

## **8. Ten Year Study of Ketamine Psychedelic Therapy (KPT) of Alcohol Dependence**

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Psychedelic psychotherapy was shown to be a potential benefit for alcoholism treatment in the "60s," but different methodologies made it difficult to generalize across studies. The requisite development of appropriate sophistication for these studies was not possible to do after they were scheduled in 1970 and their use was strictly limited. However, at about this time, ketamine was being shown to elicit "psychedelic" emergent phenomena in patients. This property of ketamine was exploited by our use of ketamine-assisted therapy of alcoholism. Ketamine has some advantages over other psychedelics as an adjunct to psychotherapy. It is safe and short acting (the psychoactive effects lasting about an hour). In addition, ketamine is not scheduled like other psychedelics. In lower doses (about one sixth to one tenth of that usually used in surgery for a general anaesthesia) it induces a profound psychedelic experience.

Psychotherapy in our model consists of the preparation of patients for the psychedelic session, the psychotherapeutic facilitation of the session and special post-session psychotherapy (Krupitsky, 1992). This post-session work is intended to help the patient integrate insights from the psychedelic experience to the everyday life and relate the experience to his life and personality problems. Moreover, psychotherapy in this manner acquires a special quality. It is considered here not only as a process of resolution of certain psychological problems, but also as an important stage in spiritual maturation. The uniquely profound and powerful psychedelic experience often helps our patients to generate new insights that enable them to integrate new, often unexpected meanings, values and attitudes about their individual selves and the world.

We carried out a controlled clinical trial of the efficacy of KPT. To determine the efficiency of the treatment, we collected follow-up information about all the patients who had taken part in this study a year after their release. According to the data, abstinence of more than 1 year was observed in 73 out of 111 people (65.8%) who had undergone the KPT. Thirty people (27.0%) had relapsed. We could not obtain data on eight patients (7.2%). In the control group of 100 patients whose treatment consisted only of conventional methods, only 24 patients (24%) remained sober for more than 1 year ( $p < 0.01$ ). Thus, the data from the follow-up study demonstrated that ketamine-assisted psychedelic therapy increases the efficacy of conventional alcoholism treatment.

Two-year follow-up data had been collected for the 81 patients who had undergone the KPT (because at the moment of the follow-up study only 81 out of 111 patients had a two-year follow-up period after KPT). According to the data, abstinence of more than 2 years was observed in 33 out of these 81 patients (40.7%). Thirty-eight patients (46.9%) had relapsed. We could not obtain two-year follow-up data on 10 patients (12.4%). Three-year follow-up data had been collected for the 42 patients who had undergone KPT. According to the data, abstinence of more than 3 years was observed in 14 out of these 42 patients (33.3%). Twenty-four patients (57.2%) had relapsed. We could not obtain three-year follow-up data on four patients (9.5%). These two- and three-year follow-up data are also evidence of the high efficacy of KPT.

We also carried out psychological, biochemical, and neurophysiological studies of the different possible underlying mechanisms of KPT.

### **Psychological underlying mechanisms**

#### **MMPI**

All patients in each experimental group were examined with the Minnesota Multiphasic Personality Inventory (MMPI) (adapted in Russia by Sobchik (1990)) before and after KPT.

According to the MMPI data, our analysis of psychological changes in the experimental group points to definite, rather expressed dynamics in the patient's MMPI profiles. Particularly, after KPT the indices were decreased for the majority of the main MMPI scales. The most expressed, statistically significant decrease in the profile was in the scale "hypochondria," "depression," "hysteria," "psychastenia," "schizophrenia," "sensitivity-repression," and also in Taylor's scale of anxiety. At the same time, the estimate in the Ego strength scale increased. On the whole, such favorable psychological dynamics testify to the fact that the patients became more sure of themselves, their possibilities, their future, less anxious and neurotic, and more emotionally open after KPT. Against the background of these general tendencies, we saw in the majority of cases some essential individual variations (e.g. concerning changes in such scales as "masculinity-femininity," "paranoia," "hypomania," and "sensitivity-repression") that reflected, as a rule, a certain harmonization of the patient's personality profiles.

### **Locus of Control**

Thirty alcoholic patients treated with KPT were examined with the Locus of Control Scale (LCS) developed by J.Rotter (Phares, 1976) and adapted in Russia by Bazhin et al. (1993). All patients were assessed with the LCS twice: before and after KPT.

