

## **Ketamine** Assisted Psychotherapy (KPT) of Heroin Addiction: **Immediate Effects and Six Months Follow-Up\***

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**IN** THE 20th CENTURY, while billions of dollars have been spent to treat addictive diseases, the search for effective medication continues. The mainstay of such treatments include therapy and counseling, AA and NA, different kinds of rehabilitation programs, drug maintenance programs, and pharmacotherapy. However, the rate of efficacy of all suggested methods of addiction treatment is poor and the need remains for new effective medications. The use of hallucinogens in the treatment of addiction could be one promising approach (Halpern, 1996).

Many studies from the 1950s and 1960s suggested that hallucinogen-assisted (psychedelic) psychotherapy might be an efficient treatment for the addiction (Grinspoon and Bakalar, 1979), but the variation in methodologies made it difficult to generalize across studies.

In the 1970s Savage and McCabe (1973) showed that LSD-assisted psychotherapy had a positive effect on the outcome of treatment of heroin addicts: 25% of the subjects treated with LSD remained abstinent from opiates for one year as opposed to only 5% of the control group of conventional weekly group psychotherapy.

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THE AUTHORS encouraged further research with hallucinogens in the treatment of addictions, but by 1973, when their study was published, human research with these substances had essentially come to an end in America because of controversy associated with their non-medical use (Halpern, 1996). Later in the 1980s and 1990s both animal studies and anecdotal human reports suggested anti-craving properties of another hallucinogen - ibogaine ("Endabuse™") (Lotsof, 1995; Mash, 1998). However, further human research with ibogaine is needed to demonstrate its antiaddictive properties as well as safety.

Ketamine is a drug for general anesthesia, but in subanesthetic doses it induces a profound psychedelic (hallucinogenic) experience (Bowdle et al., 1998). Ketamine has several advantages over other hallucinogens as an adjunct to psychotherapy in the treatment of addictions: it is safe, short-acting, and, most importantly, it is not in Schedule I drug like other hallucinogens. Our

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previous studies showed that ketamine assisted psychotherapy is an effective method for alcoholism treatment (Krupitsky and Grinenko, 1997). Ketamine could also have anti-craving properties because of its influence on the NMDA receptor, similar to other NMDA receptor ligands - acamprosate and ibogaine (Mash et al., 1998; Sass et al., 1996). All these factors led us to study the efficacy of ketamine-assisted psychotherapy for heroin dependence.

**Design**

Seventy detoxified heroin addicts were randomly assigned to one of two groups. The patients of the experimental group received psychotherapy in combination with a "psychedelic" dose of ketamine (2.5 mg/kg i.m.). The patients of the control group received the same psychotherapy combined with a very low, non-psychedelic (non-hallucinogenic), dose of ketamine (0.25 mg/kg i.m.). This low dose induces some pharmacological effects without inducing a peak psychedelic experience (see Results section below). Both a psychotherapist and a

**EXPERIMENTAL DESIGN AND METHODS**

patient were blind to the dose of ketamine. All patients were treated alike and were given the same preparation. The KPT sessions, regardless of dosage, were given under similar circumstances. 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.

**Patients**

Seventy heroin addicts were screened, evaluated and randomized in the study. 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. There were no statistically significant differences between the experimental and control groups with respect to age, duration of heroin addiction, and duration of abstinence from heroin.

Patients participating in the study were mostly young people (mean age of experimental group: 23.03 years / mean age of control group: 21.63 years). In this concern it is important to note that heroin addiction has a higher prevalence among youth in Russia. The typical age of heroin addicts in Russia is between 17 and 26. The typical duration of addiction is about 3-4 years. Many of heroin addicts die because of overdose or get imprisoned within the first several years of using heroin.

**Selection and screening**

Psychotherapy was provided by a psychotherapist (psychiatrist) specially trained in KPT. Only one KPT session was carried out for each patient. Screening evaluation for patients included a formal psychiatric examination; a standard medical examination, including blood chemistry panel (including hepatic functions), urine analysis, HIV-test, pregnancy test and EKG; and a review of previous medical and psychiatric records.

**Assessment instruments**

In choosing the battery of assessment instruments, care was taken to include those instruments we already successfully used in our previous studies of KPT for alcoholism (Krupitsky and Grinenko, 1997) to provide comparability with those studies. There was also an effort to provide a mix of instruments widely used in psychotherapy outcome research. In addition, due to the specific nature of ketamine psychotherapy, instruments were considered desirable that might indicate changes in the areas of personality, life values and purposes, spiritual development, and unconscious emotional attitudes.

**Treatment and follow-up**

All patients were asked to write a detailed self-report about their experiences during the ketamine session. These self-reports provided evidence for the presence of a peak experience during the ketamine session.

