

Internal Inhibition: A Form of Nonconflict Breaking Mental Alcohol Dependence in Narcology

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A conceptually new method for breaking mental alcohol dependence is described. The results indicate a demolishment of the alcoholic stereotype and the formation of a qualitatively new behavioral reaction to alcoholic stimuli.

Key Words: *acupuncture; alcoholism; internal inhibition; mental dependence; conditioned reflex*

The mental dependence on alcohol is the main therapeutic target in the treatment of alcoholism [6]. Drug therapy and physical methods of treating alcoholism are aimed at suppressing this dependence [6]. Still, both narcological practice and experimental data point to the failure of this therapeutic strategy in alcoholism, due to many reasons. First, the developing mental alcohol dependence is a constant, its state being intermittently latent or actualized [3], and therefore it has to be constantly suppressed, which leads to treatment dependence. Second, the craving for alcohol is characterized by a morphofunctional and neurochemical heterogenesis [7], which is why the suppression of mental alcohol dependence is associated with distorted activity of the body's centers of natural requirements. Internal inhibition is a result of an imbalance and conflict between two systems of excitation, two integral activities of the organism in the space-time structure of the inhibited conditioned reflex [1]. Basing ourselves on the theory of internal inhibition and the theory of functional systems of the body [1], we may propose that breaking the mental dependence on alcohol in the structure of the alcoholic dynamic behavioral stereotype may be achieved by disturbing the balance between conditioned stimulation

(releasing factors) and stimulation caused by failure to supply the unconditioned stimulus (alcohol). This will induce the body to engender a qualitatively new activity while preserving intact the response to old conditioned stimuli.

The present report describes a method for nonconflict breaking of mental alcohol dependence in alcoholics based on the formation of internal inhibition in the structure of the alcoholic dynamic behavioral stereotype.

MATERIALS AND METHODS

The method for treatment of alcoholics was developed at the Research and Practical Center for Reflex Therapy of Alcoholism in 1989-1993. A total of 285 male patients aged 32 to 48 were examined who were suffering from second-degree alcoholism (dipsomania or pseudodipsomania, moderately rapid progress of the disease). All the patients had previously been repeatedly treated for alcoholism: 48 had been given drug therapy, resulting in remissions lasting from 0 days to 2.5 months, 26 had undergone stress therapy (remissions from 3 weeks to 2 months), 14 acupuncture (remissions from 2 weeks to 4 months), and 8 had been subjected to conditioned reflex therapy (remissions from 2 weeks to 1.5 months). Forty-eight subjects were treated and examined; alcoholism was the underlying condition in 47 of these and a

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concomitant condition in one. The patients were not specially selected. The treatment consisted of 4 sessions. Each session was divided into three steps. The first session was carried out on days 18-19 of alcohol deprivation, the second 2 days after the first session, the third 3 days after the second, and the fourth a week after the third session. The symptoms were assessed in points during the third step of each session.

First session, step one. Development of conditioned reflex excitation in response to conditioned stimuli. For this purpose we used the method of recollections reduction. The recollections of a patient were reduced till the time when he had his last hard drinking. The purpose of the conversation was to excite a conditioned reflex reaction to specific verbal stimuli and to attain the stage of development of its autonomic secretory and weak emotional components. The physician monitored the patient's behavior, skin color, type of respiration, swallowing movements, facial expressions, tone of voice. The patient was not allowed to take a detached view of the picture of alcohol intoxication but was to immerse himself in it and to live through it again.

First session, step two. Access to smell and taste sensations is the most potent and rapid method of regression in a state of intoxication. For this purpose the patient was offered the smell of alcohol on cotton and had to inhale it at least four times. The physician then inquired about his sensations. Then 2-4 drops of a 40% solution of ethyl alcohol were administered under the tongue, and the patient described his sensations.

First session, step three. Puncture of the HE-GU points of Chinese acupuncture on the left in right-handed persons and of the auricular zone of thalamic sensitivity [5] on the right in right-handed persons, and vice versa. After puncture of the points the needles were continually rotated. This was followed by the manifestation of symptoms in a certain time order: a sense of "movement" in the stomach; intensive peristalsis; a taste of rotten food in the mouth; a bitter taste in the mouth. All the symptoms were rated in points according to the degree of their presence. The symptoms of the first session were assessed as 3 points. After a bitter taste appeared in the mouth, the rotation of needles was stopped. The time of needle rotation varied in different patients from 8 to 15 min.

