

Research at Harvard Medical School

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In 1999 I published a paper reviewing the medical literature on whether or not hallucinogens cause long-term brain damage with functional consequences (Halpern JH, Pope HG Jr. Do Hallucinogens Cause Residual Neuropsychological Toxicity? *Drug and Alcohol Dependence*, 53:247-256, 1999). For many MAPS members, I am sure it comes as no surprise that the upshot of this review is that very little research actually has been done concerning this question and that most of the existing work is filled with a variety of methodological flaws — leaving the question essentially unanswered.

Serious design flaws continue to this day: many studies of residual effects from MDMA abuse, for example, include users with a history of dependence on other compounds already known to have CNS (central nervous system) toxicity. Moreover, all neurocognitive evaluations have been performed with the assumption that the test subjects' reports of drug use are accurate. With a substantial fraction of street MDMA not containing any MDMA at all, it is difficult to be certain that any of the adverse effects reported in this population are actually the result of MDMA. Clearly, before specifically condemning MDMA or a classical hallucinogen as a cause of brain damage, it is important to determine whether these agents are truly neurotoxic, or

whether neuropsychological deficits reported in users are actually the result of other substances used on the street, or are perhaps due to unrelated confounding variables.

Returning to our question, then: do hallucinogens cause residual neuropsychological toxicity? For many people, this question is not as interesting to answer (or read about) as, say, a clinical study in which subjects are actually provided hallucinogens to assess risks

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and benefits. But, actually, the study I am completing on neurocognition is quite exciting and the information we are gaining about life-long hallucinogen use should offer a considerable improvement on previous studies. Specifically, it happens that while mescaline and its principal natural source, peyote (*lophophora williamsii*), are Schedule 1 substances, peyote is the legal sacrament for some 300,000 American citizens who count themselves members of the Native American

Church (NAC). Here, then, is a population with legitimate access to a known hallucinogen while the tenets of the religion clearly frown on the use of drugs of abuse and alcohol. Literally, when peyote is consumed as part of the expression of the faith of the Native American Church, peyote is not a drug being ingested: it is the non-drug, sacramental use of peyote.

For several years now our research team has been administering a large battery of neurocognitive tests to Native Americans who either are life-long members of the NAC (never having problems with drugs or alcohol), or Native Americans who are in good sobriety now but have a history of heavy alcoholism (never having problems with other drugs and are not NAC members), or Native Americans who are not NAC members nor ever had problems with drugs or alcohol. A total of 210 individuals are being recruited (70 in each cell) and then are tested by a psychologist who is unaware of their group assignment. Tests of executive cortical functioning (i.e. processes such as decision-making, categorizing, etc.), visuospatial functioning, IQ, memory, and other types of standardized word games and puzzles are administered over three hours. Ultimately, the study should provide answers to lingering questions of brain toxicity from extended hallucinogen use as well as reconfirming the lasting impact that alcohol has upon cognition.

I have been steadily building a research career to study the effects (positive and negative) of hallucinogens in man for 8 years now. Mostly, I have tried to keep “under the radar” of the public eye because, while the need for education is great, I believe the greatest impact of this research will be in doing this work, reporting it, and letting the facts speak for themselves. “Talk less...do more.” There are a number of “experts” out there lecturing and writing, but few are or ever have been engaged in active research projects in the United States dealing with the direct effects of hallucinogens in people. It certainly would be nice to have more colleagues working in this area, and eventually that should happen.

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In the meantime, it is the dedicated support from MAPS and the Heffter Research Institute and the National Institute on Drug Abuse (NIDA) that is making it possible for me to patiently, cautiously, methodically forge ahead a research career in this sometimes controversial area with sufficient rigor that the results should generally be accepted as scientifically sound and unbiased. I am deeply thankful to MAPS for its donation of \$10,000, which is critically assisting us with ancillary and supportive expenses that could not otherwise be paid for from my other funding sources. I am also grateful to NIDA for funding research in this controversial area. The United States has a tremendous shortage of qualified research doctors, so things move slowly these days because not enough people are going to medical school and then jumping through the years and years of hoops necessary for a medical research career with hallucinogens. This is a difficult path and it is humbling. There really is a tremendous amount of work to be done.

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