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CHEMICAL AVERSION THERAPY FOR
MORPHINE ADDICTION

THESIS

Presented to the Graduate Council of the
North Texas State University in Partial
Fulfillment of the Requirements

For the Degree of

MASTER OF ARTS

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Denton, Texas

December, 1973

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CHEMICAL AVERSION THERAPY FOR MORPHINE ADDICTION

Opiate addiction has become a major social problem in this country, and as such, has produced a great number of new treatment approaches. Many treatment centers have appeared around the country in response to the growing number of young addicts requiring help. However, poor record keeping at many experimental treatment facilities has made difficult the evaluation of success or failure of a particular treatment mode.

Synanon, a major drug treatment society, has been operating since 1958 with a better success rate than most facilities can report. In 1962, it was determined that of those addicts who remained at Synanon longer than three months, better than 70 per cent were still living there as "clean" ex-addicts. A more recent appraisal of the data suggested that this percentage of success had improved (Yablonsky and Dederich, 1965). The methods used by the ex-addict counselors are primarily based around confrontation group therapy sessions. The addicts live and work together under the supervision of the ex-addict counselors. As they prove their willingness to work toward changing their lives, they are given more and more responsibility and freedom, and many eventually become counselors themselves.

Methadone maintenance programs have proliferated in the last few years, but have been quite controversial. The addicts are given methadone orally on a daily basis under the supervision of a physician at a clinic designed specifically for this purpose. Methadone is physically addictive, but produces no euphoria or other side effects when ingested orally. In addition, it eliminates the drug craving reportedly experienced by withdrawn narcotics addicts and produces a marked tolerance to the effects of ordinary doses of other opiates such as morphine and heroin. This phenomenon has been labeled narcotic blockade by Dole and Nyswander (1965), who have investigated this method of treatment. By using this treatment approach, former addicts have been able to return to normal community living and have become self-supporting. Critics have argued that the individual is still drug dependent (Ausubel, 1966), but Dr. Jerome Jaffe (1969), current head of the President's Commission on Drug Abuse, has made this statement concerning methadone maintenance:

Thus, while patients are physically dependent on methadone, the difference between the psychologically and physiologically disruptive effects of intravenous heroin and the barely perceptible effects of oral methadone may be more significant than the fact that pharmacologically they are both narcotic drugs (Jaffe, 1969, p. 355).

A new class of drugs called narcotic antagonists have been used to block the action of narcotics. These drugs occupy the site within the nervous system at which narcotics have their actions and so prevent the user from experiencing

any drug-induced euphoria and also prevent addiction, regardless of the quantity of narcotics ingested or injected (Martin, 1966).

It has been suggested by various researchers (Lindesmith, 1965; Nichols, 1965, 1968; Wikler, 1965, 1968) that compulsive opiate use is primarily a result of conditioning. Narcotic users have acquired a complex set of instrumentally and classically conditioned responses which perpetuate their drug taking and also make relapse after withdrawal much more likely to occur. Wikler (1965) has described the process by which addiction is maintained:

The motivations for self-maintenance of addiction in man are largely unconscious ones, above all the gratification by each dose of morphine of the need for the drug engendered by physical dependence. Furthermore, it was suggested that "being hooked" furnishes the addict with a motivational basis for sustained activity ("hustling for drugs") directed to recurring but attainable goals, thereby preventing boredom and also securing approval from his peers, i. e., "addict society" (Wikler, 1965, p. 87).

Schuster (1967) has shown evidence to indicate that animals are willing to inject themselves with narcotics in order to experience the euphoria (anthropomorphically speaking) associated with the drug even when not physically addicted and in the absence of apparent tension.

Wikler (1965) has also stated this theory regarding the phenomenon of relapse:

Relapse may be attributed at least in part to two factors operating during previous episodes of addiction: (1) classical conditioning of physical dependence through repeated temporal contiguities between a specific environment and the occurrence of morphine-abstinence phenomena;

and (2) reinforcement of instrumental activity (morphine acquisitory behavior) through repeated reduction by the drug of such abstinence phenomena as developed during intervals between doses (Wikler, 1965, pp. 88-89).

Regardless of the mechanism by which opiate use is perpetuated, one of the best methods for eliminating it would be for the addict to use his narcotics in the usual manner but experience no euphoria or tension reduction as a result. The response of taking drugs could be extinguished in the natural environment in this manner.