Second session. The same steps were performed as during the first session. During the second session sensations connected with gastrointestinal peristalsis were absent, but gustatory sensations in the mouth persisted. The time of needle rotation varied from 8 to 15 min.

Third session. The same steps were performed as during the first and second sessions. The time of needle rotation was determined by the time of manifestation of a bitter taste in the mouth.

Fourth session. It was no longer possible to immerse the patient in a state of alcohol intoxication during the first step of this session. Therefore, some alcoholic situations were analyzed during this session which the patient had experienced since the onset of treatment. In the second step the patient was offered only the smell of alcohol but no drops of ethanol solution. The time of needle rotation was determined according to the third session.

RESULTS

The following reactions were recorded in all the patients during the first session after exposure to releasing factors: hypersalivation; change of respiration type; perspiration (according to CGR); changed coefficient of interhemispheric asymmetry (unpublished data [6]); animated facial expression; changed skin tone; the motivational component of craving was not recognized at this moment of the reaction. Alcoholics denied craving alcohol when first asked by the physician, for releasing factors were absent at that time. But as soon as one of these factors appeared, the subject's behavior drastically changed. The symptoms recorded during the first step of a session indicate that exposure to conditioned stimuli was conducive to the appearance of autonomic, secretory, and weakly manifest emotional components in the structure of the alcoholic dynamic behavioral stereotype. Other researchers have observed the same [2,3,9]. Proceeding from experimental findings [11], we submit that the manifestation of these symptoms in the patients represents a "jumping-ahead" reaction of an adaptive nature. Some authorities [8] believe that at the neurophysiological level excitation of the subthalamic structures responsible for the formation of alcohol motivation occurs at that moment, as well as a rearrangement of the functional activity and adaptation of all body systems to alcohol-obtaining and alcohol-consuming activity. At this point the excitation has not yet involved the motoneurons, and realization of the motor component of the conditioned reflex reaction has not yet started. Therefore, the induced conditioned reflex reaction at this time is probably at the stage of afferent synthesis, the stage of formation of the efferent mechanism of action.

After puncture of the acupuncture points and needle rotation, a sense of "movement in the stomach" was recorded in 44 subjects, increased

intestinal peristalsis in 42, a taste of rotten food in the mouth in 48, and a bitter taste in the mouth in 48 subjects. These data indicate a changed reaction of the gustatory and olfactory analyzers and of the motor activity of the gastrointestinal tract to conditioned alcohol stimuli, evidently under the effect of nonreinforcement by the unconditioned stimulus (alcohol) and of afferent signals from the acupuncture points. The excitation by nonreinforcement is enhanced by excitation from the acupuncture point receptors. Subthreshold stimulation with the acupuncture needle sends a potent afferent signal to the hypothalamic structures of the brain and changes the activity of neurons of the prime biological motivations [4] with which the formation of alcohol motivation is associated in alcoholics [11]. By this time a "focus" of motivation, an overpowering alcohol motivation, appears in the subhypothalamic structures as a result of releasing factors. This motivation "focus" attracts an artificially induced afferentation discharge [10] and, in accordance with P. K. Anokhin's concept, afferent synthesis changes and a new efferent behavioral apparatus forms on account of this attraction.

A regressive time course of symptoms was observed during the sessions. The first session was assessed as 3 points. At the second session no gastrointestinal symptoms were recorded (2 points). At the third session the patients felt only a bitter taste in the mouth (1 point). At the fourth session only a weak bitter sensation in the mouth was felt or nothing at all (0 points). Afferent signals from acupuncture points promote the formation of a new action acceptor as early as during the first session, breaking the alcoholic behavioral stereotype. This is confirmed by the fact that if a patient happened to be in the company of drinkers after the first session (24 subjects), he developed in response to releasing factors (pouring of alcohol into glasses, smell of alcohol, etc.) nausea (18 subjects) or even vomiting (6 subjects). We believe that such situations help the physician fix the conditioned inhibition obtained in the first session. All the symptoms ran their course more rapidly during subsequent sessions in these 24 patients and were less pronounced (rated, respectively: 1; 0; 0 during sessions).