It was established that locus of control in the personality of alcoholic patients became significantly more internal after KPT (from  $11.1 \pm 4.8$  to  $30.3 \pm 5.3$ ;  $P < 0.01$ ). This means patients became more sure about the ability to control and manage different situations of their life, they became more responsible for their life and future after KPT.

### **Psychosemantic Changes**

#### ***Color Test of Attitudes and Personality Differential***

We also studied changes in the psychosemantic domain induced by KPT. The study used the data from 69 alcoholic in-patients treated with KPT in our hospital. All patients were examined by the personality differential test (PD) (Bazhin and Etkind, 1983) (a personality oriented version of Osgood's semantic differential (Osgood et al., 1957)) and also by the color test of attitudes (CTA) (Etkind, 1980) before and after the treatment.

The analysis of the CTA results revealed that after KPT there occurred significant positive changes in the nonverbal emotional attitude to a psychotherapist, close relatives, to the ideal image of self, and to the image "Me sober," At the same time, the attitude to the image "Me drunk" became more negative. According to the PD data, significant positive changes occurred after KPT only in respect to the attitude toward the person himself (Krupitsky, 1992).

After KPT there occurred a considerable decrease in differences between certain indicies of the CTA and that of PD in respect to the same images. This decrease was evidenced by the reduction of the difference between the verbal (realized) and nonverbal (unrealized) assessments of personal attitudes. Such reduction was mainly related to the change in the CTA indices and appeared to be the strongest for the sphere of attitudes to a psychotherapist, relatives, the image "Me sober," and the ideal image of self.

Thus, KPT produced considerable and significant positive changes in the domain of personality attitudes, which took place due to the transformation of nonverbal (unrealized) emotional attitudes. KPT resulted in a decreased level of dissonance between isosemantic indices as measured by CTA and PD which could be interpreted as a reduction of dissonance between verbal/conscious and non-verbal/unconscious thoughts and feelings regarding alcohol use and personality characteristics and relationships.

One should also underline the fact that, according to the CTA data, there occurred strong positive changes in patients' nonverbal (unrealized) assessments of the attitudes toward the psychotherapist, close relatives, to the image "Me sober," and to the ideal image of self. This means that the patient has internally grown to emotionally accept these images and, in turn, the attitudes toward sobriety connected with them. Thus KPT of alcoholism may be of benefit by transforming unconscious attitudes, particularly those related to sobriety. The enhancement of the relationship to the therapist may have enhanced transference issues which may also have had a therapeutic effect.

A special note should be made of the discrepancies between the verbal and nonverbal estimates of a patient's personal attitudes registered before KPT. These discrepancies, obviously, reflect the presence of an essential discord between the conscious and unconscious estimates of a personality's attitudes. This discord reflects a peculiar difference between the subject's unconscious and conscious mind, and possibly characterizes the ambivalence of the patient's position and the disagreement between what is declared at the verbal level and what takes place at the level of the immediate emotional experience. Such discord may give rise to psychological discomfort, internal tension, to difficulties in communication with the environment, i.e. to the reduction of a person's adaptation, which after all leads to alcoholism relapse. Therefore, the reduction of such discord due to KPT should be considered as an achievement of a personality's psychological status which favors sobriety.

#### **A study with repertory grids (Kelly matrixes)**

Ten alcoholic patients were tested with verbal and special nonverbal (color) repertory grids before KPT and after it. Then we calculated the mean verbal repertory grid (MVRG) and mean color (nonverbal) repertory grid (MCRG) for all 10 patients together. Four MVRG and MCRG (2 before KPT and 2 after KPT) were processed by the standard programs of repertory grid computer-assisted analysis (Fransella and Bannister, 1977), and then semantic spaces of the personality were built (Fig. 1 and 2). The semantic space of the personality (built on the basis of multidimensional assessments of elements with constructs) shows semantic interrelationships and interconnections between elements and/or constructs of the repertory grid.

