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Preface

Learning, as it is used for this monograph, refers generally to changes in behavior due to experience, whether these changes are in lifestyle or in cellular activities. For the successful treating of drug and alcohol abuse, relearning is necessary at the social, individual, and biologic levels.

Our current understanding of how learning contributes to drug and alcohol abuse is covered in several of these reports, as we are shown how drug abuse "teaches" the body and the nervous system to react to previously unimportant events in new and sometimes life-threatening ways.

In systematic and carefully controlled animal studies, Siegel shows us that repeated experience with a drug can establish a tolerance to it that occurs only in the drug-associated environment. This tolerance derives from the animal's developing a drug-opposite response to repeated exposures to the drug in certain settings. This association between drug and environment, in some instances, means that setting predicts tolerance better than does the amount, frequency, or duration of drug used.

The implications of these findings for human drug abuse are serious. When tolerance has not been learned in a new setting, the unsuspecting drug abuser may take an accustomed dose only to overdose and perhaps die.

Similarly striking in Schindler et al. is the demonstration of the power of learning factors over monkeys working for drug to the extent that a drug-associated stimulus exerted stronger control of behavior than the drug itself, a finding that has important implications for treatment and prevention techniques.

Learned reactions resulting from drug use occur to both internal (moods) and external (people, places, things) cues. Among these

reactions are: drug abstinence syndrome, drug craving, positive expectations about use, and intoxication reactions. All of these reactions can occur in drug-associated settings by persons detoxified from the drug for perhaps many years. As Childress et al. show, hypnotically induced moods such as anger or joy can trigger drug or alcohol use, indicating how varied and complex are the learned responses due to substance abuse.

Appreciating the variety of simultaneous stimulus variables that control the behavior of drug taking, Fischman et al. conduct research in a life-like human living environment. This experimental environment helps to bridge the procedural gap from the animal laboratory to human drug abuse that is controlled simultaneously by many variables, including social access to others. Experiments with marijuana, for instance, confirm the popular notion that it can raise the probability of eating and socializing.

O'Brien et al. discuss the clinical relevance of laboratory studies of conditioning in drug abusers and point out that treatment must take into account transitions in what controls drug taking from first, to casual, to chronic use and dependency, and recognize the importance of stimuli remote from the point of drug taking that may start the chain of behaviors leading to use.

De Leon describes the therapeutic community approach to treatment as recognizing the need to teach or reteach the drug abuser. As with any treatment program, techniques that work are used whether or not they have been subjected to rigorous scientific testing. The concept of "internalizing" new beliefs and social values, for example, seems clearly to be an attempt to remove control by the external environment filled with drug-associated cues and to return control to the individual. It is worth noting that the gradual step-by-step process of socialization and education that characterizes the therapeutic community is consistent with the basic principle of learning by successive approximation to behavioral targets.

Learning occurs not only in the abuser but in those who make their living by selling drugs. Lerner and Raczynski describe learning aspects of the drug economy, including techniques of marketing learned by drug suppliers. Not the least of the skills learned by the drug dealer are techniques for assisting the recovering drug user to relapse to drug use.

The role of punishment in treating drug abuse is controversial, but Crowley finds it to be an important element in a program that has helped addicted physicians stay drug free. He finds that deliberately imposed negative consequences for drug use may be necessary to counteract the inherent reinforcing power of the drugs themselves and that this has policy implications for controlling drug abuse.

Bickel and Kelly make the point that the cues controlling drug taking change from when a person first uses to the time dependency sets in and that controlling cues are so various for an experienced user that zero frequency of drug use in any one setting cannot be interpreted to mean no drug dependency in others.

Monti et al. demonstrate the value of specific social skills training for alcoholics in the first 6 months following treatment, and reveal that even social skills become drug related. In this connection, Meyer's finding that chemical blocking agents appear to directly reduce craving for alcohol and opiates leads to his suggesting that they offer the recovering addict protection from craving in social settings. The recognition that stimulus cues and learned skills are so important to successful drug treatment encourages future investment in this area of research.

Special thanks to Dr. Beny Primm who presented an accurate and compelling picture of the human misery arising from drug abuse and whose contribution of personal time to the administration's war on drugs prevented his preparing a chapter for this monograph.

The challenge for treatment research is to find practical ways to reeducate the body and brain of experienced drug abusers such that ordinary environments do not trigger relapse.

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Drug Anticipation and the Treatment of Dependence

Shepard Siegal

INTRODUCTION

It has long been recognized that the process of "detoxification" and the crisis of withdrawal are not the major impediments to effective drug abuse treatment. Rather, the major problem is relapse following the completion of the withdrawal crisis. The high relapse rate following apparently "successful" treatment (or prolonged abstinence due to incarceration) has been documented in many studies (Siegel 1983), and the typical scenario has been described by several investigators. For example:

> The patient was a 28-year-old man with a 10-year history of narcotic addiction. He was married and the father of two children. He reported that, while addicted, he was arrested and incarcerated for 6 months. He reported experiencing severe withdrawal during the first 4 or 5 days in custody, but later, he began to feel well. He gained weight, felt like a new man, and decided that he was finished with drugs. He thought about his children and looked forward to returning to his job. On the way home after release from prison, he began thinking of drugs and feeling nauseated. As the subway approached his stop, he began sweating, tearing from his eyes, and gagging. This was an area where he had frequently experienced narcotic withdrawal symptoms while trying to acquire drugs. As he got off the subway, he vomited onto the tracks. He soon bought drugs, and was relieved. The following day he again experienced craving and withdrawal symptoms in his neighborhood, and he again relieved them by injecting

heroin. The cycle repeated itself over the next few days and soon he became readdicted. (O'Brien 1978, p. 533)

PREDRUG CUES AND RELAPSE

Results of recent research indicate that the occurrence of withdrawal distress and relapse, long after detoxification, are not readily predictable from an individual's drug history (e.g., length of addiction, type, and purity of drugs used). Rather, understanding the phenomenon requires an appreciation of drug-predictive environmental signals, as well as pharmacological considerations. This is apparent in both the experimental literature (with animals), and the clinical and epidemiological literature (with humans).

ENVIRONMENTAL CUES AND RELAPSE

Animal Studies

An early demonstration that environmental cues play an important role in relapse was provided by Thompson and Ostlund (1985). In the first phase of their experiment (addiction phase), rats were orally addicted to morphine by having it as their only available fluid for 60 days. They were then withdrawn from morphine by replacing the opiate solution with water for 30 days. Finally, during the readdiction phase of the experiment, the rats were again permitted to drink the morphine solution. For half the rats, readdiction occurred in the same environment as that used during the addiction phase. For the remaining rats, readdiction took place in a very different environment. During readdiction, rats displayed greater avidity for morphine solution when it was presented in the environment where original addiction had occurred than when readdiction occurred in an alternative environment.

More recently, Hinson et al. (1986) confirmed and extended the results of Thompson and Ostlund (1965). In the Hinson et al. (1986) experiment, rats received a series of morphine injections in one environment (the DR, or "distinctive room" environment), and also a series of saline injections in another environment (the HR, or "home room" environment). When subsequently given the opportunity to consume morphine solution in both environments, the rats drank significantly more morphine solution in the morphine-associated DR environment than in the saline-associated HR environment.

Anecdotal evidence of the contribution of environmental cues to relapse is provided by Ternes' (1977) description of the behavior of monkeys that were repeatedly injected with morphine in the presence of an arbitrary auditory cue-tape-recorded music. This music became capable of eliciting withdrawal symptoms and relapse in these monkeys after a considerable period of abstinence:

> After the animal had been weaned from the drug and maintained drug-free for several months, the experimenter again played the tape-recorded music and the animal showed the following signs: he became restless, had piloerection, yawned, became diuretic, showed rhinorrhea, and again sought out the drug injection. (Ternes 1977, pp. 167- 168)

Human Studies

There is considerable evidence that relapse in human addicts, like relapse in experimentally addicted animals, is influenced by drug-associated cues. As indicated in the above quote from O'Brien (1976), the physical environment in which drugs had previously been used frequently elicit withdrawal symptoms in the individual who had been drug free for a considerable period of time. Often the association between environmental cues and relapse is noted, but the role of the environment is minimized. Wikler has described a typical instance of this incognizance:

> . . . After being detoxified and having served their sentence at the U.S. Public Health Service Hospital, the postaddict felt fine and had no craving for heroin or morphine but just before his release, or on his way home, or after arriving in his drug-ridden environment, he felt sick, craved a fix, and then hustled to obtain it. Some postaddicts described the sickness in more detail: running nose, watery eyes, sweating, chills, nausea and vomiting-'like the flu, doc.' One postaddict, a physician, remarked that the sickness resembled heroin abstinence phenomena, but he dismissed that interpretation as preposterous. (Wikler 1977, p. 35)

Not only is relapse in humans related to the presence of drug-associated cues, but successful abstinence is related to the absence of these cues. Evidence in support of the salutary effect of protection

from drug-associated cues is provided by follow up studies of returning Vietnam veterans who were addicted to heroin while in Vietnam:

> During the summer and fall of 1971, drug use by United States servicemen in Vietnam had, by all estimates, reached epidemic proportions. (Robins 1973, p. 1)

> The high rates of narcotic use and addiction there were truly unlike anything prior in the American experience. (Robins et al. 1975, p. 980)

A study of a sample of enlisted men departing Vietnam in September 1971 indicated that approximately 20 percent were addicted to heroin while in Vietnam (Robins et al. 1974). Although known heroin users were treated before release, a substantial social problem was anticipated. Since there is a very high relapse rate following all known forms of treatment, It was expected that a new, large population of relapsing heroin addicts would substantially add to the indigenous civilian addict population:

> This will obviously lead to crime and other problems with law enforcement when he (the returning Vietnam heroin user) brings his addiction home . . . . They will be unable to cut off this drug use. (Senate Testimony 1972, p. 481)

Unlike most civilian addicts, following treatment, these Vietnam addicts returned to an environment very different from that in which they used drugs. They also evidenced much less relapse than civilian addicts. In one report, narcotic use in the United States by returned veterans addicted in Vietnam was compared to that seen in addicts of comparable age treated at the large Federal facilities in Lexington, KY, and Fort Worth, TX (Robins et al. 1975). Those addicted in Vietnam (and returned to a very different environment) were much less likely to relapse than those addicted in the environment to which they subsequently returned. Indeed, the veterans evidenced “rates of remission unheard of among narcotics addicts treated In the United States” (Robins et al. 1975, p. 958). Many of Robins’ conclusions have been substantially confirmed in a more recent follow up study of a different population of returned soldiers who were addicted in Vietnam (O’Brien et al. 1980).

In addition to the Vietnam veteran findings, other data suggest that alteration in the addict’s environment promotes long-lasting abstinence. Ross studied 109 opiate addicts in Detroit and noted that

physical relocation was significantly associated with abstinence from illicit drugs:

> It appears that for a large group of a treatment population (almost 40%) cessation of illegal drug use meant moving away physically from an area of high drug use. (Ross 1973, p. 561)

Frykholm evaluated 58 intravenous drug users in Sweden who had been abstinent for 3 years or more. Residence relocation was considered a prime factor in achieving this abstinence:

> When asked what they had done to change their lives in order to give up drugs, a majority of the respondents answered that they had felt it necessary to change residence. (Frykholm 1979, p. 376)

More recently, Maddux and Desmond (1982) studied patterns of abstinence in heroin addicts in San Antonio, TX. They found that frequency of l-year abstinence was three times higher in relocated respondents than in respondents staying in San Antonio. These and many other reports (see review by Maddux and Desmond (1982)) all indicate that environmental alteration favors long-term drug abstinence.

ENVIRONMENTAL CUES, DRUG TOLERANCE. AND DRUG DEPENDENCE

Findings that environmental cues are important contributors to relapse are accommodated in a model of drug tolerance and dependence that emphasizes learning principles. The model will first be discussed with respect to tolerance, and then the relevance of this analysis of tolerance to dependence will be discussed.

Enviroment Specificity Tolerance

It has become increasingly apparent that the pharmacokinetic or pharmacodynamic principles usually used to explain tolerance are insufficient. Rather, a complete account of tolerance requires an appreciation of environmental influences.

The importance of environmental cues in tolerance is illustrated by the results of a number of studies that have demonstrated that

tolerance is not the inevitable result of repeated drug administration. Rather, the drug-experienced organism may or may not display the hyporesponsivity to the drug that characterizes tolerance, depending on whether the drug is administered in the usual drug administration environment or an alternative environment.

Early studies of the environmental specificity of tolerance evaluated tolerance to the analgesic effect of morphine. A number of experiments by Mitchell and colleagues (e.g., Adams et al. 1969) demonstrated that rats displayed the expected analgesia-tolerant response to the last of a series of morphine injections only if the final injection occurred in the same environment as the prior injections in the series. Results of many subsequent experiments have confirmed and extended Mitchell's observations, in several species (including humans), using a range of morphine doses, a variety of analgesiometric procedures, and various modifications of Mitchell's original design (Siegel and MacRae 1984). Additional research has indicated the environmental specificity of tolerance to the thermic and locomotor effects of morphine, and to the lethal effect of diacetylmorphine hydrochloride (heroin) (Siegel and MacRae 1984). The environmental specificity of tolerance has also been demonstrated with many nonopiate drugs: ethanol, pentobarbital, amphetamine, scopolamine, haloperidol, and a variety of benzodiazepines (see reviews by Siegel (1983, Siegel (1986), and Siegel (1987)). Such findings have inspired analyses of tolerance that emphasize learning principles.

Tolerance and Learning

Several investigators have indicated parallels between tolerance and learning. Both processes frequently exhibit great retention, both are disrupted by electroconvulsive shock and frontal cortical stimulation, both are retarded by inhibitors of protein synthesis, and both are facilitated by antagonists of these metabolic inhibitors (Siegel 1988). Although there are several ways in which learning may contribute to tolerance, a dearly articulated model of tolerance that emphasizes the contribution of learning is based on Pavlovian conditioning principles.

The Pavlovian Conditioning Situation. In the Pavlovian conditioning situation, a contingency is arranged between two stimuli. Typically, one stimulus reliably predicts the occurrence of the second stimulus. Using the usual terminology, the second of these paired stimuli is termed the "unconditional stimulus" (UCS). The UCS, as the name

implies, is selected because it elicits relevant activities from the outset, i.e., unconditionally, prior to any pairings. The stimulus signalling the presentation of the UCS is "neutral," i.e., it elicits little relevant activity prior to its pairing with the UCS, and is termed the "conditional stimulus" (CS). The CS, as the name implies, becomes capable of eliciting new responses as a function of, i.e., conditional upon, its pairing with the UCS. In Pavlov's (1927) well-known conditioning research, the CS was (for example) a bell, and the UCS was food (which elicited a conveniently monitored salivary response).

Conditioning of Drug Responses Pavlov (1927) suggested that the usual drug administration situation corresponded to the conditioning paradigm: environmental cues uniquely present at the time of drug administration constitute the CS (e.g., location of injection, or drug administration rituals), with the actual systemic effect of the drug constituting the UCS. Subsequent to Pavlov's original demonstrations, there have been many studies concerned with the conditioning of drug effects (Siegel 1985).

Compensatory Pharmacological Conditional Responses (CRs). The development of an association between the environmental CS and the pharmacological UCS may be seen by administering an inert substance in the presence of the usual drug-signalling cues. The nature of the pharmacological CR observed in these circumstances depends very much on the nature and mechanism of the drug effect (Eikelboom and Stewart 1982). For many effects of many drugs, the CR is an anticipatory compensation: drug-associated environmental cues elicit responses that are opposite to the drug effect. For example, the subject with a history of ethanol administration (and its hypothermic consequences) displays a CR of hyperthermia (Siegel 1987). Similar drug compensatory CRs have been reported with respect to a variety of effects of morphine (analgesia, temperature, locomotor activity, and gastrointestinal transit time), as well as many other drugs (Siegel 1983; Siegel and MacRae 1984).

Although most studies of pharmacological conditioning have been conducted with animals, there is evidence that humans display drug-compensatory CRs too. Most of this human research has been conducted with alcohol, and evidence of alcohol-compensatory conditional responding has been reported by several investigators (see review by Siegel (1987)). A compensatory CR has also been reported with respect to caffeine in humans (Rozin et al. 1984).

Compensatory Pharmacological CRs and Tolerance. As indicated above, organisms with a history of drug administration frequently evidence CRs opposite to the drug effect, as revealed by presentation of the usual predrug cues without the usual pharmacological consequences. When these predrug cues are followed by the usual pharmacological consequences, the compensatory CR would be expected to attenuate the drug effect. As the association between the environmental CS and the pharmacological UCS is strengthened by repeated pairings, the effect of the drug becomes increasingly attenuated. Such a progressively diminished response to a drug over the course of repeated administrations defines tolerance.

Comparison With Nonassociative Interpretations of Tolerance. It should be noted that the analysis of tolerance that emphasizes the importance of environment-drug associations is not an alternative to traditional interpretations. Rather, the conditioning model is complementary to views of tolerance that do not acknowledge a role for learning. Many such nonassociative analyses of tolerance emphasize the role of drug-elicited homeostatic corrections that restore pharmacologically induced physiological disturbances to normal levels. Several investigators have indicated that the potential adaptive advantage of these homeostatic corrections actually antedate the pharmacological insult (e.g., Siegel et al. 1987; Wikler 1973). Pavlov was certainly aware of the importance of such anticipatory responding:

> It is pretty evident that under natural conditions the normal animal must respond not only to stimuli, which themselves bring immediate benefit or harm, but also to other physical or chemical agencies-waves of light and the like-which in themselves only signal the approach of these stimuli. (Pavlov 1927, p. 14)

Pavlovian conditioning provides a mechanism for such anticipatory responding. On the basis of a conditioning model, the systemic alterations that mediate tolerance occur not only in response to pharmacological stimulation, but may also occur in response to reliable environmental signals of this stimulation.

Evidence for the Conditioning Model Tolerance

A considerable amount of evidence has been published that supports the conditioning analysis of tolerance. Much of these findings have

been reviewed elsewhere (Siegel 1983; Siegel 1986; Siegel 1987) and are only briefly summarized here.

Environmental-Specificity of Tolerance. The observation that there often is pronounced environmental specificity to the display of tolerance is readily interpretable by an analysis of tolerance that Incorporates Pavlovian conditioning principles. If the repeatedly drugged organ&m receives the drug in the context of the usual pre-drug cues, the compensatory CR partially cancels the drug effect thus, tolerance is observed. On the other hand, if this drug-experienced organism receives the drug in the context of cues not previously associated with the drug, there would be no pharmacological CR cancelling the drug effect, and the tolerance attributable to such a CR would not be observed. An especially dramatic demonstration of the environmental specificity of tolerance concerns tolerance to the lethal effect of opiates.

Environmental Specificity Tolerance and Opiate Overdose. The conditioning model of tolerance has been elaborated to account for some Instances of overdose in human heroin addicts (S. Siegel 1984; Siegel and Ellsworth 1986; Siegel et al. 1982). Although deaths from overdose are prevalent, the mechanisms of many of these deaths are far from clear. Some deaths result from pharmacological overdose (Huber 1974), but often victims die following doses that would not be expected to be fatal for these drug-experienced, and presumably drug-tolerant, individuals (see reviews by Brecher (1972) and Reed (1980)). Indeed, the victims sometimes die following self-administration of a heroin dose that was well tolerated the previous day (Government of Canada 1973). Some fatalities may result from a synergism between the opiate and other drugs concomitantly administered or from adulterants (especially quinine) in the illicit heroin, but many deaths do not result from such drug interactions (Brecher 1972; Government of Canada 1973; Reed 1980). Thus, it has been suggested that “the term ‘overdose’ has served to indicate lack of understanding of the true mechanism of death in fatalities directly related to opiate abuse” (Greene et al. 1974, p. 175). Some instances of these enigmatic failures of tolerance may be interpretable by the conditioning analysis. According to this analysis, an organism is at risk for overdose when the drug is administered in an environment that has not previously been paired extensively with the drug (and thus does not elicit the compensatory pharmacological CR that attenuates the effect of the drug).

Results of an experiment by Siegel et al. (1982) support the Pavlovian conditioning interpretation of heroin overdose. Rats injected with high doses of heroin in the same environment as that previously associated with the drug were more likely to survive than rats with the identical pharmalogical history receiving the final drug administration in an alternative environment.

The role of predrug cues in overdose has also been evaluated by interviewing drug addicts who have survived a heroin overdose. Findings obtained in such retrospective studies are mixed: S. Siegel (1984) reported that novel predrug cues typically accompany such overdoses, but Neumann and Ellis (1986) reported that there is typically nothing unusual about the predrug cues on the occasion of the overdose.