**Treatment procedure**

Patients and the psychotherapist were both blind to the dose of ketamine. There were up to 10 hours of

psychotherapy provided before the ketamine session in order to prepare patients for the session. There were up to 5 hours of psychotherapy provided after the ketamine session to help patients interpret and integrate their experiences during the session into everyday life.

An anesthesiologist was present throughout the ketamine session to respond to any complications. The length of the ketamine session was about 1.5 - 2 hours. Only one ketamine session was carried out for each patient. The patient was instructed to recline on a couch with eyeshades. The pre-selected stereophonic music was used throughout the ketamine session. The psychotherapist provided emotional support for the patient and carried out psychotherapy during the ketamine session. Psychotherapy was existentially oriented, but also took into account the patient's individuality and personality problems (Krupitsky and Grinenko, 1997). The same psychotherapeutic technique (see below) was used regardless of the dose of ketamine. Patients were discharged from the hospital soon after the KPT.

#### **Description of the psychotherapeutic technique**

Three main stages in our method of KPT can be distinguished (Krupitsky and Grinenko, 1997). The first stage is preparation. In this stage, preliminary psychotherapy is carried out with patients. During these psychotherapeutic sessions it is explained to the patients that the relief of their dependence from heroin will be induced in a special state of consciousness in which they will have deep experiences that will help them to realize the negative effects of heroin abuse, and the positive aspects of life without drugs. We explain that the ketamine session may induce important insights concerning their personal problems, their system of values, notions of self and the world around them, and the meaning of their lives. All of these insights may entail positive changes in their personality, which will be important for their shift to a new lifestyle without heroin. During the ketamine sessions, patients often experience the separation of consciousness from the body and the dissolving of the ego, so it is very important to prepare patients carefully for such an unusual experience. The therapist pays close attention to such issues as the patient's personal motives for treatment, his goals for his new life without drugs, his idea of the cause of his disease and its consequences, and so on. An individually tailored "psychotherapeutic myth" is formed during this dialogue. It becomes the most important therapeutic factor responsible for the psychological content of the second stage of the KPT. It is also very important to create a specific atmosphere of confidence and mutual understanding between the psychotherapist and patient during this first stage of KPT.

The second stage is the ketamine session itself. With a background of special music (generally, "New Age" composers, such as Kitaro and Jean Michel Jarre) the patient having a KPT session is treated psychotherapeuti-

cally. The content of these psychotherapeutic influences is based on the concrete data of the patient's anamnesis (case history) and is directed toward the resolution of the patient's personality problems and toward the formation of a stable orientation towards the life without drugs. We try to help our patients create a new meaning and purpose in life during this session. We emphasize the positive

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values and meaning of life without drugs and the negative aspects of drug abuse during ketamine session. It is also very important to direct carefully the patient's psychedelic experiences by verbal influences and manipulating the musical background towards the symbolic resolution of the personality conflicts as well as a final cathartic peak experience. This second stage of KPT is conducted by two physicians, a psychotherapist and an anesthesiologist, because some complications and side-effects (such as increased blood pressure and depression of breath) are possible, though exceedingly rare. After the session, the patient rests, and we ask them to write a detailed self-report of their experience later that evening.

In the third stage, special psychotherapeutic sessions are carried out within several days after the KPT session. During these sessions the patients discuss and interpret the personal significance of the symbolic content of their experience with the psychotherapist. This discussion is directed toward helping the patient establish a connection between their ketamine experience and their intra- and interpersonal problems (primarily those connected with drug abuse), and thereby to solidify their desire for a life without drugs. We try also to assist patients to integrate the insights from the ketamine session into everyday life. The uniquely profound and powerful ketamine experience often helps them to generate new insights that enable them to integrate new, often unexpected, meanings, values and attitudes about the self and the world.

#### **RESULTS AND DISCUSSION**

##### **Characteristics of the ketamine experience**

Content and features of the ketamine experience in both groups were evaluated with the Hallucinogenic Rating Scale (Strassman et al., 1994). HRS scores in the

**Treatment outcome: Six month follow-up**

Follow-up data were collected by psychiatrists who were blind to the dose of ketamine used for KPT. The follow-up data included information from patients themselves, their relatives, and urine drug testing results. According to the follow-up data, all patients were divided into four groups: patients who were abstinent, patients who relapsed, patients for whom we were unable to get reliable follow-up data, and patients with specific circumstances for abstinence. One patient of the experimental group was placed into the group with specific circumstances for abstinence: He was imprisoned on the fifth month of the follow-up for a crime committed before his admission into the treatment program.

The rate of abstinence in the experimental (high dose) group was approximately twice as high than that of the control (low dose) group, while the corresponding rate of relapse was lower. The differences between the experimental and control group in rates of both abstinence and relapse were statistically significant within the first six months of follow-up. Thus, KPT with the high dose of ketamine was significantly more effective within the first six months after the ketamine session.