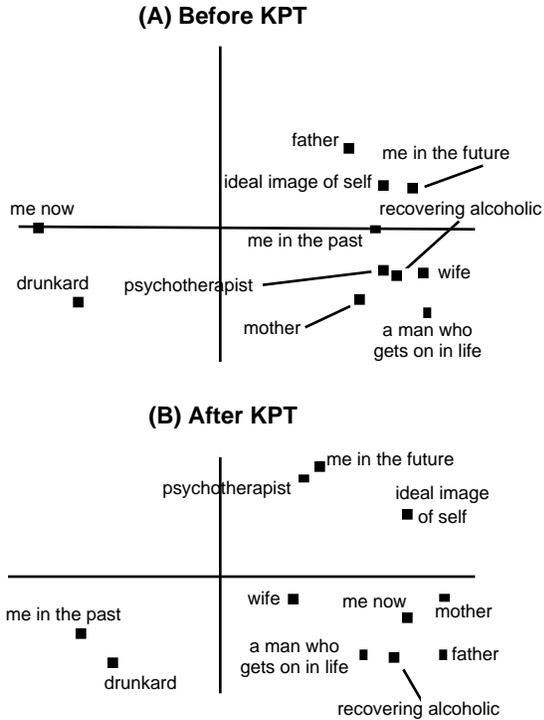


Figure 1. Semantic space of the mean color repertory grid of alcoholic patients

The results of this study have demonstrated some positive changes in the semantic space of the personality of alcoholic patients, particularly in the space of personality characteristics of the color repertory grids. The image "Me now" was close to the image "Drunkard" and far from the group of such positive images as "Recovery alcoholic," "Ideal image of self," "Wife," "A man who gets on in life," and others in the semantic space of the MCRG before KPT (Fig.1A). After KPT the image "Me now" became close to the group of positive images described above and far from the image "Drunkard" in the space of MCRG (Fig.1B). At the same time the image "Drunkard" became closer to the image "Me in the past." These data indicate that alcoholic patients emotionally perceived (identified) themselves as drunkards before KPT. After KPT their emotional perception of themselves had been changed: they emotionally identified themselves with "recovery alcoholic" and other positive images in the semantic space of personality characteristics and value orientations, and identified themselves as drunkards only in the past.

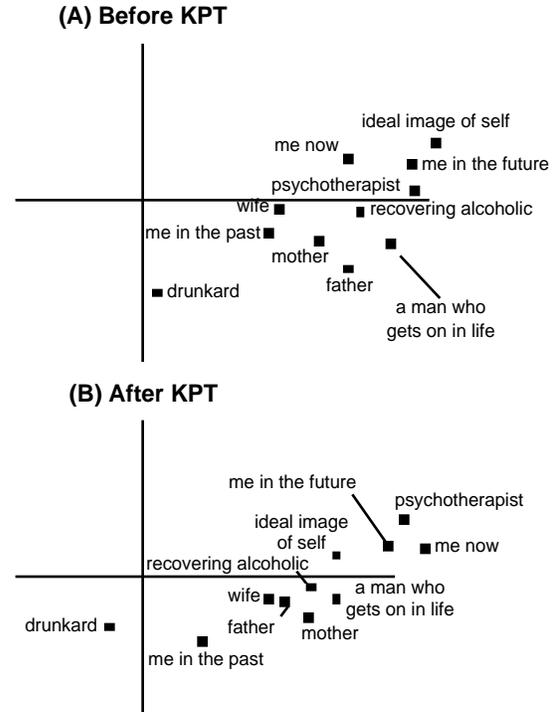


Figure 2. Semantic space of the mean verbal repertory grid of alcoholic patients

The changes in the verbal repertory grids were not so significant as in the color repertory grids (Fig.2A and 2B). The image "Drunkard" only became a little bit more distant from the group of positive images and closer to the image "Me in the past." It is interesting to note that patients already identified themselves with positive images at the level of verbal self-identification in the semantic space of personality characteristics and value orientations before KPT, whereas they identified themselves in the same way at the level of nonverbal (unaware, mostly emotional) perception only after KPT. This can be interpreted to mean, first of all, that KPT creates a profound nonverbal association with the sobriety self-concept, and second, that KPT brings about the attainment of similarity (resemblance) of verbal (realized) and nonverbal (unaware) perception by the patients of their individual self and the world.

These data show that KPT positively transformed primarily the nonverbal (unaware, mainly emotional) perception by alcoholic patients of their individual self. Thus, it is possible to conclude that KPT positively transformed mostly the emotional self-identification (self-concept) of alcoholic patients.