A recent report suggests that Pavlovian conditioning may be relevant to some instances of death from overdose of medically prescribed opiates (Siegel and Ellsworth 1986). A single case is described-a patient receiving morphine for relief of pain from pancreatic cancer. The circumstances of this patient's death from apparent overdose of licitly used morphine are readily interpretable by the Pavlovian conditioning account of tolerance: on the occasion of his final morphine administration, he was in an environment very different from that associated with prior morphine administrations.

Extinction of Tolerance. Following CR acquisition, presentation of the CS without the UCS causes a decrease in the CR strength, i.e., "extinction." If drug tolerance is partially mediated by drug-compensatory CRs, extinction of these CRs should attenuate tolerance. That is, established tolerance should be reversed by placebo administrations. Such extinction has been demonstrated with respect to tolerance to both the analgesic (e.g., Siegel et al. 1980) and lethal (Siegel et al. 1979) effects of morphine, as well as a variety of effects of amphetamine, midazolam (a short-acting benzodiazepine), and the synthetic polynucleotide Poly 1:C (see reviews by Siegel (1986) and Siegel (1987)).

Another procedure for extinguishing a CSUCS association is to continue to present both the CS and the UCS, but in an unpaired manner (Mackintosh 1974). That is, the subject receives both conditioning stimuli, but the CS does not signal the UCS. Rather, the UCS is presented only during intervals between CS presentations. It has been reported that such unpaired presentations attenuate tolerance to the behaviorally sedating effect of morphine in rats

(Fanselow and German 1982). In this experiment, morphine was administered on a number of occasions in the presence of a distinctive environmental cue. When tolerance was established, continued presentation of the drug and cue, but in an explicitly unpaired manner, eliminated tolerance. That is (as expected on the basis of a conditioning analysis of tolerance), despite the fact that morphine-tolerant rats continue to receive morphine, tolerance is reversed if the continued morphine administrations are unpaired with a cue that was initially paired with the drug. Such a finding would appear uninterpretable by any view of tolerance that does not acknowledge the contribution of learning.

Retardation of Tolerance. A variety of nonpharmacological procedures retard the acquisition of CRs. According to the conditioning interpretation of tolerance, similar procedures should retard the development of tolerance. One technique for attenuating the strength of an association is to repeatedly present the CS alone prior to pairing it with the UCS. The deleterious effect of such preconditioning exposure to the CS has been termed "latent inhibition" (Mackintosh 1974). If drug tolerance is mediated, at least in part, by an association between predrug cues and the drug, it would be expected that rats with extensive experience with administration cues prior to the pairing of these cues with the drug should be relatively retarded in the acquisition of tolerance (compared to rats with minimal preexposure to these cues), despite the fact that the groups do not differ with respect to their histories of drug administration. Such latent inhibition of tolerance has been reported with respect to the analgesic effect of morphine (Siegel 1977; Tiffany and Baker 1981) and the immunostimulatory effect of Poly 1:C (Dyck et al. 1986).

Another procedure for decreasing the strength of a CSUCS association is partial (as compared to consistent) reinforcement. That is, if only a portion of the presentations of the CS is paired with the UCS, CR acquisition is retarded (compared to the situation in which all presentations of the CS are paired with the UCS; see Mackintosh (1974)). This literature has clear implications for a Pavlovian conditioning account of morphine tolerance: a group in which only a portion of the presentations of the drug administration cues is actually followed by morphine (i.e., a partial reinforcement group) should be slower to acquire tolerance than a group that never has exposure to environmental cues signalling the drug without actually receiving it (i.e., a continuous reinforcement group), even when the two groups are equal with respect to all pharmacological parameters.

Such a finding has been reported with respect to tolerance to the analgesic, thermic, and anorexigenic effects of morphine (Krank et al. 1984; Siegel 1977; Siegel 1978).

Other evidence for the conditioning Analysis of Tolerance. In addition to the research summarized above, results of many other experiments have provided further evidence that Pavlovian conditioning contributes to tolerance to many drugs. These experiments demonstrate that nonpharmacological manipulations of predrug environmental cues affect both CR acquisition and tolerance in a similar manner. For example, tolerance to both morphine (Fanselow and German 1982; Siegel et al. 1981) and pentobarbital (Hinson and Siegel 1986) is subject to inhibitory learning. Furthermore, morphine tolerance is subject to sensory preconditioning (Dafter- et al. 1983) and "external inhibition" (Siegel and Sdao-Jarvie 1986), and can be manipulated by compound conditioning phenomena such as "blocking" (Dafters et al. 1983) and "overshadowing" (Dafters and Bach 1985; Walter and Riccio 1983). A full discussion of these findings is beyond the scope of this review, but it should be emphasized that a variety of additional experiments support the conditioning analysis of tolerance.

Pavlovian Conditioning and Withdrawal Symptoms

According to most current views, tolerance and withdrawal symptoms are both manifestations of homeostatic mechanisms that correct for pharmacological disturbances: the feedback mechanisms that mediate tolerance when the drug is administered are expressed as withdrawal symptoms when the drug is not administered (Siegel et al. 1987). It has become increasingly apparent that, just as feedforward, or anticipation (as well as feedback), contributes to tolerance, it also contributes to withdrawal symptoms. Thus, some "withdrawal symptoms" are due not to alterations in feedback mechanisms induced by past drug administrations, but rather to the anticipation of the next drug administration. That is, some drug "withdrawal symptoms" are, more accurately, drug "preparation symptoms"; they result from drug-Compensatory CRs.

In discussing the role of compensatory CRs in so-called withdrawal symptoms, it is important to make a distinction between the acute withdrawal reaction seen shortly after the initiation of abstinence (which typically lasts for days or, at most, weeks), and the apparently similar symptoms often noted after detoxification is presumably complete (Hinson and Siegel 1982). In the latter case, it is likely

that it is the anticipation of the drug, rather than the drug itself, that is responsible for the symptoms:

> Consider the situation in which the addict expects a drug, but does not receive it; that is, no drug is available, but the addict is in an environment where he or she has frequently used drugs in the past, or it is the time of day when the drug is typically administered, or any of a variety of drug-associated stimuli occur. Research with animals demonstrates that presentation of cues previously associated with drug administration, but now not followed by the drug, results in the occurrence of drug-compensatory CRs . . . . In the situation in which the drug addict expects but does not receive the drug, it would be expected that drug-compensatory CRs would also occur. These CRs normally counter the pharmacological disruption of functioning which occurs when the anticipated drug is administered. However, since the expected drug is not forthcoming, the CRs may achieve expression as overt physiological reactions, e.g., yawning, running nose, watery eyes, sweating . . . or form the basis for the subjective experience of withdrawal sickness and craving. (Hinson and Siegel 1982, p. 499)

Actually, the role of environmental cues in the display of withdrawal symptoms and relapse has been known for a long time. The following observation is from *The Anatomy of Drunkenness,* written in 1859:

> Man is very much the creature of habit. By drinking regularly at certain times he feels the longing for liquor at the stated return of these periods-as after dinner, or immediately before going to bed, or whatever the period may be. He even finds it in certain companies, or in a particular tavern at which he is in the habit of taking his libations. (Macnish 1859, p. 151)

More recently, many other investigators have noted that environmental cues affect the display of the symptoms of withdrawal from a variety of drugs.

Observation of Addicts One way to evaluate the role of environmental cues in withdrawal distress is simply to ask addicts to recall the circumstances in which they suffer such distress. Several investigators have done just this, and have noted that both opiate addicts

and alcoholics report that such distress is especially pronounced in the presence of drug-associated cues (see reviews by Siegel (1993) and Siegel (1987)). Several clinicians have reported that opiate withdrawal symptoms are displayed when, during behavior therapy (even with long detoxified former addicts), drugs are discussed (O'Brien 1978; Wikler 1977) or the paraphernalia of addiction (syringe and tourniquet) are viewed (Teasdale 1973). The appearance of such symptoms in these circumstances can be enigmatic to an observer not acquainted with the phenomenon of pharmacological conditioning, as one of Wikler's recollections demonstrates:

> On two separate occasions, psychiatrists at the U.S. Public Health Service Hospital told me that in group therapy with long detoxified postaddicts, the patients would suddenly begin to blow their noses, wipe their eyes, and yawn incessantly when the subject under discussion turned to dope. The psychiatrists, unaware of this theory of relapse, were puzzled by the reappearance of opioid abstinence phenomena 3 to 8 months after detoxification. (Wikler 1977, p. 35)

One's own personal experience may provide similar evidence of the importance of drug-associated cues in withdrawal distress and craving-environmental cues associated with smoking (or seeing others smoking, or talking about smoking) often elicit craving for a cigarette in individuals addicted to nicotine.

In the case of orally ingested drugs, such as alcohol and tobacco, an especially effective cue for the drug's systemic effects should be the flavor of the drug. It has been reported that cigarette smokers will display nicotine withdrawal symptoms if they experience the taste of the cigarette without the usual accompanying nicotine administration, i.e., they puff on a cigarette containing much less than the usual amount of nicotine (Schachter 1977). It is well known that alcoholics find the taste of alcohol a potent elicitor of craving (e.g., Ludwig and Stark 1974) and have difficulty in refraining from drinking if they sample an alcoholic beverage (Hodgson and Rankin 1978). This "loss of control" is apparently elicited by the taste cue since, if the taste of the alcoholic beverage is masked, a sip does not elicit such craving (Merry 1988).

Drug-associated olfactory cues can apparently also elicit withdrawal sickness and craving. Teasdale (1973) noted that several heroin

addicts who had usually injected themselves in public lavatories reported that a lavatory smell elicited craving.

Many other anecdotal reports of environmentally elicited withdrawal symptoms and craving are reported by Biernacki in his study of recovery from heroin addiction:

> Those in the study who were able to isolate the source of their cravings to use drugs again usually pointed to some olfactory or visual cue that they associated in their past experience with obtaining the drug and/or using it. Being in an area where they once had obtained the drug, seeing old addict associates, or (especially) witnessing another person using drugs were the most frequent reported events that engendered craving to use opiates. One man, who had been addicted for five years prior to his being interviewed, recalled how drug cravings were prompted when he saw a group of actors seem to inject heroin in a movie that he was watching on television. (Biernacki 1986, pp. 107- 108)

Another of Biernacki's respondent's displayed remarkable insight. He "likened himself to one of Pavlov's dogs when he felt the nausea accompanying a craving. He explained: 'I had the objectivity to even see my own behavior for what it was and that was like getting nauseous whenever I'd even think about fixing. Like one of Pavlov's dogs'" (Biernacki 1988, p. 115).

Experiments Concerning Environmental Elicitation of Withdrawal Distress. There are several laboratory demonstrations of the ability of drug-associated cues to elicit withdrawal distress. For example, it has been noted that former addicts display physiological signs of narcotic withdrawal when they performed the "cooking up" ritual while being monitored by a polygraph (O'Brien et al. 1976). Teasdale (1973) showed addicts slides of both opiate-related material, e.g., inserting a syringe into a vein, and non-opiate-related material, e.g., a hand holding a cup of coffee. On the basis of a variety of psychometric measures, Teasdale (1973) concluded that the opiate-related slides induced more emotional responding and evidence of withdrawal distress than the non-drug-related slides. Sideroff and Jarvik (1980) also reported that drug-associated cues elicit symptoms of withdrawal. They presented a videotape depicting scenes of heroin preparation and administration to groups of both heroin addict patients and nonaddicts. They found that the videotape elicited evidence of withdrawal (changes in heart rate and galvanic skin

response, and subjective ratings of anxiety and craving) in only the addict group.

Similar findings have been reported with respect to alcohol. Ludwig and colleagues (Ludwig et al. 1974; Ludwig et al. 1977) have presented results of experiments demonstrating that alcoholics, in the presence of laboratory-reconstructed alcohol-associated cues (e.g., a mock barroom or the odor of bourbon) display withdrawal sickness, subjective reports of alcohol craving, and (if liquor is available) relapse to drinking.

IMPUCATIONS FOR TREATMENT

According to the conditioning model, those drug-compensatory CRs which contribute to tolerance when the anticipated drug is administered contribute to withdrawal symptoms when the anticipated drug is not administered. It follows that treatment techniques should address the crucial contribution of environment-drug associations to dependence (Poulos et al. 1981).

As described previously, when treatment consists primarily of a period of "detoxification" in an insulated treatment environment, and the released patient is returned to the original addiction environment, treatment success is poor: the vast majority of the treated addicts quickly relapse following reexposure to predrug cues. The conditioning analysis suggests several factors which should be considered in a treatment program to minimize such relapse.

Environmental Change and Treatment Effectiveness

As discussed previously, transfer of an addict to an environment not associated with drug use should promote recovery. This is what happened with soldiers addicted while in Vietnam (e.g., Robins 1973) and with experimentally addicted rats (e.g., Hinson et al. 1986; Thompson and Ostlund 1985). As discussed in the beginning of this chapter, results of several epidemiological studies suggest that environmental change is frequently associated with long-lasting abstinence.

Of course, environmental change may be a good prescription, but it is not one that can readily be implemented. Since such changes usually do not occur, a function of treatment might be the extinction of the pharmacological associations that are responsible for relapse, and/or the teaching of other, overriding behaviors in response to drug CSs.

Extinction of Responses to Drug-Associated Cues

The primary treatment implication of the conditioning analysis of withdrawal is that the usual predrug cues must be subjected to extinction. There are reports of the effectiveness of extinction-like procedure in eliminating the ability of predrug cues to elicit craving and withdrawal distress (Siegel 1983). The study by Blakey and Baker (1980) provides an example of how extinction procedure may be used with alcoholics. One of the cases they described (W.R., case 1) illustrates the procedure. The drinking history of the patient was first analyzed in terms of the events which "triggered" craving for alcohol and relapse to consumption. For this patient, these stimuli included "tiredness after long hours of work, boredom, smell of drink on customers, bouts of illness, travelling home past a particular pub at night, and the taste, smell, and sight of alcohol" (Blakey and Baker 1980, p. 320). Treatment involved extinction of the capacity of these usual predrug cues to elicit craving by presenting the we and not allowing drinking. At first, presentation of one of the usual predrug cues elicited strong craving, trembling, and feelings of depression. With repeated presentations of the cue not followed by the drug, these symptoms diminished. When the capacity of one cue to elicit craving had been extinguished, another predrug cue was introduced and subjected to the same extinction procedure. The extinction procedure continued until most of the "trigger" stimuli had undergone extinction, after which the patient apparently successfully gave up drinking.

Blakey and Baker (1980) report other cases involving the same general procedure for eliminating the capacity of the usual predrug cues to elicit craving: identification of the usual predrug cues for the individual patient and systematic exposure to each of the cues while not allowing alcohol consumption until the capacity of that cue to elicit craving is diminished. In some cases, it was necessary that the extinction program be conducted outside the institutional setting. For example, treatment for one patient who repotted that being in a pub in the company of friends was the most powerful elicitor of craving involved sitting in the pub with one or two therapists while he and they drank soft drinks. Later sessions included being in the presence of people drinking alcohol, going into a well-known pub, and going into a pub alone.

Ronald Siegel (1994) has reported the use of extinction therapy to treat cocaine dependence. Patients being treated for cocaine addiction were provided with vials that contained a chemical that

duplicated the odor of “street” cocaine. They could sniff the *vapors ad libitum.*Such exposure to a cocaine odor was an effective adjunct to treatment for the majority of the users who participated in the study:

> Repeated sniffing of the aroma unaccompanied by cocaine itself appears to result in some ‘extinction’ of the cocaine craving itself. (R.K. Siegel 1984, p. 81)

“Extinction therapy” has also been used to treat opiate addiction (O’Brien and Ng 1979). Although dramatic successes have not been reported, a problem in implementing this procedure with these patients is the difficulty in reconstructing predrug environmental cues. As indicated by O’Brien and Ng (1979), “for optimal effectiveness it might be necessary for patients to be desensitized in situations that clearly resemble their own neighborhoods” (O’Brien and Ng 1979, p. 198). Obviously, such realistic presentation of drug-associated cues may present special problems, although it has been used in some cases, such as Kraft’s (1970) procedure of having amphetamine-barbiturate (Dexamyl, or “purple hearts”) abusers go to areas of the city where they usually obtain the drug and refrain from buying it.

A promising extinction procedure has the patient actually self-inject the opiate in an environment similar to that in which heroin is usually self-administered, but the effects are blocked by a long lasting narcotic antagonist such as cyclazocine or naltrexone (Meyer and Mirin 1979).

SUMMARY AND CONCLUSIONS

Results of much research demonstrate that tolerance is not the inevitable consequence of repeated drug exposure: the drug-experienced organism often demonstrates tolerance when the drug is administered in the context of the usual predrug cues, but not in the context of alternative cues. Such findings raise the importance of learning factors above that of the purely physiological factors in substance abuse. Incorporated in a model of tolerance that emphasizes the Pavlovian conditioning of an association between predrug cues and the systemic effect of the drug are findings that learned tolerance leads to death by overdose. A history of association results in drug-compensatory conditional responses, and these conditional pharmacological responses may be displayed as “withdrawal symptoms” and craving when the organism with a history of drug

administration is confronted with the usual predrug cues without the usual pharmacological consequences.

An implication of the conditioning analysis is that successful treatment of drug addiction should acknowledge not only pharmacodynamic and pharmacokinetic principles, but also the powerful evocative effects of drug-predictive environmental cues. Permanent abstinence is most likely if the treated addict is either protected from reexposure to these predrug cues (for example, by residence relocation), or treated with a protocol which incorporates extinction of the association between these cues and the drug. As Hamlet suggested to his mother (Act III, Scene 4):

> Assume a virtue if you have it not
> . . . refrain tonight;
> And that shall lend a kind of easiness
> To the next abstinence: the next more easy;
> For use almost can change the stamp of nature
> And master ev'n the devil or throw him out
> With wondrous potency.

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Classically Conditioned Responses in Opioid and Cocaine Dependence: A Role in Relapse?

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INTRODUCTION

For several years our research group has studied the conditioned responses associated with chronic opioid use on the hypothesis that these responses, particularly conditioned craving and conditioned withdrawal, may help trigger relapse to drug use in the abstinent patient (O'Brien 1975; O'Brien et al. 1977; O'Brien et al. 1986; Childress et al. 1984; Childress et al. 1985; Childress et al. 1986a; Childress et al. 1986b; Childress et al. 1986c; Childress et al. 1986d; Childress et al. 1987a; Childress et al. 1987b; Mclellan et al. 1986). The history and theoretical complexity of these studies is described elsewhere in this volume. This chapter provides an overview of our attempts to elicit, document, and reduce conditioned drug-related responses in four different clinical populations: (1) methadone outpatients; (2) detoxifying methadone inpatients; (3) abstinent opioid users; and, most recently, (4) abstinent cocaine users.

For all of these populations, the basic strategy has been similar. First, we try to find out the kinds of conditioned responses experienced by the patients and target the responses that we feel might be important in relapse to drug use. Next, we try to find stimuli that reliably elicit these responses. We then develop extinction (nonreinforced exposure) procedures to help reduce or eliminate these responses. Finally, we compare the clinical outcome of patients who have had their conditioned responses reduced (through extinction) with others who have not, as a way of helping to determine whether these responses contribute to relapse. In our treatment-outcome studies, extinction is usually added to treatments such as drug counseling or professional psychotherapy, which address

the nonconditioned factors (unemployment, psychiatric problems, etc.) important in drug use and relapse (Woody et al. 1983).

TARGETING RELEVANT CONDITIONED RESPONSES

Drugs are powerful and complex stimuli, exerting multiple direct and indirect unconditioned effects (O'Brien et al. 1986). It is difficult to know a *priori* which of these effects will become conditioned and, of those, which will be of the greatest clinical significance. Our general approach has been to target responses with theoretical and face relevance, e.g., conditioned withdrawal and conditioned craving, and then to develop meaningful measures of these responses. In our initial work with opioids, for example, we devoted considerable effort to studies of conditioned withdrawal responses and also to conditioned euphoria or "high." This was based on the hypothesis that these responses might be contributors to relapse. To measure conditioned withdrawal we have used the patient's global ratings of subjective withdrawal, a technician-administered checklist of withdrawal-associated signs and symptoms, and physiological measures of heart rate, respiration, skin resistance, and peripheral skin temperature, which can reflect arousal and withdrawal-like changes. We have used a similar approach to measure conditioned high (drug-like) effects, using the same physiological measures but different (drug-like) signs and symptoms.