This highly desirable result could be accomplished if the addict could be made to take enough narcotic antagonist to prevent the narcotic from reaching its receptor site in the body. This approach has been experimentally evaluated by Jaffe (1967) and Jaffe and Brill (1966), and research is being continued in order to develop the most effective antagonist for this purpose.

Behavioral approaches to drug addiction have been rare until the last few years. Most of those which have been done have used an aversive conditioning paradigm. Raymond (1964) used apomorphine to induce nausea during an aversion treatment of a woman addicted to physeptone for six years. The treatment was successful, and the woman was drug-free two and one half years later.

Liberman (1968) used a similar technique with two morphine addicts. One of the subjects was drug-free one year after treatment, but the other subject relapsed after an initial period of abstinence.

Aversive conditioning using a portable shock apparatus was done by Wolpe (1965) with a physician addicted to demerol. Wolpe reasoned that the craving for the drug occasionally may arise internally rather than as a result of external stimuli and should be dealt with at the time it is experienced. The shock was self-administered whenever the physician felt the craving for demerol, as well as when observable stimuli produced the urge to take the drug. The subject remained totally abstinent for three months following treatment but relapsed during a period of excessive stress. Wolpe suggested that periodic booster shocks might have prevented the eventual relapse.

The effects of the drug succinylcholine (also called anectine or scoline) have been used as an aversive stimulus by a variety of researchers. This drug induces respiratory paralysis and an accompanying sensation of horror in the patient. Vandewater, et al. (1963) have described the full range of physiological changes resulting from the injection of this substance. Campbell, et al. (1964) investigated the ability of this drug to produce classically conditioned responses in human subjects. The results of their investigation showed that the drug was capable of producing conditioned responses which did not extinguish over time but rather became stronger in spite of repeated extinction trials.

The first researchers to actually pair this aversive stimulus with an undesirable behavior were Sanderson, et al.

(1963). Of fifteen alcoholic patients treated, twelve showed some signs of aversion to alcoholic beverages as a result of treatment. They concluded, however, that the respiratory trauma was not sufficient to produce a complete loathing for alcohol.

The same group of researchers headed by Madill (Madill, et al., 1966) again applied this treatment to alcoholics, using three treatment groups--conditioning, pseudo-conditioning, and placebo. Significant decreases in drinking were found in the two conditioning groups but not the placebo group, but other aspects of behavior investigated in the same study provided more ambiguous data.

Clancy, et al. (1967) treated another group of alcoholics and compared the efficacy of respiratory trauma conditioning to "placebo," "other therapy," and "no treatment" groups. Chemical aversion therapy produced the greatest percentage of increased abstinence, but the difference between that method and the placebo group was not significant, while the other group differences were.

Another study was done by Farrar, et al. (1967) in which twelve alcoholics were given a one-trial extinction by punishment procedure using succinylcholine as the unconditioned stimulus. After a one-year follow-up, only two subjects reported continued abstinence.

A replication of the study done by Sanderson, et al. (1963) was attempted by Holzinger, et al. (1967). Of twenty-one

alcoholic patients treated in that manner, only two were not drinking at all when they were contacted four months after treatment. No explanation was offered as to their lack of success as compared to Sanderson's relative success.

The only reported use of respiratory trauma with narcotic addicts was done by Thomason and Rathod (1968) in Great Britain. Of the ten addicts who completed treatment, eight had not used heroin or any other intravenous drug since the treatment was terminated. The remaining two subjects lapsed once after treatment, but one became completely drug free following another series of treatments. The remaining subject used chloral hydrate upon release from the treatment facility but did not use it intravenously as had been her habit. At the last follow-up, the other nine patients had been drug free for an average of thirty-three weeks.

These studies led the experimenter to investigate the use of chemical aversion therapy using anectine as the aversive stimulus with a morphine addict. The success of Thomason and Rathod with heroin addicts suggested that their experimental method would be useful as a reference while designing this study.

The treatment hypothesis was that the patient's use of intravenous narcotic drugs would be eliminated through the application of chemical aversion therapy. Chemical aversion therapy was operantly defined as the injection intravenously of anectine into the patient concurrent with his self-injection of his narcotic of choice.

Method

Subject

The subject was a nineteen-year-old hospitalized male who had a two-year history of multiple drug use. He had been using morphine and related compounds regularly for approximately six to eight months and habitually injected them intravenously.