### Content Analysis Data

We also carried out content-analysis of psychedelic experiences written down by our patients after their KPT sessions. It is of interest to note that a content analysis from the written self-reports of 108 male alcoholic patients whose personality

characteristics were defined by the MMPI demonstrated a number of statistically reliable correlations between some MMPI scales and the content of the psychedelic experience described in self-reports. Thus, one may conclude that the ketamine psychedelic experiences are to a certain extent determined by the personality characteristics of patients.

In addition we also have demonstrated the relationship (statistically reliable correlations) between the content of the ketamine session experiences and the MMPI profile changes caused by KPT. That is, the content of the ketamine session experiences to a certain extent determines the personality changes caused by KPT.

### **Effect on Life Values**

Thirty patients assessed with the LCS were also examined with the Questionnaire of Terminal Life Values (QTLV) developed by Senin (1991) and based on Rokeach's approach to human values and beliefs (Rokeach, 1972, 1973). Patients were examined with QTLV twice: before and after KPT.

This study has demonstrated a number of significant positive changes in patient's values as a result of KPT. KPT enhanced the importance of such life values as creativity, self-perfection, spiritual contentment, social recognition, achievement of life purposes and individual independence. These changes were mostly expressed in such areas of life values actualization as family, education and social life. It is evident that such a positive transformation of a patient's life values system brings about enhanced motivation for a sober life and favors sobriety.

### **Effect on grasping the meaning of life (purposes in life)**

Ten alcoholic patients were studied before and after KPT with the Purpose-in-Life Test (PLT) elaborated by Crumbaugh (1968) and based on Frankl's concept of man's aspiration for the meaning of life. The PLT was adapted in Russia by Leontiev (1992) in the Department of Psychology of the Moscow State University.

This study has shown that KPT causes a significant increase in the index of grasping the meaning of life in alcoholic patients (from  $89.7 \pm 5.7$  to  $115.3 \pm 3.2$ ;  $p < 0.01$ ). Before KPT, the index was below the average normal level, but after KPT it was greater. These changes mean that after KPT patients were able to grasp better the meaning of their lives, their life purposes, and perspectives. Their life became more interesting, emotionally saturated, and filled with meaning for them after KPT. They felt themselves more able to live in accordance with their concept of the meaning of life and life purposes as a result of KPT. Such changes favor a sober life, particularly from the standpoint of Frankl's approach

which considers alcoholism as an "existential neurosis," as a consequence of losing the meaning of life and the appearance of a specific "existential void" (Frankl, 1978), which KPT we believe is able to fill, at least to some extent.

### **Effect on Spirituality**

We have studied the influence of a profound mystical (transformative) experience during KPT on the level of spiritual development of the alcoholic patients in this study. For the assessment of changes of spirituality we used our own special Spirituality Scale based on a combination of the Spirituality Self-Assessment Scale developed by Charles Whitfield, who studied the importance of spirituality in alcoholism therapy in Alcoholic Anonymous (Whitfield, 1984), and the Life Changes Inventory developed by Ken Ring to estimate the changes of values and purposes of life produced by near-death experiences (Ring, 1984). It was demonstrated by our Spirituality Scale that the increase in the level of spiritual development of our alcoholic patients due to KPT was comparable to the increase induced in healthy volunteers by a special course of meditation and was much greater than the changes in spiritual development induced in alcoholics by a training program of relaxation techniques and self hypnosis (autogenic training). It is evident that the increased spiritual development induced by KPT in alcoholic patients is very auspicious for sobriety. Moreover, the results of the study of KPT's influence on spirituality demonstrate that KPT is much more than simply the creation of an attitude in alcoholic patients toward a sober life. These results show that KPT brings about profound positive changes in life values and purposes, in attitudes toward the different aspects of life and death, and, in turn, in the alcoholic's world view. Many reports suggest religious or spiritual conversion as an important factor in "spontaneous" recovery from drug abuse, and Alcoholic Anonymous programs have a distinct spiritual/religious orientation (Whitfield, 1984; Corrington, 1989; Grof, 1990). A therapy that enhances the likelihood for a conversion type experience therefore might have utility in the treatment of substance abuse. Psychedelic drug-assisted psychotherapy may represent one method to elicit religious spiritual experience in patients with chemical dependence.