Conditioned drug craving has been an extremely prevalent subjective response to opioid-related stimuli, and its importance has been underscored with the advent of our cocaine work, where it is by far the most common response to cocaine "reminder" stimuli. Though we record a full set of subjective and physiological responses to cocaine-related stimuli, cocaine craving has become the focus of our recent attention because, although not well understood or easily measured, conditioned craving seems closely related to episodes of cocaine use.

It is perhaps worth noting the obvious: we are limited to targeting conditioned responses that we can measure, either with our crude autonomic measures or by asking the patient to accurately label what he is feeling. These measures are very rough analogs of important central nervous system (CNS) events that are not as readily measured. However, with increasingly available technology for imaging brain activity, the day is not far off when we will be able to locate and monitor the CNS sites of these conditioned drug-related responses.

DEVELOPMENT OF EFFECTIVE ELICITING STIMULI

Over the past 5 years, we have worked closely with a number of patients to develop an extensive series of standard drug-related stimuli that reliably elicit both conditioned physiological changes, subjective reports of "high," "craving," and/or "withdrawal" feelings. We now have a full complement of drug-related stimuli for eliciting both opioid- and cocaine-related conditioned responses (Childress et al. 1986e). Our opioid-related stimuli are injection focused and include audiotapes of explicit drug talk by experienced users; color slides of local drug-buying locations and actual drug injections; color videotapes of simulated buy/sell sequences, actual drug injections, and postinjection behavior; and a collection of injection paraphernalia (syringes, cookers, bags of simulated heroin, etc.).

In our pilot work with cocaine patients (Childress et al. 1987a; Childress et al. 1987c), we quickly discovered that, to be most effective, the eliciting or "trigger" stimuli should be modality-specific, i.e., directly related to the route of cocaine administration for a given patient. Pilot patients insisted that seeing or hearing tapes of cocaine use in a nonpreferred modality could actually be a "turn-off;" the tendency would be to scornfully dismiss the other users as obviously not knowing the best way to use cocaine. We have now developed three separate sets of eliciting stimuli (each set containing audiotapes, videotapes, and paraphernalia) for cocaine "snorters," "freebasers," and "injectors" (Childress et al. 1986e). Virtually all of our patients presenting for cocaine abuse treatment have been either freebasers or injectors.

We have referred to our testing stimuli as "standard" because they represent sights, sounds, and experiences that are common to the use patterns of a majority of drug-abusing patients. As we will discuss later, there are also a great number of stimuli specific to the individual history of each patient that are likely to be even more important and evocative than the standard stimuli.

ASSESSMENT OF CONDITIONED DRUG RESPONSES IN OPIOID AND COCAINE ABUSERS

In the course of studying each treatment population, we usually collect data from three different settings: (1) from laboratory test sessions, where the patients' subjective and physiological responsivity to drug-related stimuli is assessed prior to any treatment intervention, at the end of treatment, and at a followup session after

the completion of treatment; (2) from extinction sessions, which are usually conducted in the ward or clinic; and (3) from the patients' natural environment, based on prospective weekly reports of conditioned response episodes.

Laboratory Testing

A crucial part of our work has involved the multimeasure (physiological and subjective) assessment of patients' conditioned drug responses in our specialized testing laboratory. Patients are seated in an environmentally controlled, video-equipped chamber where neutral and drug-related stimuli can be presented according to a consistent protocol. Patients can also engage in drug-related rituals or control activities while being recorded in the chamber. Simultaneous physiological measurements are obtained using a Grass polygraph and an IBM XT computer, and a Bio Med package for analysis of physiological data. Baseline and during-session subjective measures are recorded along with physiological responses.

These detailed laboratory assessments are an essential adjunct to our extinction procedures, allowing the measurement of all patients' conditioned responses prior to extinction or other control treatments. Responses are then reassessed during and at the end of treatment and at l-month followups. We have now conducted well over 350 of these laboratory assessment sessions, testing opioiddependent (methadone) patients, detoxifying opioid abusers, abstinent opioid abusers, and, most recently, abstinent cocaine abusers.

Pretreatment laboratory assessments in a large (n=89) sample of methadone patients clearly established a differential responsivity to drug-related vs. neutral stimuli (videotapes, activities), with patients generally experiencing greater arousal (decreases in galvanic skin response [GSR], analysis of variance [ANOVA] p<,.O1), greater reductions in peripheral skin temperatures (p<.01). increased craving (p<.O1), and an increased probability of withdrawal symptoms in response to the drug-related stimuli (Childress et al. 1984; Childress et al. 1985; Childress et al. 1986d. Figure 1 illustrates the differential skin temperature response to drug-related vs. neutral stimuli in one methadone patient.

The response to each stimulus is represented as the change in peripheral skin temperature in Fahrenheit degrees from a predetermined physiological baseline period. Approximately one-third of

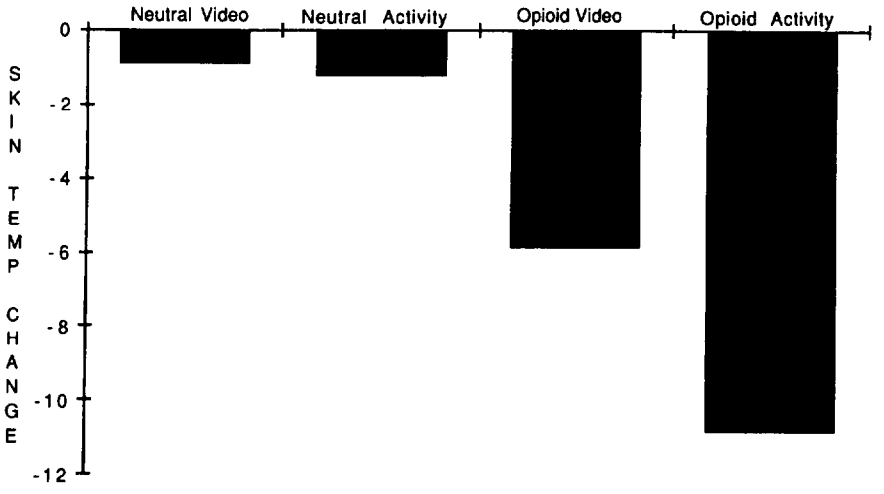

FIGURE 1. *Differential response to neutral vs. drug-related stimuli*

the methadone patient sample responded with a clear differential change in physiologic response to drug-related vs. neutral stimuli.

Assessments in a subsample of detoxifying patients (n=23) showed a generally similar profile of physiologic and subjective conditioned responses, except that these patients were even more likely to acknowledge withdrawal in response to drug-related stimuli. Our more recent assessments in abstinent opiate-abusers (n=15) also revealed a differential responsivity to drug-related vs. neutral stimuli, reflected primarily in measures of peripheral skin temperature ($p<.05$, paired t-test following overall ANOVA, GSR arousal, $p<.05$, and opioid craving $p<.0001$). The prevalence of increased craving in response to our drug-related test stimuli in abstinent opioid-users was 90 percent, a rate almost twice that observed in our methadone-maintained patient sample. Our pilot work assessing conditioned responses in abstinent cocaine abusers (n=16) indicates that they, too, show a differential responsivity to drug-related vs. neutral stimuli. For example, they respond to drug-related stimuli with Increased physiological and subjective arousal, increased craving ($p<.005$), and even reductions in peripheral skin temperature ($p<.007$) in response to the drug-related stimuli.

Extinction Studies

Over the past 5 years we have developed a series of increasingly effective procedures for extinguishing conditioned drug-related responses. The findings summarized below are detailed in the referenced publications. Our most recent and most effective extinction protocol is detailed in the *Manual: Guided Extinction Procedures for Opioid and Cocaine Dependence* (Childress et al. 1986e). This publication has also been made available to other investigators in the interest of standardizing procedures in this area.

Methdone Patients. In early pilot work with opioiddependent methadone patients, we used a "trials to criterion" extinction format, in which each class of eliciting stimuli, (self-produced verbal stimuli, audiotapes, slides, videotapes, and drug paraphernalia) was presented until the patient no longer experienced increased arousal, craving, withdrawal, etc. This early extinction procedure established the reliability and effectiveness of the eliciting stimuli (Childress 1984; Childress 1985) and helped determine the optimal number of exposures for each class of stimuli.

In a large scale treatment/outcome study of extinction in methadone patients (Childress et al. 1984; Childress et al. 1985; Childress et al. 1986c; McLellan et al. 1986), a fixed-trials format determined the number of exposures to each stimulus class (audio, video, etc.). Ten-minute exposures to eliciting stimuli were preceded by a brief psychotherapy session and followed by deep relaxation. The integration of extinction with other more conventional treatments (psychotherapy and relaxation) was well-received by the patients, and this integrated approach addressed both the conditioned and nonconditioned (psychiatric, social, vocational, etc.) factors in drug use. Patients given up to 35 treatment sessions showed a significant reduction (extinction) of conditioned craving in response to the drug-related stimuli (repeated measures ANOVA, $p<.001$), but withdrawal symptoms persisted without significant reduction. Figure 2 illustrates the group reduction in craving in response to drug-related stimuli as a function of extinction sessions. Both therapy and therapy plus extinction groups showed significantly greater clinical improvement at followup than the control group which received only extra drug counseling (paired group comparisons following an overall significant analysis of covariance [ANCOVA], $p<.05$). Note also that the control group (figure 2) reported little or no craving at the time of the session, but the experimental group reported craving evoked by the drug-related stimuli, but decreasing (extinguishing) with repeated

exposures. During laboratory sessions conducted at termination, and at 1- and 6-month followups, the nonextinction patients showed responses to the drug-related stimuli that had not diminished over time.

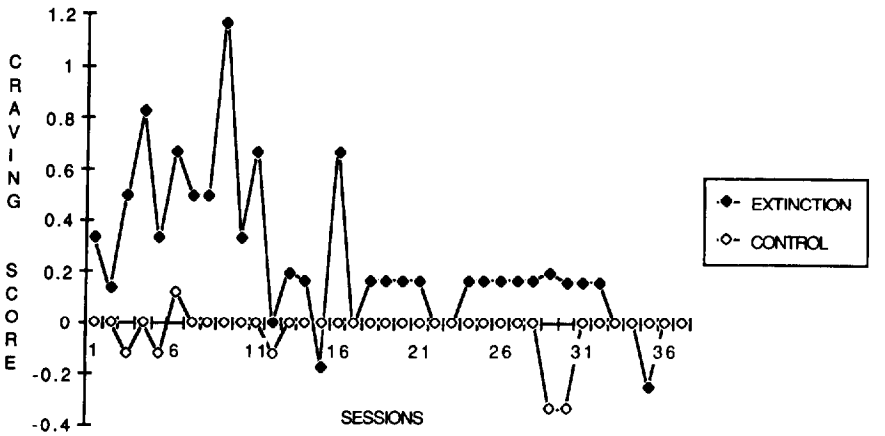

FIGURE 2. *Opioid craving in two groups of methadone outpatients*

This large outpatient study (102 patients tested for presence of conditioned responses, 52 of whom agreed to be randomly assigned to treatment) provided us with systematic information about the wide prevalence of conditioned responses in opioid-abusing patients (Childress et al. 1986a; Childress et al. 1986c), and gave us good indication that an extinction approach could be effective in reducing drug craving. However encouraged we were by these findings, other results from this study were more problematic. Very few of our methadone patients chose to detoxify during the course of the study (despite therapeutic support and small financial incentives), meaning that we could not adequately assess the impact of extinction upon relapse to drug use, which is necessarily evaluated in an abstinent population. Moreover, our outpatient extinction procedure did not produce complete reduction of withdrawal symptoms, either because the amount of nonreinforced exposure was inadequate, or, perhaps as likely, because the outpatients would sometimes engage in drug use, leading to reinstatement of the conditioned responses. Finally, some patients commented that our standard extinction stimuli were less evocative for them than other more individualized cues (e.g., the sight of their own paycheck) or even shifts in their own mood state.

From these findings, we developed a set of design needs that would guide the next phase of our extinction work:

- the need for an abstinent patient population to properly assess the impact of extinction upon relapse to drug use;

- the need for a controlled therapeutic environment in which to conduct initial extinction trials, to prevent drug use that would reinstate conditioned responses;

- the need for increased stimulus exposure in an attempt to completely reduce both physiological and subjective conditioned responding; and, finally,

- the need to address individualized and mood-related stimuli, which seemed to account for substantial amounts of conditioned responding.

Mood Influences on Conditioned Responding During Extinction. In the course of completing our work in the methadone outpatient study, experiences with several patients suggested that changes in mood state could significantly influence both the nature and intensity of conditioned responses to the same set of external stimuli. Figure 3 shows the extinction curve of one of these patients, who happened to have a confrontation with a hospital policeman prior to session 23. During the angry mood, withdrawal symptoms were again evoked by the same stimuli that had lost their ability to evoke withdrawal responses in prior sessions during the basal state. This chance finding, repeated in several patients, led us to explore this phenomenon in a subsequent study with detoxifying methadone inpatients (n=7). We systematically explored the power of hypnotically induced mood states (euphoria, anxiety, depression, and anger) to elicit conditioned craving, withdrawal, or high responses in these subjects. We demonstrated that induced negative mood states, particularly depression and anxiety, could *by themselves* elicit increased craving and withdrawal, while induced euphoria reduced these same responses (ANOVA, main effect of mood on withdrawal and withdrawal symptoms, $p<.02$; subsequent paired comparisons, euphoria vs. depression, $p<.05$) (Childress et al. 1987b). This is illustrated in figure 4, which shows the increases in withdrawal symptoms (from baseline through mood induction) in a representative subject exposed to the moods of depression and anxiety, the lack of significant change in symptoms under the mood of anger, and the decrease in withdrawal symptoms during euphoria.

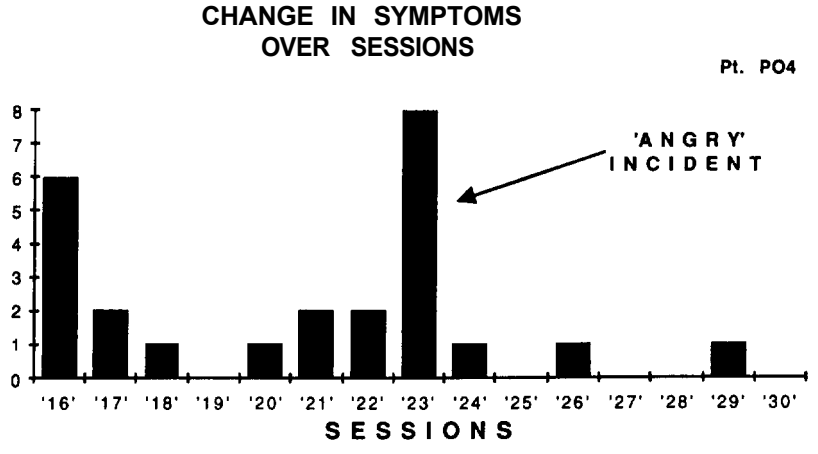

FIGURE 3. *Reinstatement of withdrawal symptoms in response to angry mood*

Detoxifying Methadone Patients. *To* address the need for an abstinent patient population and the need for a controlled setting during initial extinction trials, we initiated an inpatient treatment protocol with patients detoxifying from methadone maintenance (n=23). Extinction stimuli and treatment packages were essentially the same as those in the methadone outpatient study, and were delivered in the course of a 30-day inpatient stay. Initial results from this approach indicated that detoxifying inpatients also responded to the early presentation of these extinction stimuli with increased craving and subjective withdrawal, similar to our findings in the methadone-maintained patient sample. However, some of these detoxifying patients were experiencing mild withdrawal symptoms at the beginning of extinction sessions, even prior to exposure to the drug-related extinction stimuli. The presence of withdrawal symptoms presumably related to methadone dose reductions made extinction sessions difficult for these patients. The withdrawal symptoms also made it difficult for us to assess conditioned responses against a fluctuating physiological and subjective baseline.

Abstinent Opioid Users. To study the impact of extinction in abstinent, physiologically stable opioid abusers, our most recent protocol (Childress et al. 1986d; Childress et al. 1987a) has been conducted with patients from a nearby therapeutic community who have already completed 30 days of abstinence. This protocol incorporates all of the previously acquired knowledge into an optimal

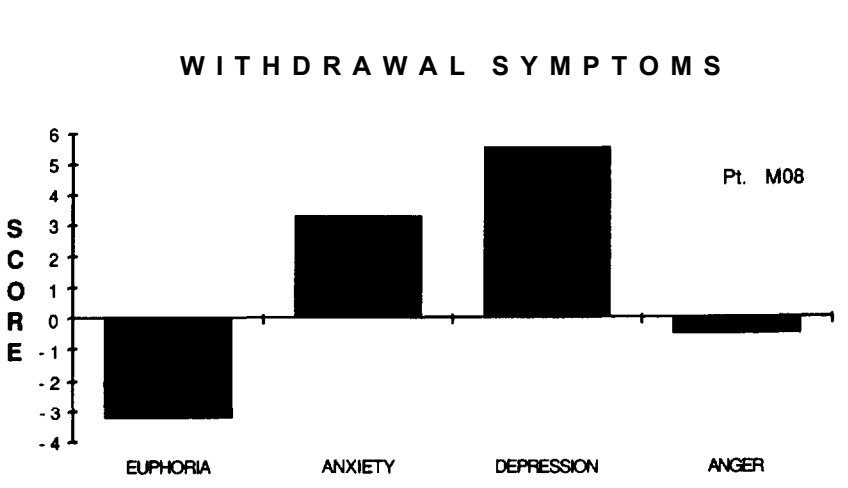

FIGURE 4. *Mood influences*

extinction package featuring: (1) abstinent, stabilized patients; (2) initial inpatient setting; (3) greatly intensified exposure to extinction stimuli totalling over 20 hours during the inpatient phase; and (4) incorporation of individualized and mood-related stimuli during an 8-week outpatient treatment phase that follows the inpatient stay. Patients are randomly assigned to psychotherapy or counseling plus intensive extinction or control activities. The recent decrease in pure opioid abusers due to the easy availability of cocaine has slowed patient accrual to this study. However, there is already clear evidence that abstinent patients experience craving and increases in withdrawal symptoms upon exposure to our extinction stimuli. This is illustrated in figure 5, which shows that the abstinent group had substantial ratings of craving in response to the drug-related stimuli during the early extinction trials (average of 7 on a l0-point scale). Further, this figure indicates the important finding that this revised extinction regimen (providing 6 to 7 times more stimulus exposure) was effective in virtually eliminating the conditioned craving responses to the drug stimuli by the 18th session (repeated measures ANOVA, reduction in craving, $p<.07$; reduction in withdrawal symptoms, $p<.07$). These early results have been so encouraging that we have adopted several features of this extinction procedure for our current project with abstinent cocaine abusers.

Abstinent Cocaine Users During the course of our extinction work with opioid abuse patients, there has been a dramatic increase in the number of patients seeking treatment for cocaine dependence. Given

FIGURE 5. *Abstinent former opioid users*

the need for innovative treatment strategies in this disorder and the particularly high rate of relapse after treatment for cocaine dependence, we began to explore the possible role of conditioned responses in relapse to cocaine use. In initial interviews, patients reported episodes in which encounters with talcum powder, powdered sugar, or even the sight of a cocaine-using friend would trigger arousal and strong drug craving. Because of the rich experience acquired through the study of conditioned opioid-related responses, we were able to efficiently begin a pilot study of the conditioned responses in cocaine-abusing patients and have begun work on a pilot extinction protocol. The transfer of technology enabled by our prior work with opioid-abusing patients has led to the rapid accumulation of findings, including the following:

(1) Abstinent cocaine abusers experience physiological arousal (decreases in peripheral skin temperature, a fall in galvanic skin resistance) and strong drug craving when exposed to cocaine-related vs. neutral stimuli. Figure 6 shows the differential skin temperature response to neutral vs. cocaine-related stimuli in a group of abstinent cocaine-abusing patients (ANOVA, $p<.007$).

(2) A preliminary extinction protocol employing 15 hours of repeated exposure to cocaine-related audiotapes, videotapes, and objects shows virtually complete reduction of cocaine craving (repeated measures ANOVA, $p<.008$) by the 15th hour of exposure (figure

7). Physiological arousal is often still in evidence at the 15th hour and may require further extinction.