During high school, the patient had normal interests and had excelled in athletics. Prior to entering college, the patient had married; he and his wife had one child. When he began to use drugs heavily, his wife left him and ultimately obtained a divorce and custody of their child. Although his stated ambition was to become a lawyer, he was unable to finish his first semester of college due to his constant drug usage. He had not held a job for over a year at the time of treatment. He had received some support from his parents during his marriage and had been obtaining drugs by robbing drug stores when no one was there. Part of the drugs he obtained were sold, and the rest he used himself.

When he finally indicated to his parents that he would like to quit using drugs, they offered to pay for hospitalization and treatment. The hospital at which the treatments were given was an in-patient private facility with a patient population of seventy-five. The subject was housed in a locked building and shared a room with another young man. When in the locked building, the patient spent his time in occupational and recreational therapy, played pool with other

patients, and attended a teenage group therapy session twice a week. He had been hospitalized for one month when the aversion series was begun. At the time treatment was begun, the subject was fully withdrawn from all addicting drugs and was in very good health.

Apparatus

One room with a moveable hospital bed was used for all treatments. A red light was placed in front of the patient as a discriminative stimulus to begin injecting the drug.

Three injectable drugs were used during the procedure; they were demerol, anectine, and narcan. Demerol was used as the drug with the most similar effects to the usual drug of choice of the patient. Within about one minute after injection, the drug produces sensation commonly referred to as "being high."

Anectine is a chemical which produces temporary muscular paralysis and respiratory inhibition or arrest. Within five to ten seconds after injection, the onset of these effects can be observed. The duration of the drug effects is from five to seven minutes. This drug produces subjective sensations of horror due to the patient's inability to move, and his belief that he is suffocating. No physical damage or pain is associated with this chemical.

Narcan is a narcotic antagonist which blocks the acceptance of any opiate derivative at the cellular receptor

site within the body. About two minutes after injection, any opiate-induced effects will be cancelled, and Narcan will continue to block the effects for up to six hours, depending on the dosage. This drug was used to prevent the patient from experiencing any demerol effects after the Anectine wore off.

An artificial resuscitator and oxygen were made easily accessible in the treatment room so that prolonged respiratory arrest could be terminated, should it occur.

All medical paraphernalia were kept behind the patient during treatment. A screen was utilized to keep the patient from watching the other injections being given him.

Procedure

Prior to the treatments, it was explained to the patient that the effects of the chemical to be used were very unpleasant. He was also told that as a result of these treatments, this unpleasantness would become associated with the drugs he had been using prior to hospitalization. He was also given an opportunity to observe a person who was experiencing the effects of anectine before beginning his own treatment.

A total of seven treatments were given during a two-week period. The treatments were given at random intervals, no more than one each day. The patient had no advance warning as to when he would undergo each treatment. During each of the treatments a psychiatrist, two psychologists, and a nurse were present. The patient was allowed to prepare the demerol

injection himself in order to make the procedure as realistic as possible. He was instructed to sit on the hospital bed, straddling it, and to watch the red light in front of him. He was to inject the demerol when the light went on. Within one and a half minutes, he was given the anectine injection in his other arm by the nurse. A screen blocking his vision prevented his knowing exactly when this injection was given. Approximately five seconds later, the anectine produced observable effects in the patient. As he lost control of his muscles, he was assisted in lying back on the bed. Although he could not speak or move, he was conscious and could hear and feel the presence of objects touching him. During this period of paralysis, a hypodermic needle was repeatedly rubbed over his forearm, and he was helped to grasp the syringe and feel it. His eyelids were held open and a used syringe was placed within his field of vision.

Verbal suggestions were continually whispered in his ear in order to make a conscious connection between his current condition and future drug usage. Typical admonitions were, "This is the way it feels to die from a drug overdose. This is the way it will feel if you ever use drugs again. Whenever you even think of doing drugs, this is the way you will feel." When the effects had completely worn off, he was given several minutes to relax before returning to his room. He was then offered a syringe containing demerol to take with him back to his room; he was told he could use it as he wished.

On every occasion, he refused to take the syringe. He was observed closely for the rest of the day by the nursing staff to make sure that no adverse post-treatment effects occurred.