It is important to note that almost 50% of patients in the experimental group and 60% of subjects in the control group relapsed within the first three months after KPT. Thus, it might be possible that repeated sessions carried out within the first few months after KPT would provide a higher rate of abstinence. J. Halpern in his review of the studies of hallucinogen-assisted psychotherapy of addiction (1996) came to a similar conclusion. However, testing of that hypothesis is a subject for a separate study.

**KPT influence on craving for heroin**

KPT sessions significantly reduced craving for heroin as evaluated by the Visual Analog Scale of Craving in both experimental and control groups. However, the decrease of craving in the experimental group was significantly greater than in the control group right after KPT as well as at one and three months after the ketamine session. Also, craving in the experimental group was significantly decreased for each of the six months following KPT, while in control group this was the case for only the first month. Thus, KPT with a high dose of ketamine produced greater and longer-lasting decreases in drug craving in heroin addicts than that seen in the low-dose group. It is interesting to note that other NMDA receptor antagonists, like ibogaine and acamprosate, have a similar influence on craving (Sass et al., 1996; Mash et al., 1998).

**KPT influence on the syndrome of anhedonia**

The amelioration of the syndrome of anhedonia is an important aspect of relapse prevention (Krupitsky et al., 1998). Thus, the positive effect of KPT on the syndrome of anhedonia in heroin addicts might be important for relapse prevention and maintaining abstinence from heroin. KPT reduced the severity of the syndrome of

**high dose group provided evidence that patients in the**

experimental group had a profound psychedelic (hallucinogenic) experience. The scores in the high ketamine dose group are similar to ones induced by high (psychedelic) dose of another hallucinogen - dimethyltryptamine (DMT) in Strassman's study in healthy volunteers (Strassman, 1996). Average scores in the experimental group are also similar to the scores received by Bowdle and co-authors with the high level of ketamine in the blood (200 ng/ml) (Bowdle et al., 1998).

HRS scores in the low ketamine dose group suggests that patients did not have a full-blown psychedelic (hallucinogenic) experience. However, HRS scores in the low dose group were much higher than those seen in placebo groups in Strassman's (1996) and Bowdle's (1998) studies. Subjects in the low dose group demonstrated affective and cognitive effects that were close to a psychedelic dose of DMT. Thus, patients in the control group had experiences of what might be referred to as "sub-psychedelic." This could be the effect of set and setting combined with a relatively low dose of ketamine. Similar effects were noted in Kurland et al. (1971) study many years ago. They used 500 mcg of LSD as their high dose, and 50 mcg for their low dose, in treating alcoholics. They thought 50 mcg would be an active placebo. They found the frequency of peak experiences similar in both groups. This is also a strong statement about the importance of set and setting in determining the responses to hallucinogenic drugs.

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HRS scores in the experimental and control groups in our study were statistically significant for all HRS subscales except Volition. That means that the experiences of the high ketamine dose group were different than those in the low dose group. Patients in the experimental group had a deep psychedelic experience while patients of the control group experienced something like a ketamine-facilitated guided imagery (Lerner, 1977). However, patients of the control group were often very much impressed by their experiences and considered them as useful as therapeutic ones.

anhedonia more quickly than did traditional treatment with selective serotonin reuptake inhibitors (SSRIs) which takes at least three weeks. Also, KPT reduced the severity of all components of the anhedonia syndrome, including a cognitive one, while SSRIs influence mostly affective and behavioral components (Krupitsky et al., 1999).

#### **KPT influence on anxiety and depression**

KPT in both experimental and control groups significantly reduced elevated pre-treatment levels of both state and trait anxiety, measured with the Spielberger Anxiety Scale and depression, measured by the Zung Depression Scale. The level of anxiety was within normal limits by six months of abstinence in both groups. The level of depression was relatively low within the first six months after KPT in both groups.

#### **KPT influence on personality**

KPT in the experimental group produced a decrease in scores for the following MMPI scales: depression, conversion hysteria, paranoia, schizophrenia, and Taylor scale of anxiety. The self-sufficiency score significantly increased after KPT. On the whole, such favorable psychological dynamics suggest that patients became more sure of themselves, their possibilities and their futures, less anxious, less depressed and neurotic, and more emotionally open after KPT. These changes are very similar to those noted in alcoholics after KPT (Krupitsky and Grinenko, 1997) and are favorable for abstinence. KPT in the control group decreased scores of the following scales: hypochondriasis, depression, conversion hysteria, masculinity-femininity, paranoia, psychasthenia, schizophrenia, sensitivity-repression, and Taylor scale of anxiety. The self-sufficiency score significantly increased after KPT. Positive MMPI changes in the control group were similar to those in the experimental group and included even more scales. However, the scores for the lie scale significantly increased while those for the validity scale decreased in the control group. This may mean that control group patients tried to present themselves in a more positive, more socially acceptable way while they were answering MMPI questions after KPT. Thus, positive MMPI changes in the control group might reflect to some extent patients' desire to be appear in a more positive light.