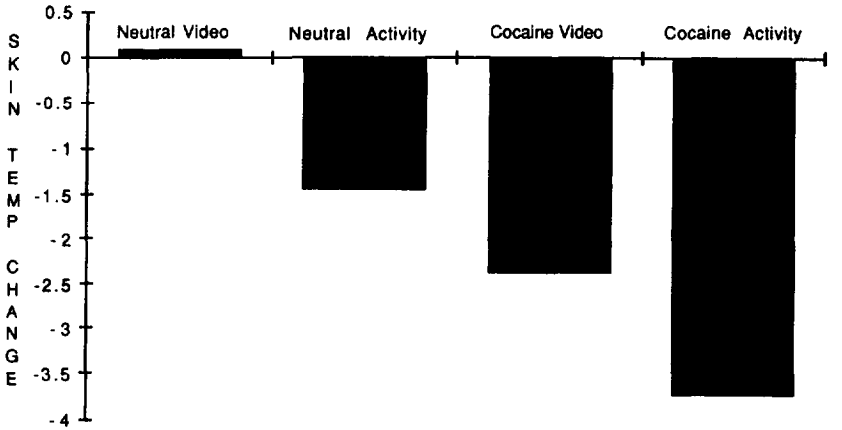

FIGURE 6. *Skin temperature responses in abstinent cocaine a&users (n=14)*

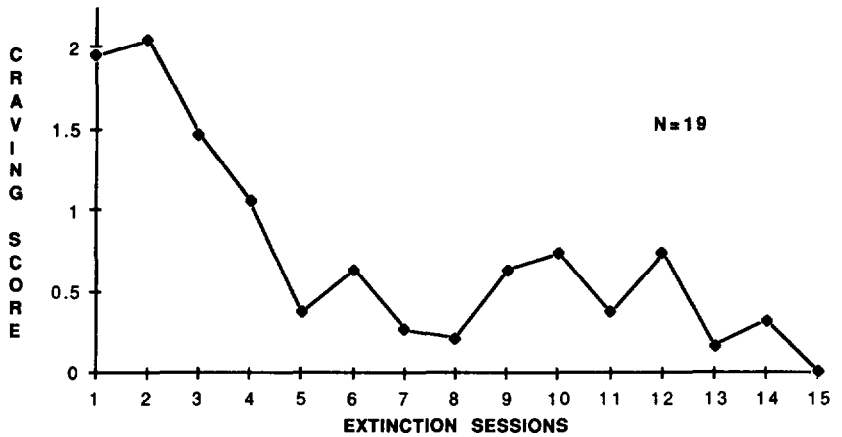

FIGURE 7. *Reduction in cocaine craving reports as a function of extinction trials*

REVIEW AND DISCUSSION

(1) We studied a population of patients maintained on methadone using standard drug-associated stimuli in a psychophysiological laboratory setting. In support of prior interview and questionnaire data, we found a wide variety of apparent conditioned responses on exposure to the drug-related stimuli. These include reports of high, craving, and withdrawal; physiological arousal; and decreases in peripheral skin temperature. The responses for the group as a whole were significantly different for the drug-related stimuli as compared to the neutral stimuli (ANOVA).

(2) Studies in abstinent former opioiddependent patients at least 30 days after detoxification revealed a similar pattern of conditioned responses. These patients had been protected from exposure to drug-related stimuli by remaining in the therapeutic community. The fact that these patients were still so responsive to drug-related stimuli after what is considered to be standard treatment suggests that they were vulnerable to relapse when exposed to similar stimuli after leaving the hospital.

(3) The incidence of drug-related conditioned responses is greatest in the natural environment, where response opportunities are more frequent and drug-related stimuli are more varied and more naturalistic than those in the laboratory setting.

(4) Abstinent cocaine abusers also respond to cocaine-related stimuli with physiological arousal, decreases in peripheral skin temperature and subjective reports of arousal and intense cocaine craving.

(5) Extinction procedures are effective in reducing the response to both opioid- and cocaine-related stimuli.

(6) Ongoing treatment/outcome studies with both abstinent opioid and abstinent cocaine abusers will help determine the possible clinical benefits of extinction, and by extension, the importance of conditioned drug-related responses in relapse.

in the course of gathering the data summarized above, we have expanded our research focus to include substances, stimuli, and responses additional to those targeted in our earliest work (table 1). Our earliest research efforts, for example, focused on conditioned

responses associated with chronic opioid use, particularly conditioned withdrawal. This initial focus was a function of Wikler's original clinical observations of presumed conditioned withdrawal-like responses in abstinent opioid abusers, and his hypothesis that conditioned opioid withdrawal was a crucial factor in relapse to drug use (Wikler 1948). Early focus on conditioned withdrawal was not difficult to understand: these phenomena were compelling and observable-and they offered a mechanism to help explain the mystery of relapse.

We also studied conditioned drug-like ("high") responses, but we found them to be relatively uncommon as a response to our test stimuli. Conditioned "highs" in response to saline self-injection were readily extinguished in most patients and we judged them to be less relevant than conditioned withdrawal to the clinical problem of relapse. The focus on conditioned withdrawal in turn shaped the search for important conditioned stimuli: stimuli were selected based on their ability to reliably elicit conditioned withdrawal. Though many different kinds of stimuli can elicit conditioned opioid withdrawal responses (in fact, in Wikler's early reports (Wikler 1948), the patient's own stories of his former drug use were potent triggers), we found stimuli proximal to drug administration to be particularly potent and reliable elicitors of conditioned withdrawal (table 1). Thus, most of our early extinction efforts were geared toward giving patients repeated, nonreinforced exposures to a standard set of external stimuli: syringes, cookers, white powder, even asking them to undergo nonreinforced "sham" injections. With considerable effort, we developed extinction procedures that could, in fact, produce a reduction in conditioned withdrawal-in patients who experienced it.

This last point has always been somewhat problematic for theories of conditioned withdrawal and relapse to opioid use; at least one-third of any patient sample we tested denied any "sickness signs" when exposed to drug-related stimuli. Conditioned drug craving, on the other hand, was nearly universally acknowledged: almost every patient either experienced in response to our stimuli or could recount episodes of drug craving in particular circumstances. In our discussions, we have often used the terms "conditioned withdrawal" and "conditioned craving" almost interchangeably, with the assumption that craving might be a form of mild withdrawal. Our patients did not, however, always subscribe to this position; reports of craving usually showed low correlations with reports of withdrawal. To paraphrase one indignant user, "No, Doc, craving is when you want

TABLE 1. *Change in research focus*

	Early Focus	Current Focus
SUBSTANCE	Opioids	Opioids and Cocaine
STIMULI	Proximal To Drug Administration	Proximal to Decision to Use
	Standardized	Individualized
	External	External and Internal
RESPONSES	Conditioned Withdrawal	Conditioned Craving
	Conditioned "High"	Conditioned Arousal
		Conditioned Withdrawal

it–want it so bad you can almost taste it. . . but you ain't sick. . . sick is, well, sick."

The recent tide of cocaine-abusing patients offered an important opportunity to advance our understanding of drug craving and the other conditioned phenomena associated with drug use and relapse. Cocaine is highly addictive, yet pharmacologically quite distinct from opioids. By inhalation or injection, it produces arousal, brief euphoria, and intense "roller waster" highs and lows. High doses or binge use can result in paranoia; termination of a binge often results in a "crash," characterized by lethargy and negative mood. Which of these many possible responses would become conditioned? And what would be the relevant eliciting stimuli?

Though we are still in the process of collecting data from cocaine-abusing patients, it seems evident that cocaine craving is by far the most common subjective response to cocaine "reminder" stimuli. Reports of increased arousal are not uncommon, and reports of "crash" or withdrawal-like feelings can also occur. The conditioned

physiological responses to cocaine-related stimuli are very similar to those found in response to opioid-related stimuli, including increased arousal and decreased peripheral skin temperature.

In selecting the eliciting stimuli for cocaine craving and other cocaine-related conditioned responses, we no longer focus exclusively on stimuli proximal to drug administration, but we now include stimuli that would occur earlier in the stimulus chain, supposedly proximal to the decision to use (table 1). Our move to include these earlier stimuli was prompted by patients' comments that most "real world" encounters with cocaine paraphernalia, for example, would have been preceded by a decision to use cocaine and that they would probably act on this prior decision, even if they experienced substantially less arousal or craving as a result of repeated exposures to the paraphernalia during extinction. We have continued to emphasize individualized stimuli (e.g., the patient's paycheck stub, his particular drug-buying corner) in the outpatient phase of treatment, to maximize the relevance and generalization of extinction. Some of the most important trigger stimuli for cocaine craving, as with opioid craving, may be internal mood states (e.g., depression) that have been repeatedly paired with cocaine administration (Childress et al. 1987b).

SUMMARY

We have shown that conditioned phenomena occur in a number of drug-related settings and that they can be reliably elicited and studied. Our recent work suggests that conditioned craving is an extremely prevalent, if poorly understood, response to drug-related stimuli and that it can occur independent of conditioned withdrawal responses. Our current extinction protocols are effective in reducing the conditioned responses to both opioid and cocaine-related test stimuli. How well this extinction training generalizes to the "real world," is, of course, the crucial clinical question. We are trying to maximize the generalization of extinction through use of realistic, individualized drug "reminders." The final clinical impact of these extinction procedures awaits completion of our ongoing treatment/ outcome studies in abstinent opioid and cocaine abusers.

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Types of Conditioning Found in Drug-Dependent Humans

Charles P. O'Brien, Anna Rose Childress, A. Thoms McLellan, Ronald Ehrman, and Joseph W. Ternes

INTRODUCTION

The evidence that drugs produce conditioned responses dates back to the studies of Pavlov in the early part of this century. Pavlov and colleagues noticed that dogs repeatedly injected with morphine by the same experimenter began to show the appearance of morphine effects at the mere sight of the experimenter with the syringe (Pavlov 1927). The dog would begin to salivate, vomit, and become sedated even though no morphine had yet been received. Collins and Tatum (1925) also reported the conditioning of a morphine-induced salivary response. These were the earliest reports that pairing drugs with neutral stimuli produced a conditioned response (CR); in this case the conditioned response seemed to be similar to the effects of the drug itself.

It was Abraham Wikler who first drew the connection between conditioning of drug effects and the problem of relapse to drug addiction (Wikler 1948). Wikler noticed that while inpatients at the Addiction Research Center in Lexington, KY, were having group therapy sessions, they often found themselves talking about drugs, effects of drugs, and ways of administering drugs. Despite the fact that these men had been completely detoxified many months before, they would, on certain occasions, show the signs of opiate withdrawal. Wikler noticed that they would rub their eyes as though they were tearing, yawn, and act as though they might be going through mild withdrawal while the topic of drugs was being discussed.

When Wikler interviewed patients who had returned to Lexington after having relapsed, he often heard a puzzling story. Typically, the former addict felt fine just after leaving the hospital: however, on

returning to his home, which was usually New York City, the former addict began to feel ill. When he began to see the sights of New York City, the former addict, who may have been drug-free for several years, would again begin to feel the signs and symptoms of opiate withdrawal. Sometimes the patient would become nauseated and actually vomit. Patients also reported a strong urge to inject heroin during this period just after returning home. Usually the patient would give in to this craving within the next few days and quickly become readdicted.

Stimulated by these clinical anecdotes, Wikler began a series of animal studies aimed at confirming in the laboratory that withdrawal symptoms could be conditioned (Wikler and Pescor 1967). In one of his studies, Wikler and colleagues injected rats with morphine once a day in their home cage and then moved the animals to a distinctive environment as the effects of morphine were fading. As the rats became tolerant and dependent on once-daily morphine injections, they experienced a period of withdrawal each day in the distinctive environment. Thus, a specific environment (complex conditioning stimulus) was paired with the morphine withdrawal syndrome. At the end of 6 weeks, the morphine injections were terminated, and the rats were allowed to detoxify. When the now drug-free rats were returned to the environment where they had repeatedly experienced withdrawal, the animals showed withdrawal-like behavior. The most striking and quantifiable behavior exhibited by rats in withdrawal was a shaking movement called “wet-dog shakes.” Since the pioneering studies of Wikler, other investigators have demonstrated that opiate withdrawal can be conditioned in animals, although it has not been clearly shown in animal studies whether this conditioned withdrawal can actually enhance the probability of relapse to dependence on drugs.

We became interested in pursuing Wikler’s observations in human subjects because of their potential clinical significance. In the early 1970s, we began a series of systematic studies in which we interviewed patients about the possibility of conditioned responses. We found that drug-free patients frequently reported situations that produced feelings of craving for drugs and, at times, the signs and symptoms of withdrawal (O’Brien 1975). Some of the patients, certified drug-free by urine testing and counseled in the drug-free section of our treatment program, were able to list a hierarchy of stimuli that produced feelings of craving or withdrawal. We also noticed that patients on methadone maintenance reported similar kinds of responses even though their pharmacological need for opiates

was satisfied by a steady dose of methadone. Our patients indicated to us that these responses seemed to come “out of the blue” and were experienced as being “real.” The patients also indicated that sometimes these responses could only be relieved by taking drugs.

In a related series of studies, we found that a significant number of patients who applied for admission to our methadone program only appeared to be dependent on opiates. These patients had evidence of opiate use in their urines and needle marks on their arms, but they did not have evidence of current physical dependence when tested by naloxone. We found that about 27 percent of patients fell into this category (O’Brien 1975). Blachly (1973) also reported that as many as 40 percent of patients fell into this category. Thus, it appeared that there were factors other than physical dependence that were causing patients to persist in the use of street opioids.

EXPERIMENTAL EVIDENCE OF CONDITIONED WITHDRAWAL IN HUMAN SUBJECTS

Our initial clinical studies convinced us that there were phenomena present in drug-dependent patients that could not readily be explained by the known pharmacology of opiates. A conditioning explanation seemed plausible, but it would be necessary to try to study the phenomenon directly. To do this, it would be necessary to produce the phenomenon in the laboratory.

We designed an experiment for humans, patterned after the work of Goldberg and Schuster (1970) who reported conditioned withdrawal in monkeys. These investigators paired a red light conditioning stimulus (CS) with nalorphine-precipitated withdrawal symptoms in morphine-dependent monkeys. The nalorphine (unconditioned stimulus (UCS)) produced immediate suppression of lever pressing for food and the prompt onset of physiological signs of precipitated opioid withdrawal (unconditioned response (UCR)). After only 10 red light/nalorphine pairings, the morphine was withdrawn, and the animals were maintained drug free. However, in these postaddict monkeys, the red light (CS) was now able to elicit a CR consisting of suppression of bar pressing for food, as well as heart rate decreases, vomiting, and excessive salivation.

Our human studies of conditioned withdrawal consisted of two separate experiments using two different groups of eight subjects per experiment (O’Brien et al. 1976; O’Brien et al. 1977). A mild unconditioned withdrawal symptom (UCR) was precipitated in

methadone-maintained volunteers by means of a very small (0.1 mg total dose) intramuscular injection of naloxone (UCS). The unconditioned withdrawal reaction consisted of tearing, rhinorrhea, yawning, decreased skin temperature, increased respiratory rate, subjective feelings of drug craving, and sickness of about 30 minutes duration. These symptoms were paired with a tone and odor of peppermint (compound CS) over 12 training trials. On test trials, the CS was paired with a saline injection and this produced autonomic, behavioral, and subjective changes resembling a naloxone-precipitated withdrawal reaction. This apparent withdrawal reaction was interpreted as a CR similar to the UCR but on the average less severe.

We used 12 training trials, but conditioning occurred much earlier and generalized from the specific CS to include the test chamber itself. Thus, after several trials, the reaction began to occur even before the subject entered the test room. With repeated unreinforced trials, the effect began to extinguish, although there is anecdotal evidence that the reaction to the peppermint odor persisted in two subjects for several months.

Conditioned withdrawal responses that have been experimentally produced have been remarkably long-lasting. Wikler and Pescor (1967) observed withdrawal signs (increased wet-dog shakes), in association with the abstinence environment for about 5 months after the last exposure to the UCS. Goldberg and Schuster (1970) found withdrawal symptoms (suppression of bar pressing for food and heart rate changes) in monkeys on presentation of the CS (red light) for up to 4 months after last exposure to the UCS.

The model used for explaining this conditioning procedure is given in figure 1. Episodes of withdrawal symptoms occur repeatedly in the same environment. Environmental cues act as a complex CS, and, with repeated pairing of the withdrawal symptoms and the environment, the environment acquires the ability to elicit withdrawal symptoms in the absence of a pharmacological basis for withdrawal. This means that if the patient returns to this environment later in a healthy, drug-free state, the withdrawal symptoms would recur.

The conditioning procedure described above requires that initially the subject be opioid dependent so that withdrawal symptoms can occur and can be paired with environmental stimuli. At a later time, when the individual is no longer dependent, the environmental cues alone would be enough to elicit the symptoms of withdrawal. Nondependent

Unoconditioned Stimulus *Opioid metabolized Receptors evacuated*	——>	**Unconditioned response** *Rebound* activity: *adrenergic, cholinergic, etc. (tearing, rhinorrhea, tachycardia, nausea, diarrhea, etc.). Drug-opposite effects*
Conditioning Stimlus *Drug procuring or using environment: sights, sounds,* smells, situations, fantasies	——>	**Conditioned Response** *mild version of* above *symptoms drug-opposite effects*

FIGURE 1. *Conditioned withdrawal (dependent subject)*

drug users could not develop conditioned withdrawal symptoms by the paradigm described in figure 1 because they never experienced the unconditioned drug withdrawal required to be associated with environmental cues. There is, however, another theoretical mechanism which could apply not only to drug users who have experienced episodes of withdrawal, but also to users who have never experienced withdrawal symptoms as well as to nondependent users of drugs. This mechanism is described below and diagrammed in figure 2.

CONDITONED WITHDRAWAI AND CONDITIONED TOLERANCE

In the experimental demonstrations of the conditioned withdrawal syndrome, the pharmacological withdrawal was paired with a CS by controlling the onset of withdrawal either by timing of opioid dose (Wikler and Pescor 1967) or by administration of an antagonist that precipitates immediate withdrawal (Goldberg and Schuster 1970; O'Brien et al. 1977). An addict who maintains his habit to avoid withdrawal sickness would have little or no opportunity to acquire conditioned withdrawal by pairing sickness with environmental cues. However, he might still acquire conditioned drug-opposite responses that would resemble conditioned withdrawal if unopposed by the immediate injection of opioid. The proposed mechanism (figure 2) can account for a portion of observed tolerance phenomena and is described in detail by Siegel (1975), Siegel (1976), and Siegel (1978).

Thus, the cues repeatedly associated with drug procurement or injection provide a signal that warns the subject to "prepare" for the

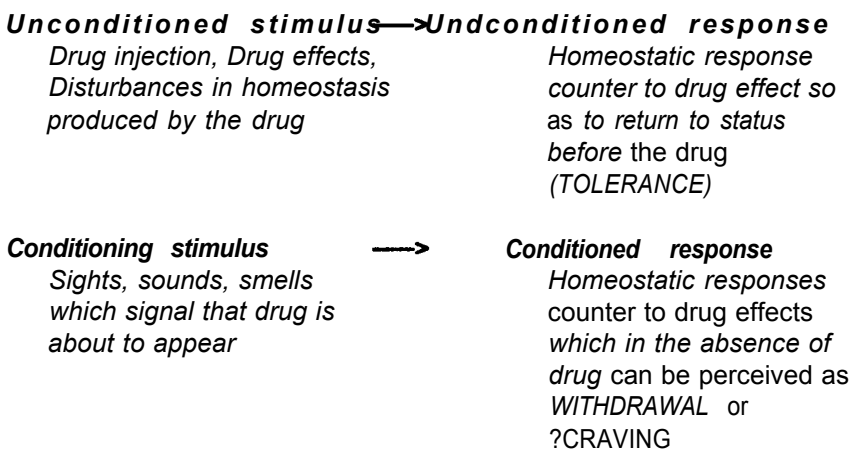

FIGURE 2. *Conditioned tolerance (dependent or nondependent subject)*

effects of the drug by initiating homeostatic responses (tolerance) that are opposite to drug effects. These conditioned drug-opposite or tolerance responses can occur in a drug user who has not had repeated episodes of withdrawal sickness in a specific environment, but, since they are physiologically similar to withdrawal responses, they may be perceived as withdrawal-like. Those drug users who have had repeated episodes of withdrawal in a specific environment will, therefore, have two mechanisms for producing conditioned withdrawal-like symptoms: the first by the "conditioned withdrawal" paradigm described in figure 1 and the second by the "conditioned tolerance" mechanism described in figure 2.

Clinical Relevance of Conditioned Withdrawal

Wikler's description of conditioned abstinence or withdrawal caused clinicians to begin looking for such phenomena in their patients. Relapse occurs in the vast majority of detoxified patients, and, when asked about reasons for relapse, most patients report very little insight into their own behavior. The first drug use after a detoxification usually appears to be an impulsive act.