Thus, KPT brings about positive changes in personality characteristics, nonverbal emotional attitudes and self-concept, positive transformation of value orientations and grasping the meaning of life, and also spiritual growth. All these psychological changes favor a sober life.

### **Underlying Biochemical Mechanisms**

We also carried out biochemical investigations of the underlying mechanisms of KPT. The results of

the biochemical investigations have shown that during the ketamine session there occurred a real decrease in the activity of MAO-A in blood serum and MAO-B in blood platelets, and there also was an increased dopamine level in blood. Plasma serotonin and GABA concentrations were not altered significantly. An increase of ceruloplasmin activity was statistically significant and the (-endorphin level increased during the KPT session (Krupitsky et al., 1990).

Changes in neurotransmitter metabolism could have some notable aspects. First, they allow some speculations about the underlying neurochemical mechanisms of the psychedelic action of ketamine (Krupitsky et al., 1990). For example, an increase of ceruloplasmin activity causes a corresponding increase in the conversion of monoamines into adrenochromes which have been speculated to possess hallucinogenic activity. This would be particularly true under conditions of inhibited MAO activity and increased dopamine levels. It is of interest that such conditions occur during the action of many hallucinogens (Hamox, 1984; McKenney et al., 1984).

Second, the fact that the pharmacological action of KPT affected both monoaminergic and opioidergic systems, i.e. those neurochemical brain systems that are involved in the development (pathogenesis) of alcohol dependence, is an important result of this biochemical investigation. It is possible that these changes are related to a certain extent to the efficiency of this method.

### **Underlying Neurophysiological Mechanisms**

According to the data from computer-assisted EEG analysis we discovered that ketamine increases delta activity (a 1.5-2 fold increase) and particularly theta activity (a 3-4 fold increase) in all regions of the cortex. This is evidence of limbic system activation during ketamine sessions, as well as evidence for the reinforcement of the limbic-cortex interaction. This fact can also be considered to a certain extent to be indirect evidence for the strengthening of the interactions between the conscious and subconscious levels of the mind during the KPT.

### **Clinical observations**

Our clinical observations suggest that KPT might also be helpful for the treatment of dependence on other drugs (e.g. heroin, ephedrone). Our method involves the repeated injection of small doses of ketamine, which allows for the maintenance of a constant verbal relationship with the patient. We believe that KPT might induce in some drug abusing patients the same psychotherapeutic effects that we have seen in alcoholics.

Ketamine psychedelic therapy proved to be effective for the treatment of personality disorders in

alcoholic patients (Ivanov et al., 1995). Sixty-four alcoholic patients with different personality disorders (avoidant - 20 patients, histrionic - 21 patients, and borderline - 23 patients) were treated with KPT. Data from clinical (Bekhterev Psychoneurological Research Institute rating scales) and psychological (MMPI, Spielberger State-Trait Anxiety Scale, T. Leary test of interpersonal relationships) studies showed the differential efficacy of ketamine psychedelic psychotherapy in the different groups of patients. KPT proved to be very effective in patients with avoidant personality disorders, less effective in patients with histrionic personality disorders and least effective in patients with borderline personality disorders. It should be noted that KPT positively influenced on the personality characteristics assessed by MMPI in all groups of alcoholic patients with personality disorders.

The potential of ketamine-assisted psychedelic therapy is not restricted to the treatment of addiction. According to data from our pilot study (20 patients, 7 male and 13 female), ketamine-assisted psychedelic therapy is also quite effective in treating neurotic disorders. This research has demonstrated that the efficacy of ketamine psychotherapy differed with various forms of neuroses: psychedelic therapy proved most effective in treating neurotic (reactive) depression and post-traumatic stress disorders, and least effective in treating obsessive-compulsive and phobic neuroses. Hysterical neurosis appeared to be most resistant to psychedelic therapy.

### **Conclusion**

We have been working with KPT since 1985 and have already treated more than 1000 alcoholic patients with KPT without any complications such as protracted psychoses, flashbacks, agitation, or ketamine abuse. KPT appears to be a safe and effective method for treatment of alcohol dependence. It seems to be an especially powerful tool in Russia, where there was no psychedelic revolution in the 1960s, where almost no one knows the meaning of "psychedelic," or can even imagine that this drug might be used for recreation, or for fun. In Russia, therefore, KPT looks particularly unusual and powerful.

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