The intensity of the reaction of the gustatory and olfactory analyzers and of the gastrointestinal tract appears to conform to the degree of abatement of conditioned reflex reactions under the effect of nonreinforcement and acupuncture and to the formation of a qualitatively new behavioral reaction to alcoholic releasing factors.

The last catamnestic examination was carried out in all the patients in May, 1993. Complete remission was recorded: from 20 months to 2 years in 34 patients and from 15 to 19 months in 12 patients. Two patients had relapses: one of them suffered from manic-depressive psychosis, and the relapse was associated with an exacerbation of the underlying disease, in the other a stressful situation (the death of his mother) led to hard drinking for 6 days, and treatment had to be repeated; by May, 1993 the remission had lasted 16 months.

The patients were questioned to detect signs indirectly indicating actualization of the primary pathological craving for alcohol during remission [3]. The data of the interviews were as follows: two subjects complained of poor general health and two of a change in appetite; none of the patients mentioned "missing something", general anxiety, dissatisfaction, boredom, fixation on alcoholic stimuli, more frequent talking about alcohol and related topics, increased tobacco smoking, short outbreaks of unmotivated anxiety, general motor anxiety, or animated responses to alcoholic stimuli; two subjects complained of insomnia.

Interviews with the patients' relatives in May, 1993 showed that all the patients had good social relationships after therapy: no cases of hot-tempered or aggressive behavior were observed (such situations had proved particularly troublesome for the relatives when they appeared after a previous course of alcohol treatment; the patients were in a good mood, did not display miserliness or litigiousness, and did not make unrealizable plans; there were no cases of pathological jealousy or attempts to "educate" their children.

Analysis of the results showed that during remissions after therapy there were no signs of the changes in somatovegetative state and behavior that are characteristic of patients in the period of actualization of the primary pathological craving for alcohol when it is not reinforced with alcohol, and that alcohol abstinence was not a conflict situation for these patients. The conditioned inhibition induced in these patients broke down the alcoholic dynamic behavioral stereotype, shaped a qualitatively new reaction to alcoholic stimuli, and differentiated the behavioral reaction by motor and emotional components. The data provide evidence that internal inhibition is an indispensable component of acquired activity.

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MICROBIOLOGY AND IMMUNOLOGY

Phosphoinositide Metabolism in Endothelial Cells of Human Umbilical Vein Effected by *Y. pestis* Toxin

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Histamine stimulates the metabolism of inositol phosphates and raises the level of prostacycline in endothelial cells. The activatory effect of histamine markedly decreases when incubation is performed in the presence of PT, whereas the baseline level of phosphoinositide metabolites does not change in endothelial cells.

Key Words: plague toxin; endothelium of human umbilical vein; phosphoinositide metabolism

Thrombohemorrhagic syndrome, or the syndrome of disseminated intravascular coagulation (DIC) is characteristic for plague and plague intoxication [1,3]. The damage inflicted on endothelial cells (EC) both by the pathogenic organism itself and by its toxins is one of the numerous factors which provoke the development of DIC in bacterial intoxications [3]. The biochemical mechanisms underlying the damaging effect of *Y.pestis* toxins are not clear. It is known that the regulation of vascular tonus and of thromboresistance is mediated by neurotransmitters and hormones via specific receptors

which are situated on the outer surface of endothelial cell membranes [13]. In addition to cAMP-regulating receptors there are so-called Ca-mobilizing receptors [4,12], whose effect is mediated by the hydrolysis of phosphatidylinositol-4,5-biphosphate (IP) to yield inositol-1,4,5-triphosphate (IP3) and 1,2-diacylglycerol (DAG). IP3 increases the intracellular concentration of Ca due to its mobilization from the intracellular depot [4,6,7]. DAG is the activator of protein kinase C and is a source of arachidonic acid, which metabolizes into prostacycline, thromboxane, and other eicosanoids in EC [9].

In this study we examined the effect of plague toxin (PT) on phosphoinositide metabolism (PIM)

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