The typical street addict engages in behavior, especially drug-taking behavior, without thinking. The impulsivity is so marked that the individual often really does not know why he performed a given action. When questioned about the reasons for a particular drug

administration, the typical response is, “I wanted to get high.” Addicts usually do not talk spontaneously about relieving withdrawal or discomfort, but, in actual practice, the injection of opioids often simply relieves withdrawal and may not produce the desired euphoria. McAuliffe (1962) interviewed 40 street heroin addicts in an attempt to assess the role of conditioned withdrawal in relapse. All of these subjects had experienced a period of abstinence on the street. While 27.5 percent reported being aware of conditioned withdrawal, only two (5 percent) gave this as a reason for resuming drug use. The author concluded that conditioning factors were unlikely to be a major cause of relapse. Of course, it is difficult to extrapolate self-report data from active street addicts and apply those data to the problem of relapse after treatment. it is probable that there are multiple factors leading to relapse, and conditioned craving or conditioned withdrawal may be included among those factors.

It is difficult to find a valid method to assess the clinical importance of conditioning phenomena in relapse. In our studies of the relapse problem, we began by doing structured behavioral interviews with three types of patients: (1) those who had just been detoxified and were in danger of relapse; (2) former patients who had been drug-free for months or years: and (3) patients who had recently relapsed. By verbally taking these subjects through behaviors and situations step-by-step, we were able to determine more precisely the sequence of their relapse or near relapse. In these interviews, we were careful not to lead the subject into responding in a certain way. Often there was initial resistance to a detailed behavioral analysis and resistance to questions about feelings and reasons for actions. Subsequently, however, many patients have reported insights about their own impulsivity and regarded the interviews as therapeutic.

The reasons found for relapse were quite varied in several series of patients. One-third to one-half of our patients were able to identify places or situations that made them feel unexplainably ill, anxious, or in need of a fix (Childress et al. 1986a; Childress et al. 1986b; Childress et al. 1986c; O’Brien 1975). Also certain moods (e.g., depression or anger) were found to trigger drug craving or sickness (Childress et al. 1987). It is of interest that in these reports negative feelings, affects, or even withdrawal sickness (sniffing and tearing) were commonly mentioned, but euphoria was rarely experienced as a possible conditioned effect. Our patients were able to recall situations or places where they began to feel a desire (craving) or need for an injection, but they rarely reported the

opposite feelings, that is, situations that made them feel euphoric in the absence of a drug.

Most of the stimuli reported by our patients involved seeing people using drugs, seeing drugs, or possessing the money to buy drugs. We found that some patients believed they could rate these stimuli in descending order of potency. Most stimuli are found in the patient's neighborhood; ,however, some patients report that they feel illness or drug craving when watching movies or experiencing fantasies about drug use. Some of our patients even reported craving or illness when they viewed an antidrug poster in the hospital, because it showed a person "shooting-up."

Similar patient reports have been noted by others. For example, Whitehead (1974) described cases of methadone-maintained patients who showed signs and symptoms of withdrawal, despite continuing high-dose methadone, each time they encountered social or psychological conflicts. Whitehead referred to this as "pseudo-withdrawal" and invoked a learning explanation.

That conditioned withdrawal may occur during methadone maintenance is further suggested by the responses of 100 consecutive methadone patients in our clinic (O'Brien 1975). A questionnaire designed to elicit conditioned withdrawal symptoms was administered. More than half the respondents reported withdrawal symptoms (sickness) or craving for no apparent reason in response to items on a list of drug-related stimuli. The stimuli that produced craving correlated 0.8 with sickness, suggesting that, in this group of patients, the two responses could be elicited by similar stimuli.

Surveys that rely on patients' memories of past experiences are subject to many sources of potential error. To improve our source of information, we conducted an 8-week prospective study that involved weekly structured interviews concerning situations that provoked desires to use drugs. Seventeen methadone patients have been studied in this manner, and interviews of abstinent former opioid abusers are now in progress. The structured interviews enabled us to get a clearer picture of the occurrence of drug-related responses over time. Sixteen of the 17 methadone patients (94 percent) reported episodes of drug craving in real-life situations (e.g., sight of a drug-using friend) that occurred during the period of study. Sixteen of 17 patients (94 percent) also experienced episodes of withdrawal-like feelings. Though patients often attributed these withdrawal-like episodes to physical discomfort or "methadone dose not holding,"

some of these episodes may have been conditioned in origin: their occurrence was unrelated to the time since the last dose of methadone. Spontaneous high-like feelings were less commonly reported, but 76 percent of the methadone patients reported at least one such episode (Childress et al. 1986a).

Among the abstinent patients who were followed for 8 weeks, all (8 of 8 thus far) have reported episodes of opioid craving, averaging 11 episodes per patient over the 8-week period. In contrast to the frequency of craving episodes, reports of withdrawal and high-like episodes were relatively rare (totaling three and two episodes, respectively). These results are still being analyzed and are being used to develop a database on the sequence of events in relapse. We are in the process of collecting the same type of "natural incidence" data from abstinent cocaine abusers as they proceed through outpatient followup. Thus far, our longitudinal work in this area indicates that concurrent collection of data from outpatients is feasible. By this longitudinal method, we hope to obtain a clearer and perhaps more valid picture of the role of conditioning in relapse to drug dependence.

NATURAL CONDITIONING: DRUG-OPPOSITE RESPONSES

Above, we discussed the evidence that withdrawal symptoms could be produced under experimental conditions in the laboratory. There have also been studies with human addicts that have attempted to detect natural conditioning that may have occurred on the street during fortuitous pairings of environmental stimuli with either onset of drug effects or drug withdrawal effects. Our attempts to detect these naturally conditioned phenomena involved the presentation of drug-related stimuli while the subjects were being monitored, in order to detect the presence of CRs. Teasdale (1973) showed slides of drug-related scenes to postaddicts and recorded significant changes in mood scales, suggesting increased tension and confusion. He also' reported a significant increase in subjective symptoms of opioid withdrawal, when compared to the effect seen after viewing slides of neutral scenes. Our group has also reported subjective changes (O'Brien 1975; Ternes et al. 1980) after exposure to drug-related stimuli and physiological changes (Ternes et al. 1980; Hugdahl and Ternes 1981) such as tachycardia and decreased skin temperature. Sideroff and Jarvik (1980) also reported subjective discomfort and tachycardia in detoxified addicts shown videotapes of drug-related behavior.

These results (Teasdale 1973; Ternes et al. 1980; Sideroff and Jarvik 1980) suggest that the drug-related stimuli act as conditional stimuli that are capable of eliciting a withdrawal-like reaction if they are not followed by a drug effect. A very convincing demonstration of this conditioning effect has been published (Ternes et al. 1982). This study paired entirely arbitrary laboratory stimuli, Hawaiian Punch and an auditory tone, with infusions of hydromorphone. The arbitrary nature of the training stimuli is an important feature of the experimental strategy for demonstrating the power of opioid drugs to produce conditioning. The results demonstrated rapid acquisition of conditioned physiological and subjective responses that resemble the withdrawal-like reactions (for example, skin temperature decrease) seen in all of our earlier studies Ternes and O'Brien 1982). What is significant about these results is the striking similarity in the physiological responses we observed between the form of CR obtained with an arbitrary CS in the laboratory, and the putative CRs that are elicited by naturalistic CSs in these other experiments (Hugdahl and Ternes 1981; Sideroff and Jarvik 1980; Ternes et al. 1980). The form of these conditioned physiological responses has generally been opposite to those induced by unsignaled drug administration (Ternes and O'Brien 1982). Consequently, they have been described variously as conditioned compensatory responses (Siegel 1978) or as conditioned abstinence syndrome (Grabowski and O'Brien 1981).

CONDITIONED OPIATE-LIKE RESPONSES

The report from Pavlov's laboratory described in the beginning of this paper involved a conditioned response to the sight of the experimenter that resembled the unconditioned effects of morphine itself. Similar findings of drug-like conditioning have been reported by others in dogs (Collins and Tatum 1925; Lynch 1978; Rush et al. 1970) and in rats (Eikelboom and Stewart 1979; Miksic et al. 1975; Numan et al. 1975). However, Wikler (1973) presented the argument that these apparent drug-like responses are actually adaptive responses to the presence of the drug and that a direct drug effect is not being conditioned. He argued that the direct effect of morphine is stimulation of the chemoreceptor trigger zone in the medulla and that salivation, vomiting, and sleep are adaptive responses to this stimulation. Thus, although the conditioned response appears to mimic the morphine effect, what really has been conditioned is an adaptive or opposing response to the morphine. In this view, the apparent drug-like responses are only another example of the conditioned tolerance response described in figure 2.

Another example of drug-like effects is found clinically in patients known as “needle freaks” (Levine 1974). Typically, these are individuals who formerly have been physically dependent on opioids. They report euphoria from the act of self-injection. At times they have been observed to show physiological signs such as pupillary constriction after injecting saline (O’Brien 1975). A similar finding was observed in some of Meyer and Mirin’s subjects (1979). Some of these cases have been detected among applicants applying for methadone treatment. Federal regulations limit the use of methadone maintenance (except in certain special cases) to individuals who are physically dependent on opioids. If there are no signs of withdrawal in an applicant, a naloxone injection may be used to precipitate withdrawal in order to support the diagnosis of dependence (Blachly 1973). Occasionally, we have observed euphoria instead of withdrawal when the injection of naloxone is given. Subsequently, we obtained the same results when these subjects self-injected saline; thus the euphoria was not a pharmacological effect of naloxone but likely a conditioned response to any injection.

There have been few direct observations of human subjects in the act of self-injection with appropriate physiological and psychological monitoring. Our group reported a series of studies (O’Brien 1975; O’Brien et al. 1974; O’Brien et al. 1980) that described self-injections in detoxified opioid addicts being treated with the opioid antagonists cyclazocine or naltrexone. Several experimental protocols were used. In one series, the patients were randomly assigned to self-injections with either saline or opioid; in others, the patients were tested with both saline and opioid on different occasions. These experiments began with “credibility” trials in which the subject was allowed to self-inject opioid or saline (double-blind, unblocked), prior to beginning antagonist maintenance. Subsequently, we conducted extinction trials in which the subject repeatedly self-injected opioid or saline while being maintained for up to 8 months on the antagonist. The purpose of the experiments was to determine whether the clinical effectiveness of the antagonists could be enhanced by a series of nonreinforced or “blocked” self-injections.

Findings relevant to the discussion of conditioning were that saline self-injections were usually reported as pleasurable and identified as a low dose of opioid. This effect was greatest in protocols under naturalistic conditions resembling the patient’s “shooting gallery,” with the patient expecting to get “high.” The effect was diminished, but still present when the patient was placed alone in the nonnaturalistic setting of a recording chamber, with various electrodes and

strain gauges attached to him. Some subjects showed a small pupillary constriction after saline injections but never to the degree seen after unblocked opioid injections.

Although our experienced addict subjects almost always reported that initial saline injections were pleasant, subsequent self–injections produced unpleasant effects in most of the subjects. Subsequent injections occurred while the patients were being maintained on an opioid antagonist, but there is no reason to believe that their reactions to saline or to opioid were related to the pharmacological effects of the antagonist. We observed a diminution in the reported pleasant effects of the injections after the first trial, and after several trials the experience became neutral or unpleasant. These subjective effects were reflected in changes in physiological responses. Preinjection stimuli ("cook-up") produced withdrawal-like effects such as lowered skin temperature and tachycardia; after injection, subjects showed increased skin temperature and a slowing of the heart rate. After several trials, the pleasant subjective effects and the drug-like physiological changes disappeared. Subjects were reluctant to continue self-injections after the experience changed from pleasant to unpleasant. Those who were induced by cash payments to continue the injections experienced discomfort that mimicked the opioid withdrawal syndrome. In other words, the self-injection of saline appeared to produce a conditioned withdrawal response.

In various protocols studying the narcotic antagonists, cyclazocine and naltrexone, we allowed 85 subjects to perform self-injections. Of these, three were clear "needle freaks" in that the positive effects of the saline injections persisted for up to 20 trials. The rest began to experience withdrawal-like effects from the procedure after the first two to five injections.

Meyer and Mirin (1979) used a different design and also observed conditioned opioid-like autonomic effects in human subjects. Their subjects were all recently detoxified inpatients who were given either naltrexone or naltrexone placebo under double-blind conditions. The subjects were then permitted to self-inject known amounts of heroin that they had earned by performing a simple operant task. In effect, the subjects who received naitrexone placebo had the opportunity to inject "free" heroin unimpeded by naltrexone, and they injected it nearly the maximum number of times permitted by the protocol. However, the 22 subjects who received naltrexone had the rewarding effects of heroin blocked by this antagonist. Eleven of these

subjects stopped injecting heroin after fewer than 5 trials, but the other 11 subjects took an average of 16 doses of heroin despite the presence of naltrexone. These 11 subjects were found to be different from those who stopped quickly in that they showed distinct autonomic changes resembling opioid effects after the first three presumably Mocked injections. The authors interpreted these autonomic changes (pupil, heart rate, and blood pressure) as conditioned opiate-like effects and they found that these autonomic changes had disappeared (extinguished) by the time the subjects decided to stop injecting. Unlike the outpatient studies described above, the Meyer and Mirin protocol did not require the subjects to continue to inject unless they wished to do so. Since they did not continue injecting past the point at which the procedure became neutral, this probably explains why unpleasant or withdrawal-like symptoms were not reported.

Thus, the evidence for conditioned opioid-like effects in humans is based on clinical anecdotes and the self-injection studies described above. These conditioned responses are elicited by the complex CS of preinjection rituals and the act of self-injection. In most subjects, the opioid-like CR is extinguished quickly and then withdrawal-like CRs are elicited by the same CSs that previously produced opioid-like effects.

It is difficult to fit the human needle-freak data into the model of conditioned adaptive responses first proposed by Wikler (1973). It would appear that there is a third type of CR, at least in the case of opioids, which consists of a CR that resembles the drug effect and that seems to extinguish more rapidly than the drug-opposite CRs.

Extinction of Conditioned Responses Elicited by Self-Injection Rituals

The implicit hypothesis, originally argued by Wikler, is that CRs constitute, in a sense, a new illness for the chronic drug user.. Whatever the reasons for starting the use of the addicting drug, the chronic administration has created CRs which tend to perpetuate drug use. The obvious test of this hypothesis would be to extinguish the CRs and measure the rate of relapse. Our group attempted such a study (O'Brien et al. 1980) and, in retrospect, the attempt seems naive. Subjects who had been started recently on naltrexone, the long-acting opioid antagonist, were exposed to many of the presumed CSs that occur before and during the act of self-injection. They were asked to take bags of heroin, prepare the drug for injection

("cook-up"), apply a tourniquet, and inject a substance (opioid or saline, double-blind) into the vein. There was no attempt to systematically deal with earlier situations that would be involved in the decision to acquire and to administer the drug. The complex stimuli that are more remote from the act of self-injection generally evoke less dramatic CRs than the proximal stimuli, but may have pivotal importance to clinical outcome.

The results of the procedure that focused strictly on "cook-up" and "shoot-up" were interesting in that strong affects and physiological changes were evoked. The changes in valence of affective response were described earlier in this chapter. Briefly, the procedure initially produced mild opiate-like euphoria. This decreased over several trials, then disappeared, and was replaced by negative affects and gradually worsening withdrawal responses. After 5 to 10 unreinforced self-injections, most subjects became too upset to continue. The dysphoria was accompanied by reductions in skin temperature and tachycardia similar to that seen during the opioid abstinence syndrome.

The results of this study included extinction of the opiate-like responses elicited under these experimental conditions, but no extinction of the withdrawal-like responses. Followup of the experimentally treated patients 8 months after the attempts at extinction revealed a somewhat better outcome for these "partially-extinguished" patients than the outcome of a reference group of naltrexone patients who received no attempts at extinction (O'Brien et al. 1980). However, there were no concurrent randomly assigned controls in this pilot study and we concluded that the procedure evoked such strong dysphoric effects that it was not feasible as a clinical approach.

We have subsequently begun a series of controlled treatment outcome studies involving the use of an extinction procedure integrated with a comprehensive rehabilitation program. This is described by Childress and collaborators (this volume).

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The Economic Shaping of Substance Abuse

William D. Lerner and James M. Raczynski

INTRODUCTION

Substance abuse may be conceptualized as arising from two interrelated systems: an intrinsic system unique to the individual and defined by biological and psychological factors and an extrinsic system occurring externally to the individual and consisting of social, economic, and pharmacological factors. The development of a substance abuse disease arises through the interaction of components of both systems.

While biological and psychological factors certainly cannot be minimized in understanding substance abuse etiology, substance abuse disorders cannot develop without access to abusable substances, usually necessitating a purchase. It is our contention that understanding substance abuse requires examination of all these factors (including economic ones) and their interdependent relationships. Our examination of the literature found only 10 studies which have examined the economic component involved in the etiology and maintenance of substance abuse disorders. The intent of this paper is to examine the potential interaction and significance of economics with other factors in shaping substance abuse disorders.

Economic relationships predominate in several areas of substance abuse. One area (beyond the scope of the present manuscript) is the international trafficking and distribution of drugs (Holahan 1972; Preble and Casey 1969). However, economic considerations are involved at all levels of drug sales and marketing (from the supplier's perspective) and drug selection and choice (from the consumer's perspective); these considerations involve supply and demand economic relationships (Bernard 1989). Drug abuse also has a major influence

on the user's economic patterns, propelling abusers toward particular illicit activities. In addition, economic factors contribute to the development of particular peer relationships among drug addicts. Finally, economic relationships emerge in the patterns of psychopathology seen among substance abusers and may have bearing on treatment and outcome.

Economic Relationships in Drug Marketing

Substance abuse disorders, by definition, are exposure illnesses. That is, no illness can occur without exposure to a psychoactive agent. Unlike other exposure illnesses, however, a substantial expenditure must occur with substance abuse disorders. An economic system of commodity exchange must be established, with the obvious conclusion that the commodities exchanged be assessed as approximately equal by those participating in the exchange. Although one commodity may be presented in the form of services, friendship, or items, it is usually expressed in monetary terms. The value of the other commodity is related to the drug, both type and amount. Not only is type significant, but, as with any supply and demand economic situation, availability and supply are highly significant in establishing value.

Based on economic relationships, one may hypothesize that the value in dollars approximately equals the net effect of the drug in terms of euphoria. Indeed, it may well be that the street value of the drug relates to its desirability for abuse. If one looks at the stimulants magnesium pemoline, dextroamphetamine, and cocaine, it becomes obvious that, although all are stimulants, differences in street value may be considered as arising from quantitative differences in the euphoric value of these three agents. That is, equivalent doses of these drugs have a low euphoric value for magnesium pemoline, an intermediate euphoric value for dextroamphetamine, and a high value for cocaine. Street prices of these drugs increase with euphoric value. The same can be hypothesized for sedating agents, such as phenobarbitol, secobarbitol, and methaqualone. Again, although all are sedating agents, they have escalating economic values, respectively.

A further aspect of this economic system is indicated by reviewing the demand for the drug Dilaudid versus the drugs Percocet and Percodan (hydroxycodone). Dilaudid is significantly more potent than hydroxycodone and more bioavailable (readily entered into solution in water and injected). Conversely, Percoset is less soluble and very irritating to the veins, thus, it is used orally. Hence, the economic

value of Dilaudid is assessed at a significantly higher level than that of Percocet due to euphoric potential as well as mode of administration. Heroin is an interesting drug from a marketing standpoint, in that it has followed trends parallel to inflation. In the early years of widespread heroin abuse, heroin was typically marketed in a “nickel” ($5) bag. As inflationary trends occurred, heroin became available only in a “dime” ($10) bag, although there was quantitatively little difference between the “nickel” bag of the 1950s and the “dime” bag of the 1960s. During the 1970s, the “quarter” bag evolved, which at the time contained three times as much heroin as a “dime” bag. However, in the 1980s, a “quarter” bag contains quantitatively about as much heroin as the “nickel” bag of the 1950s. Studies performed in St. Louis, Memphis, and, more recently, in Richmond showed that the dose of methadone necessary to block narcotic withdrawal did not vary significantly over 7 years in the three different cities. This finding suggests that despite the increase in cost of heroin and packaging of the product the amount used by addicts has remained approximately the same.

A salient illustration of economic considerations in marketing of drugs is seen in the description of street heroin sales in New York City by Goldstein et al. (1984). Due to the large number of sellers of heroin in New York, a “buyers’ market” resulted. Heroin dealers began using labels as a marketing tactic, either by writing names on the bags or by using colored tapes indicating the particular source of the heroin (table 1). Some of the elaborate names utilized included “D.C., Death, Death Row, Death Wish, Deer Hunter, Doggie, DOA, Double X, Down and Dirty, Dragon Lady, Dragon’s Potion, Dust, Dynamite, and Dynamite it.” These brand names were utilized so that a buyer could begin to identify with one brand name and to develop trust “in the product,” creating markets for the products of particular suppliers. The authors noted that if one brand provoked an overdose and buyers became aware of that overdose, then more buyers would seek that particular brand due to its reputation of being particularly potent.