#### **KPT influence on the terminal life values**

KPT's influence on the terminal life values was assessed with the Questionnaire of Terminal Life Values (QTLV) developed by Senin (1991), based on the Rokeach's approach to human values and beliefs (Rokeach, 1973). KPT in the experimental group caused a significant increase in the importance of values such as social recognition, creativity, social contacts, and individual independence. These factors were particularly relevant to areas of life values such as actualization as professional, educational and social life. KPT in the control group brought about significant increases in the

importance of social recognition, creativity, self-perfection, achievement of life purposes, spiritual contentment, and individual independence. These changes were significant in all five areas of life values actualization. KPT-induced changes in the control group included even more QTLV scales than in the experimental group. However, the scores for individual independence and educational area of life values actualization were significantly greater after high, compared to low, dose KPT.

#### **KPT influence on understanding the meaning of one's own life**

KPT influence on understanding the meaning of one's own life was assessed using the Purpose-in-Life Test

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(PLT) based on Frankl's (1978) concept of the individual's aspiration for meaning in life. The PLT was adapted in Russian by Leontiev (1992). KPT caused a significant increase in the indices measuring understanding the meanings and purposes in life, as well as self-actualization, and the ability to control oneself and one's own life in accordance to those life purposes. PLT changes after KPT were similar in both groups. This means that after KPT (regardless of the ketamine dose) patients were better able to understand the meaning of their lives, their life purposes, and perspective. After KPT, their lives became more interesting, emotionally deeper, and filled with meaning. They felt themselves better able to live in accordance with their concept of the meaning of life and life purposes as a result of KPT. Such changes might favor abstinence from heroin, particularly from the standpoint of Frankl's approach, which considers alcoholism and addictions as an "existential neurosis," consequent to losing the meaning of life as well as the appearance of an "existential void" (Frankl, 1978). We believe KPT is able to fill in this void at least to some extent.

#### **KPT influence on spirituality**

A psychedelic ketamine experience is to some extent similar to the near-death experience (Jansen, 1997); it might be transformative and induce changes in spiritual development and even in worldview (Krupitsky and Grinenko, 1997). KPT effects on the spiritual development of heroin addicts was studied with the Spirituality Changes Scale (SCS). This instrument previously demonstrated a positive influence on spirituality by KPT in

alcoholics. It also demonstrated beneficial effects of meditation in healthy volunteers (Krupitsky and Grinchenko, 1997). In the current KPT study, the Spirituality Changes Scale demonstrated a similar increase in the level of spiritual development after KPT in both groups of heroin addicts. The SCS changes in heroin addicts were also similar to those induced by KPT in alcoholics in our previous studies (Krupitsky and Grinchenko, 1997). Many reports suggest that religious or spiritual conversion is an important factor in "spontaneous" recovery from drug abuse. Indeed, Twelve Steps and Alcoholics Anonymous programs have a distinctly spiritual/religious orientation (Cortington, 1989; Whitfield, 1984). A therapy that enhances the likelihood of a conversion experience therefore might have utility in the treatment of substance abuse. Ketamine-assisted psychotherapy may represent one method of eliciting spiritual experiences in patients with chemical dependence. The increased spiritual development induced by KPT in heroin addicts may be favorable for abstinence.

**CONCLUSION**

The results of this double-blind randomized clinical trial of KPT for heroin addiction showed that high dose (2.5 mg/kg) ketamine psychedelic psychotherapy (KPT) elicits a profound, full psychedelic experience in heroin addicts. On the other hand, low dose KPT (0.25 mg/kg) elicits "sub-psychedelic" experiences which are very similar to ketamine-facilitated guided imagery. High dose KPT produced a significantly greater rate of abstinence in heroin addicts within the first six months of follow-up than did low dose KPT. High dose KPT brought about a greater and longer-lasting reduction in craving for heroin, as well as greater positive change in nonverbal unconscious emotional attitudes. Thus, it is possible that the higher rate of abstinence in the high dose group was to some extent due to positive effects of ketamine on craving (which had been found similar in other NMDA receptor ligands). It also may be due to the positive transformation of nonverbal unconscious emotional attitudes.

KPT-induced changes in depression, anxiety, anhedonia, and psychological changes on the verbal (conscious) level assessed with verbal tests (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 hypothesis that dramatic psychological transformations induced by psychedelic psychotherapy on the verbal level do not always lead to high rates of abstinence from drugs and alcohol (Grinspoon and Bakalar, 1979).

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