The time interval between the demerol injection and the anectine injection was decreased in each successive treatment (Table I). In this manner, an attempt was made to pair

TABLE I
DRUG DOSAGE AND TIMING OF
DRUG EFFECTS

Treatment	Dosage and Timing
I.	625 mg. Demerol 90 seconds later--Anectine effects
II.	50 mg. Demerol 70 seconds later--Anectine effects
III.	75 mg. Demerol 60 seconds later--Anectine effects 1 minute later--.4 ml. Narcan intravenous 10 minutes later--.4 ml. "subcutaneous"
IV.	50 mg. Demerol 40 seconds later--Anectine effects .8 ml. Narcan
V.	50 mg. Demerol) .8 ml. Narcan) Simultaneous 60 seconds later--Anectine effects
VI.8 ml. Narcan 1'55" later--50 mg. Demerol 10 seconds later--Anectine effects 2 minutes later--second occurrence of Anectine effects
VII.	50 mg. distilled water 2 seconds later--Anectine effects

the aversive consequences with earlier behaviors in the chain leading to the drug effects. In the final treatment, the

anectine was injected simultaneously with the demerol which was, in reality, distilled water for the last treatment. The narcan injection was timed for each treatment such that no demerol effects would linger beyond the anectine effects.

Results

The data for this study consisted of verbal reports of the patient's behavior. These reports were obtained from the patient himself, his friends, and his parents. The treatment plan called for the patient to be subject to urinalyses at random intervals, but after the first one, the patient refused to cooperate. The first analysis run indicated that the patient had been drug free for at least twenty-four hours prior to that time. However, it was later reported that the patient had begun self-injection of drugs approximately two days after his release from the hospital and had continued to use a variety of drugs regularly. This report was subsequently corroborated by the information that he had been arrested for driving under the influence of drugs after he had crashed into and demolished a gas pump. Following that incident, it became impossible to contact the patient, who had begun to move from one dwelling to another. Contact with his parents indicated that he had obtained a job for the summer but had been unable to work more than fifteen days in two months.

Discussion

The criterion for success in this study was total abstinence from drug use. The criterion was not met, and in this case the results have cast some doubt on the efficacy of this treatment method. A major difference between this study and the study by Thomason and Rathod (1968) was the number of treatment sessions offered the patient. Their patients each were given forty-nine treatments, while this patient was given only seven. In addition, their patients received their aversion treatments in the context of a multifaceted and supportive therapy program which included an occupational program, special sessions with the parents of the patients, close and prolonged follow-up, both individually and in groups, and repeated urine checks for evidence of drug use.

Because of the lack of adequate controls over his behavior, the patient immediately took up his old habits for lack of new and better ways to do things. He began seeing old friends, whom he admitted were stimuli for him to inject drugs, having done so often in their presence. He was given instructions by the experimenter concerning ways in which he could maximize his chances of succeeding at remaining abstinent. These instructions included warning him to stay away from old friends who used drugs and to stay away from places where he knew he could make a "connection" for drugs. It was even suggested that he should move to a nearby town where the

student community would be very supportive of his attempt to remain drug free.

These suggestions were ignored, and the patient showed little motivation to remain abstinent upon his release from the hospital. His decreased motivation may have negated whatever conditioning resulted from the treatments.

Drug addicts often report a strong craving for narcotics even though they have been withdrawn from the addicting drug. This patient reported a high frequency of urges after having been withdrawn from morphine; had we administered a narcotic antagonist to him on an outpatient basis, his chances for success might have been greatly enhanced.

Many difficulties are inherent in attempts to use chemical aversion conditioning. One of the major complications is the existence of individual differences in reactivity to the various drugs used in these treatments. Rachman (1965) has pointed out,

People differ in the speed and extent of their reactions to the various drugs and, furthermore, the same person may react differently to the same quantity of drug on different days or at different times on the same day (Rachman, 1965, pp. 289-290).

Another problem peculiar to chemical aversive conditioning is the impossibility of taking accurate measurements of the unconditioned and conditioned responses being elicited. How strong the obtained aversion is can never be precisely determined.

Variables which should be more controlled in future attempts to use this method are environmental variables present after treatment, other elements of the treatment program, individual reactions to the drugs given (as far as can be determined), motivation of the patient, and the duration and its effect on the patient of the apnea. It might also be helpful to arrange a behavioral contract with the patient in order to insure his cooperation concerning post-treatment urinalysis tests.

