Ketamine-Assisted Psychotherapy In the Treatment of Heroin Addiction: An Update

Evgeny Krupitsky, M.D., Ph.D. (kru@lond.spb.su)
Leningrad Regional Center for Alcoholism and Drug Addiction Therapy

Note from MAPS: MAPS is now three years and $30,000 through its five-year and $50,000 pledge to Dr. Krupitsky's study using multiple-dose v single dose ketamine-assisted psychotherapy (KPT) in the treatment of heroin addicts. We are currently seeking donations for the remaining $20,000, pledged over two years.

I am pleased to inform MAPS readers of several developments in research with ketamine and ketamine-assisted psychotherapy (KPT). Most importantly, we are successfully progressing with our MAPS and Heffter-supported study of ketamine-assisted psychotherapy in the treatment of heroin addiction. The double-blind, placebo-controlled study compares multiple v single KPT sessions (more info at http://www.maps.org/research/ketamine/ketrussia.html). We have treated 59 subjects in the study to date and are beginning the third year of this five-year project. However, due to changing regulations regarding ketamine in Russia that went into effect recently, we cannot enroll more subjects until we implement new security procedures for the ketamine and obtain a new permit, though follow-up is continuing on subjects previously treated. It will probably take a few months before new patients can be treated.

"The study results I presented in Israel were from the first double-blind placebo-controlled randomized clinical trial of psychedelic psychotherapy conducted anywhere in the last thirty years."

Conferences

In September and October of 2001, I attended two major international psychiatric conferences, with assistance from MAPS. The first conference was the Annual Conference of the International Society of Addiction Medicine (ISAM) in Tel Aviv, Israel. It was initially planned for the year 2000 but had been postponed until September 2001 because of the political situation in Israel. At the Israel conference, I

presented the results of our recently finished study of high-dose v low-dose/placebo ketamine-assisted psychotherapy in the treatment of heroin addiction (for preliminary results, see http://www.maps.org/news-letters/v09n4/09421kru.html). The second conference was the International Congress of the World Psychiatric Association, held September 29– October 4 in Madrid, Spain. At the Madrid conference, I presented the results of a non-therapy ketamine study, and was able to include some discussion of our therapy study as well.

Israel Conference

The study results I presented in Israel were from the first double-blind placebo-controlled randomized clinical trial of psychedelic psychotherapy conducted anywhere in the last thirty years. Our results have been submitted for publication to the *Journal of Substance Abuse Treatment* (see the abstract of our paper below). We

Abstract of Paper Presented in Israel

Krupitsky, E. et al. Ketamine-assisted psychotherapy (KPT) for heroin addiction: Immediate effects and two-year follow-up. In press, *J. Substance Abuse Treatment*.

Seventy detoxified heroin addicts were randomly assigned to one of two groups receiving ketamine-assisted psychotherapy (KPT) involving two different doses of ketamine. There were 35 heroin addicts (27 male and 8 female) in the experimental group, and 35 heroin addicts (28 male and 7 female) in the control group. The patients of the experimental group received existentially oriented psychotherapy in combination with a hallucinogenic ("psychedelic") dose of ketamine (2.0 mg/kg i.m.). The patients of the control group received the same psychotherapy combined with a very low, non-hallucinogenic (non-psychedelic), dose of ketamine (0.2 mg/kg i.m.). This low-dose induces some pharmacological effects without inducing a peak psychedelic experience. Both the psychotherapist and patient were blind to the dose of ketamine. Otherwise, all patients were treated alike and were given the same preparation. The KPT sessions, regardless of dose, also were similar. All patients' psychological and clinical evaluations during the treatment and follow-up period were performed by a clinician evaluator other than the psychotherapist providing KPT. This rater was also blind to the dose of ketamine. KPT included preparation for the ketamine session, the ketamine session itself, and the post session psychotherapy aimed to help patients to integrate insights from their ketamine session into everyday life. During the ketamine session, the psychotherapist provided emotional support for the subject and carried out psychotherapy. Psychotherapy was existentially oriented, but also took into account the subject's individual and personality problems.