Economic Relationships to Drug Selection

Economics may be seen as playing a significant role in the choice of abused drugs as well. Alcohol, which is so inexpensive and so readily available that essentially it can be used by anyone irrespective of economic status, is a pure example of this concept. The low cost, ease of access, and adequacy of supply may well explain the popularity of alcohol with everyone from the teenager through the

TABLE 1. *Heroin labels.*

Eagle	Killer	One for the Road
Ebony Red	Killer 1	100 Proof
888	King	007
Evenings Delight	King Kong	Original
Evil Witch	Kiss of Death	Original Blue Magic
K.K.	Original T	
Feel Like Dynamite	Knock	Owl
Ferret	Knockout	
Fire 1	Kojak	Parcel Post
First Class	Kosher Poultry	Past Due
$5	Kung Fu	Pay Back
500		P.C.
Freak of the Week	Leo	Peace
F*** Me	Liberation	Pebble
F*** Me Please	Libra	Pink Panther
Lion	Pisces	
Gemini	Lips	Prophecy
Georgia Boy's	Lite 'N Lively	Prostitution

Source: Reprinted with permission from The Journal of Drug Issues. 1984.

elderly population. Given these access and exposure considerations, it is not surprising that a similar rate of alcoholism is seen across the population regardless of economic or socioeconomic level.

The relationship between cost and prevalence may also explain the current trends with cocaine. The high cost of cocaine when used intranasally, at $50 to $75 a gram, limits use to only those with adequate fiscal resources. The very high cost of using cocaine intravenously or freebasing also markedly limits the number of consumers. Based on these economic factors, cocaine was considered unlikely to become a major problem in this country as late as 1977 (Adams and Durell 1984). Recent marketing changes in cocaine distribution, however, have significantly altered this prediction.

The introduction of "crack" may be seen as a manufacturer's move based predominantly on economic rather than pharmacological factors. "Crack" has reduced the marketing dose from $50 to $75 for intranasal use to $5 to $15 for inhalable cocaine. With the sharp decrease in cost, the number of individuals able to purchase the drug

has markedly increased. However, while one can predict from an economic perspective that the overall use of “crack” may increase, cases of high-level abuse of “crack” will still be limited despite this manner of marketing. To utilize crack on a regular basis requires the expenditure of several hundred dollars per day, an amount which is still economically beyond the reach of the majority of the population.

These economic relationships are also clearly seen among adolescent drug users and in the relationship between education level and addiction history. The adolescent population with limited economic resources tend to use less expensive drugs such as alcohol, marijuana, and “crack” on a regular basis; teenagers are less frequently observed abusing expensive drugs such as freebase cocaine or Dilaudid. In regard to educational level and history of drug use, Crawford et al. (1963) found greater percentages of high school graduates as the frequency of drug use increased; this relationship may emerge as a result of the greater income potential of high school graduates, providing more economic means for increased drug use.

Drug Abuse Effects on Users’ Economics

The regular use of a drug, such as heroin, requires the ability to generate consistently the street cost of the drug. Legal activities often do not provide the drug abuser sufficient sustained income for two reasons. First, the pay schedules of most legitimate professions do not meet financial requirements of daily drug use. Drug users who are paid on a monthly basis would need to carefully ration either their finances or their drug supply to support a daily drug habit. Despite the strictest efforts to ration either financial resources or drug supplies, heroin-addicted individuals find that they eventually run short of legitimate financial means to support their habit, resulting in their turning to illegal means to purchase drugs. Second, although one might predict that the affluent could support a habit without daily income, the tolerance effects of heroin are escalated every 2 to 4 months, increasing the financial resources required to maintain the euphoric effect.

It is often assumed that illegal activities provide the heroin addict with unlimited financial resources. This supposition fails to recognize that illegal activities themselves are professions with defined economic levels. Whether a shoplifter, burglar, drug dealer, or prostitute, there are defined salary ranges and economic limitations, based, at least partially, on intrinsic factors such as ability and

intelligence. The choice of illegal activity must meet the requirements of regular generation of funds and a relatively low likelihood of interruption, e.g., arrest and incarceration, to avoid withdrawal. Therefore, illegal activities typically undertaken are those less likely to result in arrest or which carry minimal punishment. Purse snatching, prostitution, shoplifting, and car theft are examples of crimes with a low arrest rate and/or minimal prosecution. Violent crimes, where there is high likelihood of arrest and lengthy incarceration, are not typically perpetrated by narcotic addicts (Greenberg and Adler 1974).

Pharmacological factors are also a potent influence on the economics of narcotic abuse because a tolerance to narcotics develops. As a result, increasing doses of a narcotic are required to obtain the same effect over time. In a study performed at the methadone treatment program in St. Louis, in which 62 consecutive admissions for methadone detoxification were interviewed, the time lapse between increasing doses varied between 2 and 4 months, with the amount of increase ranging from 25 to 100 percent. It should be noted that these interviews were conducted on patients who were addicted for less than 1 year. This suggests that, for a significant percentage of heroin addicts, the effects of tolerance at some point in time exceed their economic ability to increase their dose of heroin. This may well explain why a significant percentage of heroin addicts seek treatment early in their addiction; these addicts may be economically incapable of maintaining an addicted lifestyle (see figure 1).

An alternative manner of dealing with the effects of tolerance is by varying the dose or type of drug used so as to never become addicted. “Chippers,” who only occasionally use narcotics, are able to avoid tolerance effects. Similarly, polydrug users may be able to vary their drug usage by type and amount to avoid tolerance effects. Thus, those drug users who are incapable of generating the financial resources necessary to develop an addiction may be shaped toward polydrug use (see figure 2).

What is also frequently overlooked is that income from illegal activities varies. Bad weather hinders the income-generating opportunities in several illicit professions, such as prostitution and petty theft. Thus, as addicts approach their economic limits, they are increasingly faced with a variety of difficulties in meeting the economic demands of their drug habits. This difficulty in meeting the economic demand of addiction increases over time as addicts develop tolerance and begin requiring an increased dosage for

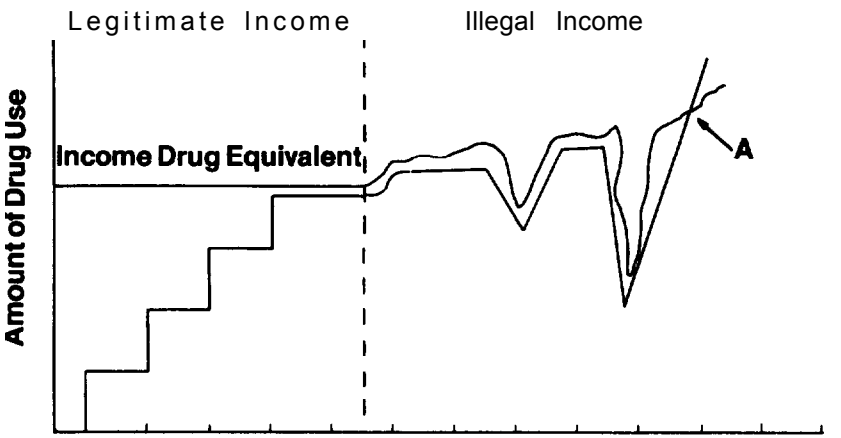

FIGURE 1. *Hypothesized relationship between economics and drug use*

NOTE: The figure characterizes the steady narcotic user who must increase drug dose every 2 to 4 months, as a result of tolerance effects, to maintain the same euphoric effect. As drug use approaches legitimate economic limits, the drug user may resort to illegal activities, which have greater income potential but generally produce more variable income, resulting in more variable drug use. At the hypothesized point A. where the addiction for the drug may exceed the illegal economic limit, the addict may resort to varying drug types and amounts, expanding Illegal activities, or entering treatment.

maintenance and may exert pressure to vary drug types and amounts, expand illegal activities, or enter treatment.

Economic Effects on Drug Addicts' Social Relationships

As noted above, one effect of less affluent narcotics addicts engaging in illicit activities to support their habit is that they begin to associate with others who also engage in illicit activities. Prostitutes associate with their "pimps" and other prostitutes, and shoplifters associate with their "fences" for their stolen merchandise.

Association with peers who also engage in illegal activities (often drug users themselves) results in peer pressure that undoubtedly has shaping effects upon narcotic addicts. As narcotics addicts approach their economic limit and begin encountering difficulty in meeting the daily economic demands of their drug habit, they may enter into

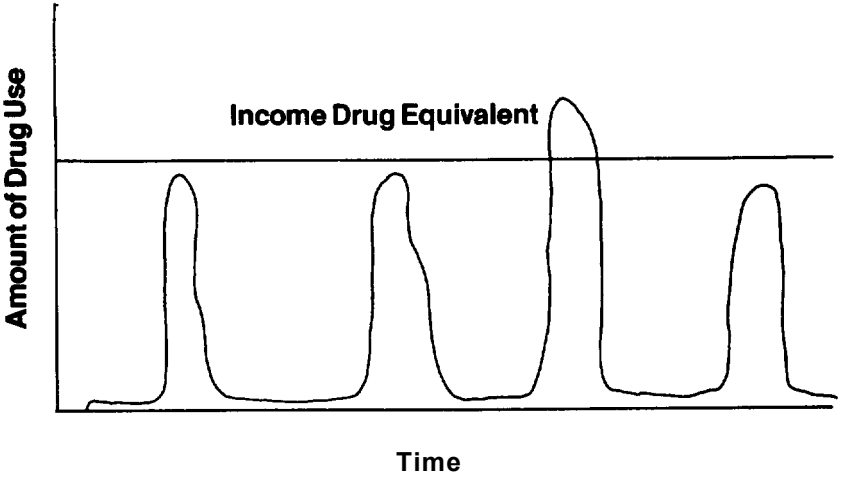

FIGURE 2. *Alternative hypothesized relationship between economics and drug use*

NOTE: The figure depcits an alternatlve means of dealing with tolerance effects by "chipping" and avoiding tolerance. By only infrequently using narcotics, sometimes at a level which would exceed financial limits if maintained, the drug user Is able to prevent the problems of tolerance effects.

social networks with other addicts; these social networks frequently foster sharing of drugs with less fortunate peers on "lucky days and borrowing of drugs from others on days when the costs of favored drugs have not been generated. The reinforcing valence of a peer who will supply drugs at a time when an addict cannot afford drugs is very strong, potentially accounting for the strength of peer relationships developed between drug abusers.

Economic Relationships to Psychopathology

Survival of long-term drug addicts requires that they be free of debilitating psychopathology so as to pursue an income adequate to meet drug needs. This notion gains strength from the observation that, over 6 years, stimulant and depressant abusers had significantly more major forms of psychopathology than did narcotics addicts.

While one interpretation of these data is that stimulant and depressant use contribute to the development of psychopathology, an alternative interpretation may be that preexisting differences between the groups in psychopathology affected their drug preference. From an economic perspective, long-term narcotic abusers who have not resorted to frequent polydrug use are most likely to possess the intellectual abilities and personality characteristics to function adequately in demanding economic situations. Stimulant and depressant users are frequently polydrug users; these individuals may not be able to maintain the economic level of narcotics users, presumably due to deficiencies in intellectual abilities or personality characteristics.

Interestingly, Kosten et al. (1985) found relationships between psychopathology, ethnic and gender variables, and history of polydrug use among opiate addicts. White male addicts had more antisocial personality characteristics and a greater history of polydrug use than black male addicts. Black male addicts had very little psychopathology. These findings are not surprising when the differential in overall societal economic opportunities between white and black males are considered; black males probably had to function more effectively to overcome their economic limitations than white males who have more economic opportunities.

Economic Factors in Treatment

Entrance into treatment may relate to economic factors. Those entering treatment early in the course of their drug abuse history may be doing so to mitigate problems in meeting the economic demands of drug abuse. Heroin addicts who cannot meet the economic demands of their drug habits may enter methadone maintenance programs within a short period of time after becoming addicted to avoid withdrawal caused by economic limitations. Alternatively, individuals who enter treatment late in the course of their addiction usually have been successful in meeting the economic demands imposed by their addiction and consequently may enter treatment for reasons other than avoiding withdrawal. It has been our experience that the prognosis for those entering treatment after a long period of addiction is usually better than for those who have a short history of addiction, most likely due to these differences in their motivation for treatment. Similarly, we have noted that those with a short addiction history are more likely to have a higher frequency of “dirty urines” than those with a long addiction history, suggesting that the former group is more likely to use drugs

recreationally once the economic pressures to maintain their habii have been minimized by methadone programs.

History of drug addiction may also have substantial implications for treatment. Since more psychopathology is generally evident in addicts with a short addiction history, these individuals may need to receive treatment for their underlying psychopathology, whereas those with a long history of addiction who have less psychopathology require a different treatment focus. This may account for the observation that those with a short-term addiction history do better with more structured/intensive treatment, whereas those with a long addiction h&tory do better with a less structured treatment program (Williams and Johnston 1972).

These strengths utilized in economic subsistence, particularly in the long-term drug abuser, might well be utilized in maintaining the recovered addict. This observation is based on the following experience of one of the authors (WDL):

Fifteen jobs were made available to patients on methadone maintenance at a local automotive assembly plant. After 3 months, only 2 of the original 15 long-term addicts were still employed, reportedly because they found the assembly line work too monotonous. When one examines the functional abilities that enable these addicts to subsist financially with their addiction over a long period, it is not surprising that they would find assembly line work boring in comparison. Interestingly, one patient who left the assembly line found employment on his own in the insurance industry. Insurance sales might be seen as more closely approximating the verbal and persuasive abilities used by addicts in their illegal activities than would assembly line work. Based on his success in selling Insurance, an additional three patients were hired by the insurance employer; all of these addicts were still gainfully employed 1 year later. This observation would suggest that the talents required for illegal activity could be reutilized in legitimate employment.

A final demonstration of the influence of economics in treatment is seen in the success of contingency contracting with certain addicted individuals. Crowley (1994) reported success with treatment of addicted healthcare professionals through contingency contracting, which based retention of professionals' licenses upon compliance with prescribed treatment regimens. Among other drug-addicted populations, contingency contracting has been found effective as long as

the contract involves a significant value. Such regimens were not found effective when the contract was not assessed as involving an economic exchange of equal or greater value to the client than remaining drug-free (Stitzer et al. 1984).

SUMMARY

It appears that economic factors have not been considered in examining the problem of substance abuse even though they have major implications. Economics must be seen as a major factor in the extrinsic system, interacting with other components of the extrinsic system as well as components of the intrinsic system. Without an understanding of this key factor, a complete picture cannot be derived. At this point, we can only hypothesize and propose conjectures as to what some of the ramifications might be. We would suggest that more formal studies, involving economic factors, be undertaken, since such studies could have major implications in a better understanding of the shaping of substance abuse.

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The Therapeutic Community and Behavioral Science

George De Leon

INTRODUCTION

The therapeutic community (TC) has proven to be a powerful approach to rehabilitating substance abusers. As described in other writings (De Leon 1988; De Leon 1986; De Leon and Beschner 1977), the TC is fundamentally a self-help phenomenon whose evolution has proceeded primarily outside of mainstream psychiatry, psychology, and medicine. Nevertheless, the TC represents a unique demonstration of the application of behavioral science principles in a human service setting.

The purpose of this paper is to narrow the gap between laboratory and field settings through exposition of the TC as a unique behavioral science model. To contrast the TC with other approaches, the initial section offers a brief overview of the aims and effectiveness of major drug treatment modalities. Next, a more detailed description of the perspective and methods of the TC is provided, followed by an illustration of the relationship between key TC concepts/practices and behavioral science principles and methods. Highlighted is the use of shaping and explicit contingencies to facilitate behavior change within a community context. Lastly, possible interactions between behavioral science and the TC are discussed.

THE EFFECTIVENESS OF DRUG TREATMENT

There are four major drug treatment modalities: detoxification, methadone maintenance, outpatient drug-free settings, and drug-free residential communities. Each modality has its view of drug abuse, and each impacts the abuser in different ways.

Considerable literature documents the effectiveness of these modalities, evaluating each in terms of its principal aims (Sells 1979; Simpson and Sells 1982; Newman 1979; Kleber and Soblentz 1979; De Leon and Rosenthal 1979; De Leon 1985). The findings show that detoxification provides a temporary treatment for withdrawal; methadone maintenance is an effective substitute for illicit opiate addiction that can maintain treatment involvement: and services in outpatient settings yield reductions in drug use, particularly for nonopiate abusers.

The principal aim of the TC is a global change in lifestyle: abstinence from illicit substances, elimination of antisocial activity, employability, and prosocial attitudes and values. A critical assumption for the TC is that stable recovery depends upon a successful integration of both social and psychological goals. Rehabilitation, therefore, requires multidimensional influences and training, which for most can occur only in a 24-hour, long-term residential setting.

For traditional long-term TCs, national surveys indicate that 30 percent of clients achieve maximally favorable outcomes (no crime, no illicit drug use, and prosocial behavior), and an additional 40 percent reveal moderately favorable outcomes (Simpson and Sells 1982). Representative results are reported for Phoenix House. Success (no crime and no drug use),rates among graduates exceed 75 percent 5 to 7 years after treatment. Among dropouts, success rates average 31 percent, but the percentages relate directly to time spent in treatment (figure 1). About 50 percent of those who remained in residence for 1 year or longer were successful across 3 to 8 years of followup, compared to about 25 percent who stayed less than 1 year (De Leon 1984; De Leon 1986).

Overall, the four modalities appear reasonably effective, considering their aims. When rehabilitation is the aim, however, it is the TC which is particularly effective. A closer look at this modality will illuminate the TC as a unique illustration of a rehabilitation model grounded in behavioral science.

TCs

The TC can be distinguished from other major drug treatment modalities in two fundamental ways. First, the primary “therapist” and teacher in the TC is the community itself, which consists of peers and staff who, as role models of successful personal change, serve as guides in the recovery process. Thus, the community provides a

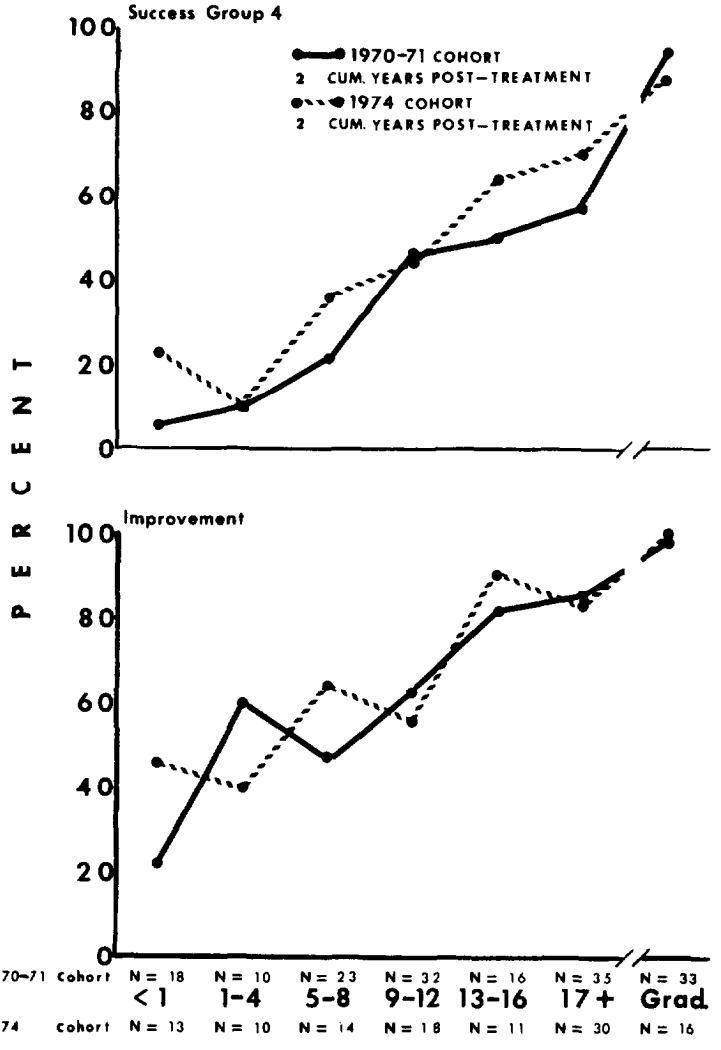

FIGURE 1. *Comparisons between the 1970-71 and 1974 cohorts through 2 years of followup for male opioid* abusers

NOTE: Success (14) and improvement rates by time in program (TIP) are shown by the 1974 TIP classifications. There were no signifcant cohort differences at any point on the curve, revealing a striking replication of the TIP function.

