestudy.org](http://www.canceranxiestudy.org).

The Heffter Institute also provides support to the Heffter Research Center, Zürich, at the University Hospital of Psychiatry, Zürich, under the direction of Dr. Franz Vollenweider. Besides Dr. Vollenweider, the research group includes Felix Hasler, Olivia Carter, and Rael Cahn, who have been working on the projects described below. The work there presently focuses on establishing a very fundamental basis for understanding how these substances work in the brain; for example, how they affect cognition, perception, memory, etc. The work coming out of our Zürich Center is of the very highest scientific caliber in the world. Indeed, this laboratory is now internationally recognized by scientists as perhaps the world leader in the study of altered states of consciousness in response to hallucinogens.

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A number of investigations into the neurobiological basis of perception and consciousness were completed late last year. One such study area has been the relationship between time perception, operationalized measures of sensorimotor integration, and ego boundary alterations in normal and altered states of consciousness induced by psilocybin (in collaboration with Marc Wittmann at Ludwig-Maximilians University, Munich).

A second area of investigation has been the determination of the level(s) in the neural hierarchy of visual perception with which psilocybin interacts (in collaboration with David Burr, University of Pisa, and Jack Pettigrew, University of Queensland). Using psilocybin and the 5-HT<sub>2A</sub> receptor antagonist ketanserin, we have also been attempting to assess the role of serotonin 5-HT<sub>1A</sub> and 5-HT<sub>2A</sub> receptors in mediating the perception of ambiguous visual stimuli (Necker cube, binocular rivalry, etc.) and their relation to cognitive functions like working memory. Further studies of the effect of psilocybin on sensorimotor gating in relationship to sensory filtering models of psychiatric illness have also been completed (in collaboration with Mark Geyer at UC San Diego). We have now implemented a neuroimaging paradigm using Positron Emission Tomography (PET), with the aim of deepening our understanding of the role of 5-HT<sub>2A</sub> receptor function underlying these phenomena, and its potential role in the pathophysiology of obsessive-compulsive spectrum disorders (in collaboration with August Schubiger, Department of Nuclear Medicine, University Hospital Zürich).

Finally, an EEG/ERP study into the neural correlates of ego-functions/sense of self and perception is now underway. This investigation aims to assess the neurophysiological correlates to the altered visual processing of ambiguous visual stimuli, as seen in our work on binocular rivalry. Further, for the first time we are directly comparing altered states and traits of consciousness as induced by psilocybin and meditation, using both subjective reports and a series of high resolution 3-dimensional EEG brain mapping techniques. The meditation portion of this study is being supported by a grant from the Fetzer Institute, and M.D./Ph.D. student Rael Cahn from UC San Diego is primarily working on that project.

As you can see, we are supporting a mix of both clinical and basic science applications. On the one hand we are establishing the safety of these agents for research in the context of fundamental studies of consciousness. These studies demonstrate to the world the unique properties of hallucinogens as tools to study consciousness, and hopefully will spur other laboratories to become involved in this fascinating area. They are of a very fundamental nature, revealing important things about who we are, with more direct payoffs in the future.

On the other hand, we are complementing these basic cognitive science studies with practical clinical investigations in attempts to identify medical indications that may have a direct and more immediate benefit to society. Our biggest limitation has been financial resources, and if those expand, the Zürich Center would potentially also become involved in developing clinical applications.

It is also one of our goals to encourage and support young scientists who wish to carry out research in this field. We are pleased to announce that one of our former grantees, Dr. Charles Nichols, who received a Heffter grant to carry out modern microarray studies of the effects of LSD on brain gene expression, has now been appointed Assistant Professor of Pharmacology at Louisiana State University, in New Orleans. He plans to continue his studies of the effects of drugs on gene expression, and the relationship of gene changes to behavior. The Heffter Institute is pleased to have been able to help this young scientist in his professional development.

In 2004, Heffter President Dave Nichols was also named the "Irwin H. Page Lecturer" by the International Serotonin Club, the new President of which, Mark Geyer, is also a Heffter Board Member. Dave presented an invited lecture in Porto, Portugal titled, "35 Years Studying Psychedelics: What a Long, Strange Trip It's Been." Finally, 2004 also saw the publication of a comprehensive scientific review on the subject of hallucinogens, also written by Dave Nichols. This review, titled simply, "Hallucinogens," was published in the journal *Pharmacology and Therapeutics*, Vol. 101, pages 131–181 (2004). Scientifically-savvy readers can consult this tome for an up-to-date perspective on what scientists know today about hallucinogens.

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