REFERENCES

- Ausubel, D. P. The Dole-Nyswander treatment of heroin addiction. Journal of the American Medical Association, 1966, 195, 945-950.
- Black, P. (Ed.) Drugs and the brain. Baltimore: John Hopkins Press, 1969.
- Campbell, D., Sanderson, R. E., and Laverty, S. G. Characteristics of a conditioned response in human subjects during extinction trials following a single traumatic conditioning trial. Journal of Abnormal and Social Psychology, 1964, 68, 627-639.
- Clancy, J., Vanderhoff, E., and Campbell, D. Evaluation of an aversive technique as a treatment for alcoholism: controlled trial with succinylcholine-induced apnea. Quarterly Journal of Studies on Alcoholism, 1967, 28, 476-485.
- Dole, V. P., Nyswander, M. E., and Kreek, M. J. Narcotic blockade. Archives of International Medicine, 1966, 118, 304-309.
- Farrar, C. H., Powell, B. J. and Martin, L. K. Punishment of alcohol consumption by apneic paralysis. Behavior Research and Therapy, 1968, 6, 13-16.
- Holzinger, R., Mortimer, R., and VanDoren, W. Aversion conditioning treatment of alcoholism. American Journal of Psychiatry, 1967, 124, 150-151.

- Jaffe, J. H. Pharmacological approaches to the treatment of compulsive opiate use: their rationale and status. In Black, P. (Ed.) Drugs and the brain. Baltimore: John Hopkins Press, 1969.
- Jaffe, J. H., and Brill, L. Cyclazocine, a long-acting antagonist: its voluntary acceptance as a treatment modality by narcotics abusers. International Journal of Addictions, 1966, 1, 99-123.
- Liberman, R. Aversive conditioning of drug addicts: a pilot study. Behavior Research and Therapy, 1968, 6, 229-232.
- Lindesmith, A. R. Problems in the social psychology of addiction. In Wilmer, D. M. and Kassebaum, G. G. (Eds.) Narcotics. New York: McGraw-Hill, 1965.
- Madill, M. F., Campbell D., Laverty, S., Sanderson, K., and Vanderwater, S. Aversion treatment of alcoholics by succinylcholine-induced apneic paralysis. Quarterly Journal of Studies on Alcoholism, 1966, 27, 483-509.
- Martin, W. R., Gorodetsky, C. W. and McClane, T. K. An experimental study in the treatment of narcotic addicts with cyclazocine. Clinical Pharmacological Therapy, 1966, 7, 455-465.
- Nichols, J. R. How opiates change behavior. Scientific American, 1965, 212, 80-88.
- Nichols, J. R. Morphine as a reinforcing agent: laboratory studies of its capacity to change behavior. Research Publications of the Association of Nervous and Mental Disease, 1968, 299-310.

- Rachman, S. Aversion therapy: chemical or electrical? Behavior Research and Therapy, 1965, 2, 289-299.
- Raymond, M. J. The treatment of addiction by aversion conditioning with apomorphine. Behavior Research and Therapy, 1964, 1, 287-291.
- Sanderson, R. E., Campbell, D. and Lavery, S. G. An investigation of a new aversive conditioning treatment for alcoholism. Quarterly Journal of Studies on Alcoholism, 1963, 24, 261-275.
- Sanderson, R. E., Campbell, D. and Lavery, S. G. Traumatically conditioned responses acquired during respiratory paralysis. Nature, 1962, 196, 1235-1236.
- Thomson, I. G. and Rathod, N. H. Aversion therapy for heroin dependence. Lancet, 1968, 2, 382-384.
- Vanderwater, S. L., Lavery, S. G., Campbell, D. and Sanderson, R. E. Some effects of succinylcholine chloride in conscious human subjects. Canadian Anesthetists Society Journal, 10, 1963, 508-515.
- Wikler, A. Conditioning factors in opiate addiction and relapse. In Wilner, D. M. and Kassebaum, G. G. (Eds.) Narcotics. New York: McGraw-Hill, 1965.
- Wikler, A. Interaction of physical dependence and classical and operant conditioning in the genesis of relapse. Research Publications of the Association of Nervous and Mental Diseases, 1968, 46, 280-287.

Wolpe, J. Conditioned inhibition of craving in drug addiction: a pilot experiment. Behavior Research and Therapy, 1965, 2, 285-288.

Yablonsky, L. and Dederich, C. E. Synanon: an analysis of some dimensions of the social structure of an anti-addiction society. In Wilner, D. M. and Kassebaum, G. G. (Eds.) Narcotics. New York: McGraw-Hill, 1965.