SOURCE: De Leon 1984.

24-hour learning experience in which individual changes in conduct, attitudes, and emotions are monitored and mutually reinforced in the daily regime. Second, the TC offers a systematic approach to achieving its main rehabilitative objective, which is guided by an explicit perspective on the drug use disorder, the client, and recovery.

The TC Perspective *

Although expressed in a social psychological idiom, the TC perspective evolved directly from the experience of recovering participants in TCs. Drug abuse is viewed as a disorder of the whole person. Although individuals differ in choice of substance, abuse involves some or all areas of functioning. Cognitive, behavioral, and medical problems appear, as do mood disturbances. Thinking may be unrealistic or disorganized. Values are confused, nonexistent, or antisocial. Frequently there are deficits in verbal, reading, writing, and marketable skills, and, whether couched in existential or psychological terms, moral issues are apparent.

Abuse of any substance is viewed as overdetermined behavior. Physiological dependency is secondary to the wide range of circumstances which influence and then gain control over an individual's drug use behavior. Invariably, problems and situations associated with discomfort become regular signals for resorting to drug use. For some abusers, physiological factors may be important, but for most these remain minor relative to the behavioral deficits which accumulate with continued substance abuse. Physical addiction or dependency must be seen in the wider context of the individual's life skills.

Thus, the problem is the person, not the drug. Addiction is a symptom, not the essence of the disorder. In the TC, chemical detoxification is a condition of entry, not a goal of treatment. Rehabilitation focuses upon maintaining a drug-free existence.

The clients in TCs are usually male (75 percent), in their mid-twenties (50 percent), and racially mixed. Most TCs are age

*This section is drawn from De Leon (1986), and it describes the TC perspective in conventional vernacular. Behavioral translation of some key concepts and terms is provided later in this chapter, in the section entitled "The TC as Behavioral Science."

integrated, with adolescents (less than 21 years old) accounting for 25 percent of the clients. A few TCs have facilities exclusively for adolescents. About half of all admissions are from broken homes or ineffective families, and 60 percent have been arrested (De Leon 1960).

Drug patterns vary; however, the chemical abused is of less importance than its meaning to the user. Drug preference depends mostly on availability, licit status, and social and peer use, although client-specific psychopharmacologic factors may also matter.

Rather than drug use patterns, individuals are distinguished along dimensions of psychological dysfunction and social deficits. A considerable number of clients have never acquired conventional lifestyles. Vocational and educational deficits are marked: middle-class, mainstream values are either missing or unpursuable. Most often, these clients emerge from a socially disadvantaged sector where drug abuse is more a social response than a psychological disturbance. Their TC residential experience can be termed "habilitation"-the development of a socially productive, conventional lifestyle for the first time in their lives.

In clients from more advantaged backgrounds, drug abuse is more directly expressive of psychopathology, personality disturbance, or existential malaise. In referring to these clients, the word "rehabilitation" is more suitable because it emphasizes a return to a lifestyle previously lived, known, and perhaps rejected.

Nevertheless, substance abusers in the TCs share important similarities. Either as cause or consequence of their drug abuse, all reveal features of personality disturbance and impeded social function. Thus, all residents in the TC follow the same regime. Individual differences are recognized but in specific treatment plans that modify the steps, not the course, of the client's experience in the TC.

In the TC's view of recovery, the aim of rehabilitation is global. The primary psychological goal is to change the negative patterns of behavior, thinking, and feeling that predispose drug use; the main social goal is to develop a responsible, drug-free lifestyle. Stable recovery, however, depends upon a successful intearation of these social and psychological goals. For example, healthy behavioral alternatives to drug use are reinforced by commitment to the values of abstinence. Acquiring vocational or educational skills and social

productivity is motivated by the values of achievement and self-reliance. Behavioral change is unstable without insight, and insight is insufficient without felt experience. Thus, conduct, emotions, skills, attitudes, and values must be integrated to ensure enduring change.

The rehabilitative regime is shaped by several broad assumptions about recovery.

Motivation. Recovery depends upon pressure-positive and negative-to change. Some seek help, pushed by stressful external pressures: others are moved by more intrinsic factors. For all, however, remaining in treatment requires continued motivation to change. Thus, elements of the rehabilitation approach aim to sustain motivation or to detect early signs of premature termination.

Self-Help. The influence of treatment depends upon the individual's motivation and readiness to change; however, change does not occur in a vacuum. The individual does not provide, but permits the impact of treatment or learning to occur. Thus, rehabilitation unfolds as an interaction between the client and the therapeutic environment.

Social Learning. A lifestyle change can occur only in a social context. Negative patterns, attitudes, and roles were not acquired in isolation, nor can they be changed in isolation. Thus, recovery depends not only on what has been learned, but on how and where learning occurs. This assumption is the basis for the community itself serving as healer and teacher. Learning is active-by doing and participating. A socially responsible role is acquired by acting the role. What is learned is identified with the people involved in the learning process, e.g., peers and staff, as credible role models. Finally, without new social connections, new learned ways of coping are threatened by isolation and its potential for relapse. Thus, a perspective on self, society, and a life philosophy must be affirmed by a network of others to assure a stable recovery.

Treatment as an Episode. Residency is a brief aspect of the individual's life which must compete with the influences of the years before and after treatment. During the relatively short P-year residency, unhealthy "outside" influences are minimized until new habits have formed and the individual is better prepared to engage these influences on his/her own. Thus, life in the TC is necessarily intense, its daily regime demanding, and its therapeutic confrontation unmoderated.

The TC Approach

Structure.Integrated recovery is facilitated through the TC structure (social organization, staff, and daily regime) and the treatment process (the individual's passage through treatment phases) within that structure.

TCs are stratified communities composed of peer groups at levels of seniority that are led by staff. Together they constitute the community, or family, in a residential facility. This peer-to-community structure strengthens the individual's identification with a perceived, ordered network of others, and it arranges relationships of mutual responsibility to others at various levels of the program.

The operation of the community itself is the task of the residents, working under staff supervision. Work assignments, called job functions, are arranged in a hierarchy according to seniority achieved by progress and productivity. The new client enters a setting of upward mobility, where job assignments begin with the most menial tasks (e.g., mopping the floor) and lead vertically to levels of coordination and management. Indeed, clients come in as patients and can leave as staff. This social organization reflects the fundamental aspects of the rehabilitative approach: mutual self-help, responsible performance, and earned success.

The TC is managed as an autocracy, with the goal of teaching self-reliance. Staff serve as rational authorities who monitor and evaluate client status, supervise resident groups, assign and supervise resident job functions, and oversee house operations. Clinically, staff conduct all therapeutic groups, provide individual counseling, organize social and recreational projects, and confer with significant others. They decide matters of resident status, discipline, promotion, transfers, discharges, furloughs, and treatment planning. Key staff, who are recovered addicts, are visible role models who illustrate the reality of personal change. Their successful rehabilitative experience qualities them to teach, to sanction, and to serve as guides and rational authorities.

Daily Regime. The daily regime is full and varied. A typical day in a TC is highly structured, beginning with a 7 a.m. wakeup and ending at 11 p.m. It includes a variety of meetings, job functions (work therapy), therapeutic groups, recreation, and individual counseling.

Although designed to facilitate the management of the community, the scope and schedule of the regime reflect an understanding of the conditions of drug abuse. The regime provides an orderly environment for many who customarily have lived in chaotic or disruptive settings; reduces boredom and distracts from negative preoccupations which have, in the past, been associated with drug use; and offers the opportunity to achieve satisfaction from a busy schedule and the completion of daily chores. In short, it ensures that productive behaviors have a chance to replace selfdestroying drug-related behaviors.

The TC Process

Within its structure, the TC prescribes explicit stages. These are sequenced to achieve incremental degrees of learning, each stage preparing the individual for learning at the next.

Stage 1 (Induction-0 to 60 Days). The main goals of this initial phase of residency are the assessment of individual needs and orientation to the TC. Important differences among clients generally do not appear until they experience some reduction in the circumstantial stress usually present at entry and have had some interaction with the treatment regime. Thus, observation of individuals continues during the initial residential period to identify special problems in their adaptation to the TC.

The goal of orientation in the initial phase of residency is to assimilate the individual into the community through full participation and involvement in all of its activities. Rapid assimilation is crucial at this point, when clients are most ambivalent about the long tenure of residency. Thus, the new resident is immediately involved in the daily residential regime. Emphasis, however, is placed not upon treatment but upon education and role induction into the community process. Therapeutic and educational activities focus on the TC perspective, its approach, and the rationale for long-term residential treatment.

Stagell (Primary Treatement - 2 to 12 Months). During this stage, the main TC objectives of socialization, personal growth, and psychological awareness are pursued through all of the therapeutic and community activities. Primary treatment actually consists of three phases separated by natural landmarks in the socialization-developmental process. Phases roughly correlate with time spent in the program (1 to 4 months, 5 to 8 months, and 9 to 12 months), and these periods

are marked by plateaus of stable behavior, which signal further change.

In each phase, the daily regime of meetings, work, recreation and groups remains the same. Progress, however, can be seen in the client's profile at the end of each phase, which can be typified in terms of three interrelated dimensions: community status, develop mental change, and psychological change.

Community status describes the degree to which residents become role models. Developmental change refers to the extent to which individuals alter their drug-involved profile in conduct, language, attitude, and outlook. This is an indication of the extent to which they internalize the TC's perspective and commitment to change. Psychological change describes the degree to which residents reveal personal growth in maturity, openness, insight and self-awareness, emotional stability, and self-esteem.

Stage III (Reentry-13 to 24 Months). Reentry is the stage at which the client must strengthen skills for autonomous decisionmaking and the capacity for self-management with less reliance on rational authorities or a well-formed peer network. There are two phases of the reentry stage.

Early Reentry (13 to 18 Months). The main goal of this phase, during which clients continue to live in the facility, is preparation for healthy separation from the community.

Emphasis upon rational authority decreases under the assumption that the client has acquired a sufficient degree of self-management. This is reflected in more individual decisionmaking about privileges, social plans, and life design. The group process involves fewer leaders at this stage, fewer encounters, and more shared decisionmaking. Particular emphasis is placed upon life skills seminars, which provide didactic training for life outside the community. Attendance is mandated for sessions on budgeting, job seeking, use of alcohol, sexuality, parenting, use of leisure time, etc.

During this stage, individual plans are shared tasks of the client, a key staff member, and peers. These plans are actually blueprints of educational and vocational programs which include goal attainment schedules and methods of improving interpersonal and family relationships as well as social and sexual behavior. Clients may attend school or hold full-time jobs either within or outside the TC at this

point. Still, they are expected to participate in house activities when possible and carry some community responsibilities (e.g., facility coverage at night).

Late Reentry (18 to 24 Months). The goal of this phase is to complete a successful separation from residency. Clients are on "live-out" status, involved in full-time jobs or education and maintaining their own households, usually with live-out peers. They may attend such aftercare services as Alcoholics Anonymous (AA) and Narcotics Anonymous (NA), or take part in family or individual therapy. This phase is viewed as the end of residency but not of program participation. Contact with the program is frequent at first and is only gradually reduced to weekly phone calls and monthly visits with a primary counselor.

Completion marks the end of active program involvement. Graduation itself, however, is an annual event conducted in the facility for completees at least 1 year beyond their residency.

THE TC AS BEHAVIORAL SCIENCE

The TC Vemacular

Behavioral science, in the broad sense of the term, is liberally reflected in the TC. However, the fit between behavioral science and TC concepts is clearly imperfect. This is most evident in the vernacular of the TC, which is an unusual mix of street idiom and language borrowed from various psychotherapeutic schools including psychoanalysis, gestalt therapy, and existential psychotherapy. The TC's vernacular reflects its view of the whole person. Self, feelings, thinking, and awareness are viewed as real dimensions of the individual. These, however, are always evident in, or inferred from, observable behavior. In this regard, the TC displays a rare behavioral bias in accepting the existence of "inner" aspects of the individual, but always addressing and/or modifying these aspects through observable behavior.

A thorough translation of the TC vernacular into behavioral terms is a task much beyond the purview of this paper. However, some of the experiential or "inner person" words of particular importance are briefly defined for purposes of clarity.

Emotions/Feelings These are the typical self-referred cognitive "feeling states," e.g., sadness, hurt, disappointment, hostility, anger,

fear, anxiety, joy, and love. They are always displayed in verbal and/or gestural, postural, and tonal ways. In the TC, experiencing and expressing feelings in appropriate ways is central to recovery. Thus, techniques are designed to evoke and teach individuals to "deal" with their feelings, that is, to label, express, and manage them appropriately before they lead to or trigger self-defeating behavior such as drug use. Examples of this are evident in a later discussion on craving and tolerance training.

An implicit but clear distinction is made between emotions/feelings and physiological states of the individual. The latter refers strictly to body events, usually labeled in terms of aches, pains, sweating, thermal changes, irritability, bowel changes, general physical malaise, etc. Since emotions are always associated with some cognitive event, they may or may not include these specific bodily states.

Insight. This key word in the TC vernacular refers to the conventional connotation of new recognition or understanding. Behaviorally, it is most evident in certain verbal statements that assert a newly identified association between the individual's actions (e.g., drug use, negative thinking, withdrawal, or hostility) and the circumstances or events that influence them (e.g., rejection, reversals, demotion, loss of relationship, criticism, or peer pressure). In addition, if the individual reports a special experience concerning this new recognition, which marks a significant change in self-awareness and in subsequent behavior, the insight is viewed as particularly important to the recovery or change process (i.e., it is a therapeutic event).

Motivation, Readiness, and Commitment. Motivation refers to the individual's verbal acceptance of a serious drug problem and desire for change; readiness refers to the individual's choice of treatment as the method for change vs. other nontreatment alternatives; and commitment refers to the individual's explicit stated intent to remain in the treatment process through completion. Some measurement distinctions among the three dimensions are offered elsewhere (De Leon and Jainchill 1988). In the TC, these terms are used interchangeably and label dimensions of the individual inferred from verbal assertions and a variety of nonverbal behaviors, e.g., job performance, punctuality, attendance, participation in activities, performance, relating to others, etc.

Internalization. This is a key progress concept which involves both new habits and cognitive acceptance: "I do this for myself rather

than others." Internalization is particularly evident when a client can transfer, i.e., generalize, what is learned in the TC about "right" living to new problems and situations outside the TC.

Maturity. This refers to age-appropriate behavior, particularly frustration tolerance, response to authority, acceptance of criticism, responsibility, and expression of emotions in socially acceptable ways.

Openess. This term refers to the extent to which the individual engages in personal disclosure, usually concerning intimate aspects of past and current events, behavior, feelings, and wgnitions.

Self-Esteem. This concept is most usually described in self-reported statements of worth and value about one's own behavior.

A variety of paradigms which are recognizable in various behavioral theories can be suitably adapted to describe what is observed in the TC. Most evident are elements from social learning, cognitive-emotional training, and role conditioning. Examples of these elements are illustrated in the TC's perspective, structure, and approach.

The TC Perspective

Overdetermined Behavior. The TC's view of drug abuse as overdetermined behavior illustrates its behavioral approach to the physical aspects of addiction. Physiological cues or triggers to drug use are less important than the cognitive-emotlonal cues arising from intra/interpersonal and social sources. Thus, withdrawal effects are seen as temporary physical upsets which can usually be managed through self-, nonmedicated detoxification. Craving, however, is viewed as more complex.

Cravings are thoughts (cognitions, images) about drug taking, as evidenced in verbal reports, which may or may not be associated with physical states nor necessarily lead to drug-taking behavior. Cravings are primarily controlled by social, emotional, and physiological cues. In the early stages of chemical detoxification, the physiological cues for craving are relatively more important than social and emotional cues. As the time since the last drug-taking episode lengthens, however, cravings are more directly under the control of social and emotional cues. For example, residents in TCs may experience cravings months after living drug free, and these are invariably related to social cues (e.g., interpersonal stress or conversations about drugs) or emotional cues (disappointment, hurt, or frustration).

In the TC, craving is addressed by Ignoring it (extinction), by distraction (interruption, blocking), or by response competition. For example, clients are encouraged to disclose thoughts of craving, which are then either ignored (extinction), blocked ("don't think about them"), or retrained to provoke new behaviors and alternative thoughts (e.g., "walk away, do exercise").

TC workers studiously avoid direct relief of the physical discomforts associated with drug abuse so as not to inadvertently strengthen poor tolerance for discomfort. Thus, there is no succor for the physical complaints associated with the discomforts of withdrawal or for craving reactions beyond that of peer understanding and encouragement to tolerate these as transient states.

The view of drug abuse as overdetermined behavior also is the fundamental premise for relocation of the client to the residential environment. The drug abuser requires temporary removal from the ordinary environment which contains the multiplicity of cues for drug abuse. This is aptly expressed in the TC (and AA) caution phrase "People, places, and things" (that is, avoid the usual settings and circumstances historically associated with drug abuse). An analogous caution is stressed concerning "internal" subjective cues for drug use. Residents, particularly in the reentry phase of recovery, are instructed not to get "too hungry, tired, or lonely" in order to prevent their thinking about or actually seeking drugs. In behavioral terms, this amounts to interrupting a chain of stimulus-response connections that would end in drug abuse.

Behavioral Orientation. Observed behavior is the primary target of change in the TC. Modifying existing behaviors involves breaking down old patterns and "wrong behavior" and substituting these with alternative, competing "right" behavior. The emphasis is on behaviors here and now rather than on the historical reasons for these behaviors.

In terms of the TC's view of substance abuse as a disorder of the whole person, every domain of behavior must be addressed. Thus, attitudes, feelings, roles, and awareness as well as conduct are regarded as valid behavioral data. For example, a resident's "attitude" on the job or in the morning meeting may elicit a response in others. In conversations or groups, this attitude will be explicitly translated into observable behaviors (gestural, postural, or verbal), which is an essential step in the process of retraining the client.

Act as if. This basic concept instructs residents and staff to behave as the person he/she should be rather than the person he/she has been. Behaving as one should behave will result in cognitive emotional changes. This concept can be contrasted with views which emphasize the need for cognitive-emotional experiential change (i.e., insight and understanding) to precede behavioral change.

Mutual Self-Help. The broad goals of recovery in the TC can only be achieved through a mutual self-help peer process. Treatment of the whole person necessitates continual observation of behavior on a 24-hour basis as well as constant, credible, and persuasive feedback to facilitate modification. The range of the behavioral agenda and the extent of training required mandate that all participants in the community serve as both trainers and trainees. Thus, the day-to-day activities of a TC are conducted by the residents themselves. In their jobs, groups, meetings, recreation, and personal and social time, residents transmit to other the main messages of recovery, right living, and the expectations of the community.

Key behavioral mechanisms evident in the mutual self-help process are:

- Confrontation and Responsible Concern:This concept is closely akin to the notion "I am my brother's keeper." It instructs residents to show responsible concern by confronting others whose behavior and attitudes are not in keeping with expectations of the TC or consistent with the goal of rehabilitation.

- Feedback: Positive and negative verbal reinforcements and suggestions continually address changes in behavior and attitude in small and large group settings and in ordinary conversation.

- Support: This is provided directly through verbal encouragement to persevere in the continual trial-and-error effort to improve and through discouragement of thoughts to leave, and indirectly (vicariously) through observation of, and identification with, others in the change process.

Role models. People are the essential ingredient in the TC. Peers and staff as role models and rational authorities are the primary mediators of the recovery process. Indeed, the strength of the community as a context for social learning relates to the number and quality of its role models. TCs require multiple role models to

maintain the integrity of the community and assure the spread of learning effects.

The role model, and role modeling, refer both to a concept and to a fundamental learning/training activity of the TC. A role model is described as an individual who reflects the behavior, attitudes, and expectations of the community. All members of the community are expected to strive to be role models. Thus, much of what is trained or taught in the TC is mediated through peer interaction, particularly through those peers who serve as role models.

Role models illustrate a variety of basic behavioral elements or mechanisms. First, they function as trainers who note elements of behavior, who reinforce but who also help establish new behaviors in newer residents through identification and imitation. In particular, role models provide proof of success, which is a motivational/ incentive cue ("hope") for newer residents who observe them as real examples of change.

Second, the status of role model in the TC brings special privileges and acknowledgment by the community itself. Thus, striving for and achieving role model status is associated with explicit practical and social reinforcements.

Third, there are subtle but powerful training effects for residents who serve as role models, mediated through their teaching and through contrast with other residents. 'The former is similar to the helper-helpee principle of self-help learning. Teaching others reinforces behaviors and attitudes of the teacher-a process which appears as a special case of behavioral rehearsal.