The results of this double-blind, randomized clinical trial of KPT for heroin addiction showed that high-dose (2.0 mg/kg) KPT elicits a full psychedelic experience in heroin addicts as assessed quantitatively by the Hallucinogen Rating Scale. On the other hand, low-dose KPT (0.2 mg/kg) elicits "sub-psychedelic" experiences similar to ketamine-facilitated guided imagery. High-dose KPT produced a significantly greater rate of abstinence in heroin addicts within the first two years of follow-up than did low-dose KPT. High-dose KPT elicited a greater and longer-lasting reduction in craving for heroin (assessed with the Visual Analog Scale of Craving), as well as greater positive change in nonverbal unconscious emotional attitudes (assessed with the Color Test of Attitudes). Thus, the higher rate of abstinence in the high-dose group may be related to KPT's effects on craving (similar to other NMDA receptor ligands) and modification of nonverbal unconscious emotional attitudes. KPT-induced effects on depression, anxiety, anhedonia, and psychological changes as assessed by the MMPI, Locus of Control Scale, Questionnaire of Terminal Life Values, Purposes-in-Life Test, and Spirituality Scale were similar in the experimental and control groups. These results support the conclusion that high-dose ketamine-assisted psychotherapy may improve abstinence in heroin addicts through reduction in craving. However, it also appears that the acute psychedelic effects induced by psychedelic psychotherapy on the verbal level do not always lead to high rates of abstinence from drugs and alcohol. Further research should explicate how high-dose KPT improves relapse rates, and how to apply more optimally acute drug-induced psychological effects towards therapeutic ends.

"I think that it is very important to present the results of rigorous scientific studies of psychedelics at international psychiatric conferences, in order to combat prejudice and to positively impact the psychiatric community's attitude toward psychedelic psychotherapy."

used a single high-dose ketamine-assisted psychotherapy session as the experimental condition and a single low-dose ketamine-assisted psychotherapy session as an active placebo. The positive results in our two year follow-up data are a strong argument for the efficacy of ketamine-assisted psychotherapy for heroin addiction. After my presentation, several Israeli psychiatrists and medical officials expressed interest in ketamine-assisted psychotherapy and the possibilities of its implementation in Israel. We are now in the process of discussing the details of a visit by Israeli psychiatrists to our facilities in St. Petersburg, Russia, in order to teach them the technique and see how they could use it in Israel.

Madrid Conference

At the International Congress of the World Psychiatric Association in Madrid, I presented the results of a non-therapeutic ketamine study which I have conducted, and I also spoke about ketamine's therapeutic and abuse potential. The study evaluated cognitive, behavioral, and ethanol-like effects of the interactions between two neuronal calcium channel ligands (blockers) in abstinent alcoholic subjects: ketamine, which is a NMDA-coupled calcium channel blocker, and nimodipine, a dihydropyridine-sensitive calcium channel blocker. We showed that nimodipine attenuates psychotogenic, hallucinogenic, cognitive and some ethanol-like effects of ketamine in abstinent alcoholic subjects. This finding is important in the study of subtle neuropharmacological mechanisms underlying mind, psychiatric disorders, and development of alcohol dependence. It is also valuable because it suggests nimodipine's potential therapeutic use in psychiatry.

Krupitsky, E. et al. (2001). "Attenuation of ketamine effects by nimodipine pretreatment in recovering ethanol dependent men: psychopharmacologic implications of the interaction of NMDA and L-type calcium channel agonists." *Neuropsychopharmacology* 25 (6):936-947.

Conclusion

I think that it is very important to present the results of rigorous scientific studies of psychedelics at international psychiatric conferences, in order to combat prejudice and to positively impact the psychiatric community's attitude toward psychedelic psychotherapy. I am very grateful to MAPS for the financial support of my visits to both Tel Aviv and Madrid, and for my KPT research, which otherwise would not have been possible. ■

"The positive results in our two year follow-up data are a strong argument for the efficacy of ketamine-assisted psychotherapy for heroin addiction."