RESEARCH UPDATE

harbor-ucla **mdma** research

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THE HARBOR-UCLA PHASE I RESEARCH investigation of the effects of 3,4-Methelenedioxymethamphetamine (MDMA) in humans has finished comprehensive study of twelve subjects administered MDMA at dosages up to 1.75 mg/kg. All subjects enrolled in the study have participated in three randomized experimental drug administration sessions, receiving different dosages of MDMA on two occasions, and an inactive placebo on a third. Subjects as well as research staff remained blind to whether active drug or placebo was administered for each particular session. A variety of measures designed to evaluate MDMA's short and long term effects have been obtained. These include basic medical status parameters (blood pressure, heart rate, temperature) during actual experimental drug sessions, psychological instruments examining subjective mental states during drug administration, analyses of serial blood samples (obtained from an indwelling intravenous catheter) for pharmacokinetics and neuroendocrine challenge testing and neuropsychological evaluation administered before the first experimental MDMA session and one week following the last. Plans for completion of this Phase I study call for the recruitment of six additional subjects who will be administered MDMA in dosages ranging form 1.75 to 2.5 mg/kg.

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Brain Imaging

Brain imaging scans have also been included in our research design in order to ascertain both short and long-term effects that MDMA has on cerebral blood flow and brain neurochemistry. Thus far, we have studied fifteen subjects (inclusive of some but not all of the subjects experimentally administered MDMA, as well as several others who were not included in the experimental MDMA administration wing of the study) with SPECT (single photon computed tomography) scans, several of whom were studied both before their first dose of MDMA and after their last. SPECT scan procedures called for co-registration with MRI (Magnetic Resonance Imaging), thus allowing for greater resolution and detail of images obtained. Magnetic Resonance Spectroscopy (MRS) has also been obtained on a large number of our subjects to examine integrity of brain neuronal membranes and to explore for the presence of abnormal CNS metabolites.

Cerebral Blood Flow

Preliminary SPECT scan findings in particular have aroused interest. Although it is premature to publish our preliminary data at this time, basic science research utilizing small laboratory animals reported in the scientific literature several years ago (McBean et al, 1990) does provide intriguing clues concerning MDMA's long-term effects. Weeks following serial administration of repeated large dosages of MDMA, these experimental animals were found to have significantly elevated rates of cerebral blood flow compared to normal control animals never administered MDMA. Given what we know of serotonergic neuronal innervation of blood vessels, such findings are not surprising. If these laboratory findings do indeed generalize to the human data, several important questions must be asked. First of all, what are the clinical implications of increased blood flow in the brain? We are aware of a variety of neuropsychiatric disorders associated with measurements of low blood flow, including Alzheimer's Disease, HIV Dementia, Major Depressive Disorders and Chronic Cocaine Abuse. However, there are no known clinical disorders or drugs which

induce long-term elevations of rates of cerebral blood flow. If indeed MDMA can reliably increase blood flow in the brain, this would presumably be an entirely novel phenomenon. And if MDMA can cause elevations of cerebral blood flow, then in order to establish what the clinical implications are, it will be necessary to evaluate the short and long term effects of MDMA on memory, cognition, mood and overall psychiatric status in a larger group of subjects.

Reports have surfaced over the years attesting to possible therapeutic and salutary effects of MDMA use. However, reports have also appeared, particularly in the neuroscience and psychiatric literatures, alleging various degrees of adverse outcome to MDMA use. Unfortunately, rigorous objective methodological assessment of this phenomenon has remained limited, in spite of the serious public health questions which still await elucidation. We believe that brain imaging investigations can provide valuable clues in helping us unravel the truth about MDMA, and whether it has genuine application as a medicine, or conversely, must be avoided because of risks for inducing brain injury. Only with additional studies of MDMA's effects on brain function and neuronal integrity will we obtain answers to these questions.

Subjects needed

Will SPECT scans of humans corroborate animal findings that MDMA increases cerebral blood flow? If this is the case, is it a dosage or time-limited phenomenon, where initial elevations are followed by decline or return to baseline? In order to address these problems, it is necessary to pursue additional investigation in human subjects. To that end, we are interested in recruiting individuals willing to undergo brain imaging procedures as well as psychiatric and neuropsychological evaluation who have personally used MDMA in excess of several hundred times. Anyone wishing more information concerning possible participation in the Harbor-UCLA Phase I MDMA research protocol can contact our research coordinator, Gayle, at (310) 222-4266. We would also like to point out that these brain imaging studies are very costly, and that in order to continue our work in this area we will need additional funding support. Given the increasing difficulties in obtaining government funding for this type of research endeavor, we are counting on private donations to allow us to move forward with our studies. Anyone interested in making such a contribution to our ongoing research efforts may do so through MAPS, or else directly to the Harbor-UCLA Research and Educational Institute, a non-profit tax-exempt research organization. With continued financial support, it is our hope that we will be able to shed new light on this critical yet perplexing area, and in so doing hasten the opportunity to pursue formal, sanctioned Phase II clinical trials with MDMA in the treatment of pain and distress in end-stage cancer patients.

We would also like to take this opportunity to thank MAPS for its generous contribution of $15,000 to our ongoing efforts conducting human research with MDMA. Without such support, it would not be possible to continue this work.•

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