Contrast, as a self-training effect, is more complex. Senior residents who are role models have the opportunity to objectively view the behaviors and attitudes of junior residents. They perceive the difference between their own behavior at an earlier time and their current behavior as role models. This perceived contrast of "where I was and where I am" functions as a reinforcement for continued change and increases the likelihood that "where I am" will prevail.

Thus, the concept of the role model in the TC most explicitly illustrates behavioral science principles. It encompasses the main elements of modeling as a training procedure. In addition, the role model as a person provides motivational/incentive cues, represents

status as reinforcement, and continues to learn through teaching and self-perceived contrast effects.

The TC Structure

The social organization of the TC, its structure, and its systems essentially constitute an environment for engineering social learning. The following key elements of the TC structure illustrate this point.

Work as Education and Therapy. In the TC, work mediates essential educational and therapeutic effects. Vertical job movements carry the obvious rewards of status and privilege. However, lateral job changes are more frequent, providing exposure to all aspects of the community. Job changes in the TC are singularly effective therapeutic tools, providing measures of, and incentives for, behavioral and attitudinal change. In the hierarchical, vertical *structure* of the TC, ascendency marks how well the client has assimilated what the community teaches and expects; hence, job promotion is an explicit measure of the resident's improvement and growth. Conversely, lateral or downward job movements also create situations that require demonstration of personal growth. These movements are designed to teach new ways of coping with reversals and change what appears to be unfair or arbitrary.

The hierarchy of job functions in the TC illustrates the TC's basic behavioral orientation to recovery. Each hierarchy represents a broadly defined behavioral repertoire that indicates competence at that level:

- Efficacy Training: The resident must engage in the behavior that produces positive change. Indeed, clinical observations and TC research demonstrate convincingly that there is a direct reiationship between efficacy and self-esteem.

- Role Conditioning: The focus is on training constellations of skills and attitudes which can be perceived and labeled and which have social status. Thus, departmental head, coordinator, director, and role model are all examples of roles trained in the TC.

- Socialization Training: This refers to classes of behaviors and attitudes which reflect dimensions of social behavior other than work roles. Typical labels for these are "responsible," "cooperative," and "mature."

Privaleges and Sanctions. Perhaps the most direct application of behavioral training principles and methods in the social organization of the TC is its system of privileges and sanctions. Privileges are explicit rewards that reinforce the behavior and value of earned achievement. Privileges are accorded by behavior, attitude change, job performance, and overall clinical progress in the program. Displays of inappropriate behavior or negative attitude can result in loss of some or all privileges. The resident is given the opportunity to earn them back by showing improvement.

Privileges acquire their importance because they are earned. The earning process requires investment of time, energy, self-modification, and risk of failure and disappointment. Thus, it is the earning process that establishes the value of privileges and hence their potency as social reinforcements.

The type of privilege is related to clinical progress and time in the program, ranging from telephone and letter–writing privileges in early treatment to overnight furloughs later on. Successful movement through each stage earns privileges for the resident that grant wider personal latitude and increased self-responsibility.

Discipline and Sanctions. TCs have their own overriding rules that guide the behavior of residents and the management of facilities. Their explicit purpose is to ensure the safety and health of the community; their implicit aim is to train and teach residents, through the use of discipline, the basic tenets of human interaction.

In the TC, social and physical safety are prerequisites for psychological trust. Thus, sanctions are invoked against any behavior which threatens the safety of the therapeutic environment. For example, breaking the TC's cardinal rule-no violence or threat of violence, verbal or gestural-can bring immediate expulsion. Even minor infractions of house rules are addressed, such as stealing mundane sundries (toothbrushes, books, etc.).

The choice of sanction depends upon the severity of the infraction, time in the program, and history of infractions. For example, verbal reprimands, loss of privileges, or speaking bans may be selected for less severe infractions; job demotions, loss of residential time, or expulsion may be invoked for more serious infractions.

Sanctions are dispensed as "contracts," a variant of contingency contracting. These vary in duration from 3 to 21 days, after which time

they are reevaluated by staff in terms of their efficacy. in most cases, the punishment element of contracts is less important than their time-out feature. Individuals may be demoted to a job of relatively menial activities, which involves some loss of status, with the instruction that they consciously review their commitment to change.

Though often perceived as punitive, the basic purpose of contracts is to provide a learning experience by compelling residents to attend to their own conduct, reflect on their own motivation, feel some consequence of their own behavior, and consider alternative forms of acting under similar situations.

The TC Approach

In its approach and daily regime, the TC has adapted familiar behavioral training methods and techniques based upon its view of the client and the recovery process. These focus on behaviors, particularly characteristic of addicts, that must be modified in the rehabilitative process.

Awareness Training. Awareness refers to client recognition or understanding of the relationship between themselves (their conduct, attitudes, and feelings), their environment, and other people. The importance of awareness is based upon the TC view of the client and recovery. Substance abusers are characteristically unaware of, or they fail to consider, how their actions affect others or how the behavior of others affects them. They either lack the skills to think of consequences or considerations or they quickly erase such thoughts through blocking, distraction, or rapidly occurring (impulsive) behavior. Understandably, awareness difficulties are also associated with poor judgement (cognitive assessment) of the positive and negative aspects of a situation, which invariably leads to negative, self-defeating consequences. Thus, awareness training is a prerequisite for teaching cognitive assessment skills.

Awareness is also essential for the stability of learned behaviors. Much of what is taught in the TC is through verbal instruction or rule-governing procedures which require awareness to be understood, followed, and remembered. Finally, awareness training is designed to promote dissonance-that is, to raise cognitive conflict between the drug abuser's own view (or personal rules) of his/her lifestyle and the TC's view of tight living. in this regard, verbal reporting of awareness is considered necessary for internalization and generalization of learned behavior to situations outside the TC.

Awareness training in the TC is an omnipresent activity. It involves social reinforcement for reporting observations of each other's behavior,* minor verbal negative reinforcement for lack of awareness, constant reminders concerning attitudes and behavior ("pull-ups"), and direct blocking of behavior or thinking that would interfere with appropriate awareness. For example, clients who appear to be distracted or to be daydreaming are simply verbally jolted back to the reality of their existing situation.

Tolerance Traning. In the TC's view, drug abusers generally have low tolerance for discomfort of any sort. Low tolerance may be a cause or a consequence of chemical abuse, or it may be the result of biological or personality predisposition or poor child-rearing practices.

The sources of discomfort range widely and include those associated with withdrawal from chemicals, wmmon illness, mood disturbances (e.g., dysphoria, depression, anxiety, and anhedonia), frustration, fear/anxiety often associated with circumstances, or vague discomfort associated with under-stimulation or boredom. The tolerance problem is also evident in the positive or neutral events in the addict's life. Addicts' characteristic inability to delay gratification reveals their difficulty in tolerating the tension of anticipation/expectation or the uncertainty associated with life's more ordinary stressors (e.g., being alone, interpersonal pressures, and demands for social responsibility). Addicts have acquired a complex repertoire of behaviors both socially and nonsocially acceptable which effectively avoid or reduce discomfort, the most prominent of which is drug use.

Based on this view, tolerance training involves raising the individual's tolerance levels (i.e., changing thresholds for responding) and developing alternative behaviors for reducing or avoiding discomfort through positive or less self-defeating responses.

In this training, effort is directed toward making the individual aware of the chain of cognitive and behavioral events which reflect poor tolerance. Any social, interpersonal, or environmental cue for discomfort can trigger sequences of behavior which lead to reduction or avoidance, most often through drug taking.

*Indeed, for many substance abusers, the requirement to observe and report on each other's behavior and attitudes is directly counter to the ethics of the "street culture."

Encounter groups or peer discussion retrace a member to a moment of discomfort (e.g., criticism, injustice, provocation, uncertainty, interpersonal hurt, or disappointment) and focus on what triggers the negative thinking or behavior that often involves drug taking. isolating these typical patterns of response (chains) that arise from poor tolerance is an essential first step leading to alternative ways of coping with the moment of discomfort.

A primary technique for increasing tolerance is to delay expected outcomes or rewards. This technique aims to teach an individual to cognitively accept disappointment, frustration, and uncertainty (e.g., about a job change or loss of furlough). Alternative behaviors, which can be characterized as persistence behaviors (e.g., staying on the job, continuing to produce, etc.), are suggested and reinforced. (Tolerance training was also illustrated earlier in teaching residents to "deal with" their craving experiences.)

The Encounter Group. This is the cornerstone training method in the TC. The systematic approach of encounters is outlined in other writings (De Leon and Rosenthal, in press). The group collectively presents their observations and reactions concerning a resident's behavior and attitudes, i.e., the group confronts the individual with how he/she is perceived by others. Thus, there is considerable use of "positive coercion" to initially raise client awareness followed by concrete suggestions (instruction) for positive alternative behavior. The group also provides support for client change.

The TC Process

The client's passage through the stages of treatment in the TC (orientation, primary treatment, early and late reentry) is guided by two interrelated behavioral principles: shaping and explicit contingencies. Behavior and attitudes are gradually modeled in stages to assure sequenced and incremental learning toward a stable recovery. The end points of each stage are well marked in terms of goal attainment levels of expected behaviors and attitudes. Achieving the goals themselves constitutes an explicit reinforcement. For example, attaining senior resident status, reentry candidacy, or graduate status achieves public acknowledgment in addition to the associated social reinforcements of privilege or highly valued job functions.

The entire staging process depends upon the fidelity of a system of explicit contingencies. The sanctions and social reinforcements at each stage are contingent upon the client's display of the expected

behaviors and attitudes usually correlated with his/her length of time in the program. The typical external social reinforcements consist of nurturance (room, board, personal needs), protection (e.g., from physical harm and outside pressures), privilege, status, and membership in the community. The latter infers powerful social reinforcements arising from friendships, support, and avoidance of loneliness or personal isolation. Staging also contains implicit reinforcements that refer to the client's own perception of change (the personal contrast effect), improvement, and movement toward the program and a self-defined picture of recovery.

Finally, in the member's passage through treatment, delivery of social reinforcements becomes less regular commensurate with the client's time in the program. For example, for more senior residents, rewards such as promotions and privileges may not be offered in predictable ways, although social approval is regularly provided for displaying patience, perseverance, and frustration tolerance. This is directly analogous to the behavioral technique of reinforcing a behavior irregularly in order to make it resistant to extinction. Having learned that payoffs come unpredictably, one is likely to persevere.

THE TC: A UNIQUE EXPERIENCE IN BEHAVIORAL SCIENCE

Although behavioral principles and methods are abundantly evident in TCs, they do not capture the complexity or distinctive features of these settings. A description of the TC in more global terms can broaden understanding of the application of behavioral science to human settings.

The TC as a Microsociety

The TC contains similarities to the larger macrosociety with the critical deletion of drug use and antisocial behavior. in its structure, progression up the hierarchy of job functions is much like the movement up the occupational ladder in the "real world." One begins at the bottom, and advancement requires hard work, discipline, good work, and social skills. Upward mobility is capable of imparting to the dysfunctional client the repertoire needed to successfully assimilate into mainstream society.

A key difference, however, is that the TC fosters trial-and-error learning providing a manipulable environment in which one can fail safely. This is contrasted with the outside world which harbors greater risk of loss, humiliation, or punishment from performance

failure. Thus, training in the TC microsociety occurs without the powerful and usual cues for drug taking but permits acquisition and generalization of new learning to the macrosociety.

Community as a Context for Social Learning

Although behavioral science principles and methods are the mechanisms for understanding change in the TC, social learning occurs within the context of everyday life as it is perceived and experienced by members of the community. Embedded in the routine activities of community life are social and psychological factors (parameters) known to strengthen the learning process. Several of these are briefly noted below.

Continous Observation. In the 24-hour regime of the TC, all dimensions of individuals can be observed: how they work, relate to peers and staff, maintain their rooms and personal hygiene, and participate in groups and community meetings. These are the everyday behaviors and attitudes that provide the steady input of data to be addressed and modified. Individuals change their attitudes, values, and conduct through continuous interaction with a community of others.

Peer Learning. Practically all learning occurs collectively in positive peer groups, which reverses the well-documented influence of negative peers or street groups on individual behavior. Thus, the use of peers in the TC incorporates the empirically demonstrated power of cohorts, teams, and groups in enhancing learning effects.

Repetition. The TC's message-its concept of recovery and right living-is continuously reiterated in virtually all of its activities (e.g., meetings, written signs, one-to-one conversations, seminars, etc.). Particular emphasis is placed upon strengthening motivation through mutual encouragement to remain in the learning process, using reminders of losses of the past, gains of the present, and goals of the future.

Affiliation. Behavioral methods govern how people learn in the TC. However, the efficacy of these methods is dependent upon the individual's receptivity to the TC's demanding regime. Skills training, role conditioning, and trial-and-error learning unfold because of perceived membership in, i.e., affiliation with, a community of similar others.

The importance of affiliation in the TC recovery process for drug abusers has been suggested in other writings (De Leon 1983). Most drug abusers who enter TCs are disaffiliated individuals who are unable or disinclined to live ordered lives or identify with mainstream values. By implication, models for changing these individuals must focus upon the goal of affiliation. This requires a socialization process, in the broad sense of that word, to assimilate the individual into a community with shared values, assumptions, and expectations in which the indlviduai is an active, successful participant.

In the TC, affiliation increases the client's amenability to remain in the learning situation. Willingness to engage in training, respond to social reinforcers, and accept disciplinary sanctions depends in part on the client's positive perceptions of the community itself. Thus, basic TC elements and activities, such as rules, three daily meetings, and varieties of group process, focus upon reinforcing positive perceptions of the community to enhance affiliation. These perceptions include nurturance (providing for daily maintenance); hope and possibility (perceived in recovered staff and peer role models); physical safety (maintaining the cardinal rules against violence or other threats); psychological safety or trust (perceived acceptance for self-disclosure); bonding, or positive interpersonal perceptions and alliances (e.g., friendships and affection).

Finally, affiliation, amenability, and training are reciprocally interactive. Behavioral progress through training strengthens community membership, which sustains continued involvement in the social-learning process.

HOW BEHAVIORAL SCIENCE CAN INFORM THE TC

The TC perspective and method emerged not from a priori theory but from the trial-and-error experiences of people in a self-recovery process. In this sense, the TC has rediscovered basic social-learning or behavioral science laws in the evolution of its methodology.

Technologies often develop without the benefit of science. However, historical examples illustrate how science can improve upon these "natural experiments." Behavioral science can inform TCs in several ways:

Staff Training. Behavioral science can assist TC staff in refining techniques for shaping behavior. Not all individuals in the TC learn at the same rate. TC staff need to better identify the smaller units

of behavior In the role-conditioning process for particular individuals. This will avoid unnecessary negative reinforcement to individuals not acquiring what is expected of them and will provide a smoother evolution toward the desired behavior in the role-conditioning process.

Training would stress identification of client-specific reinforcers. By definition, TCs "treat" all individuals the same, although individual differences are recognized throughout the stages in the recovery process. At these points, appropriate client-specific reinforcers can facilitate further change without violating the relationship between the individual and the community.

Providing Skills - Training Curricula. Behaviorally oriented therapists and researchers have considerably advanced the area of skills-training curricula. Programming the step-by-step behavioral changes necessary to achieve a working repertoire is consistent with the TC's view of incremental learning. However, most TCs are unschooled in formulating explicit curricula for a skills repertoire.

Ancillary Programs. There is a particular need for behaviorally guided programs that facilitate the member's transition to the larger outside community. For example, relapse prevention and recovery-training models can be suitably adapted to clients in the reentry stage of the TC process (Marlatt and Gordon 1985; Zackon et al. 1985).

More generally, what behavioral science can teach TCs depends upon how well it can be integrated into these human service settings. Some issues of integration are reviewed in other writings (De Leon 1979; De Leon 1980; De Leon 1974).

TCs are social-learning environments which constitute an integrated methodology for engineering a lifestyle change. To study and improve the TC requires a broader definition of behavioral science to encompass the important elements of the community as a context for learning.

From this perspective, behavioral scientists must study the setting. They can identify which activities change behavior in the TC and search for the principles that govern these effects. They can also identify what is not working in the TC setting and introduce interventions within the TC context. However, this suggestion calls for new methodologies that minimize the perturbance of the milieu that effectively produces change.

Lastly, behavioral scientists can provide functional analyses toward clarifying concepts which are consistent with behavioral science laws. These, however, must also be valid in the language and consciousness of the everyday experience in the TC.

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Learning and Unlearning Drug Abuse in the Real World: Clinical Treatment and Public Policy

Thomas J. Crowley

INTRODUCTION

Although years of laboratory and clinical research tell us much about drug abuse, clinical treatment and public policy do not evolve in a controlled research environment. In the real world, with drugs available almost *ad* libitum, how do we stimulate behaviors that can replace, or block the development of, drug-using behaviors? If every neighborhood builds a youth center, will adolescents be too busy to take up the abuse of tobacco, alcohol, cocaine, or other drugs? If we find jobs for unemployed heroin addicts, will that structuring of time help to maintain their abstinence? This paper outlines general principles that emerge from a wealth of drug abuse research data-principles that should guide the formulation of individual treatment plans and public policies. The paper lists factors associated with the development or continuation of substance abuse and highlights those factors that can be controlled or reversed to prevent or stop drug abuse in an individual or in a society.

MULTIPLE CONTRIBUTORS TO DRUG ABUSE

Picture yourself sitting on Olympus with the Gods, whiling away the hours by betting on which of the millions of youths down on Earth will become abusers of drugs. What factors would you use as predictors? Based on my best understanding of the scientific literature, I would use the nine factors presented in figure 1. I arrange them as a seesaw; seven press on that end of the seesaw associated with an increased risk of drug abuse, while two press on the seesaw to reduce the risk of drug abuse. Let us consider each of them.

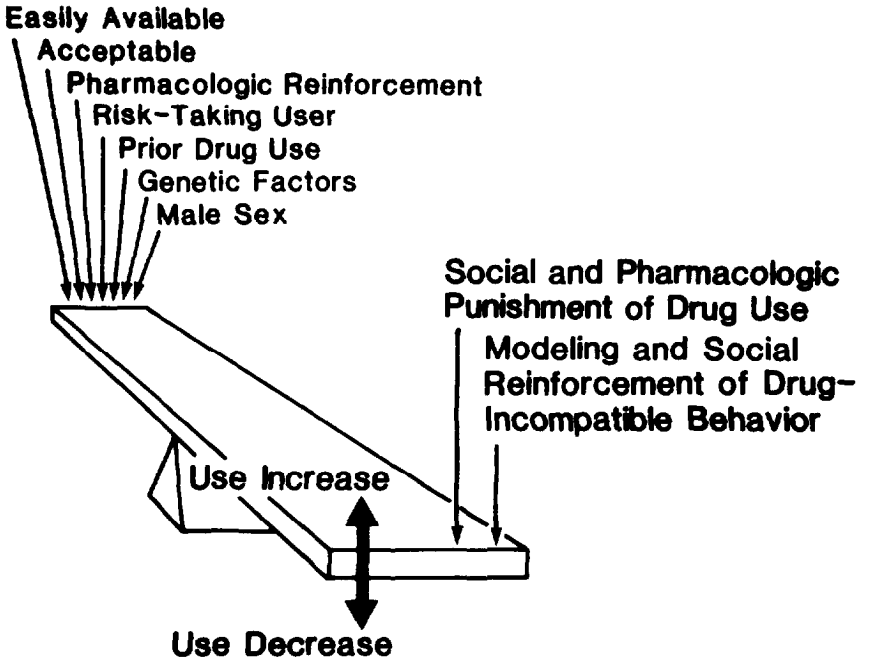

FIGURE 1. *Multiple contributors* to *substance abuse*

SOURCE: Crowley and Rhine 1985, Copyright 1985, Williams and Wilkins.

Availability and Acceptability

If I were betting at the top of Olympus, the first two factors that I would use for predicting the risk of drug abuse in a particular youth would be the availability and acceptability of drugs in that youth's environment.

National Alcoholism Rates. Figure 2 shows that alcohol is used much more (i.e., much more available and acceptable) in France, where annual per capita consumption of absolute alcohol approaches 20 liters, than in Jordan or Syria, where average consumption is only a fraction of a liter. In addition, figure 2 shows staggering differences in cirrhosis rates among different countries; rates in grape-growing France and Germany are extremely high, while rates in alcohol-proscribing Moslem Syria and Jordan are very low. The prevalence of cirrhosis in a society is a reasonably good public-health measure of the prevalence of alcoholism, so that comparing cirrhosis rates among

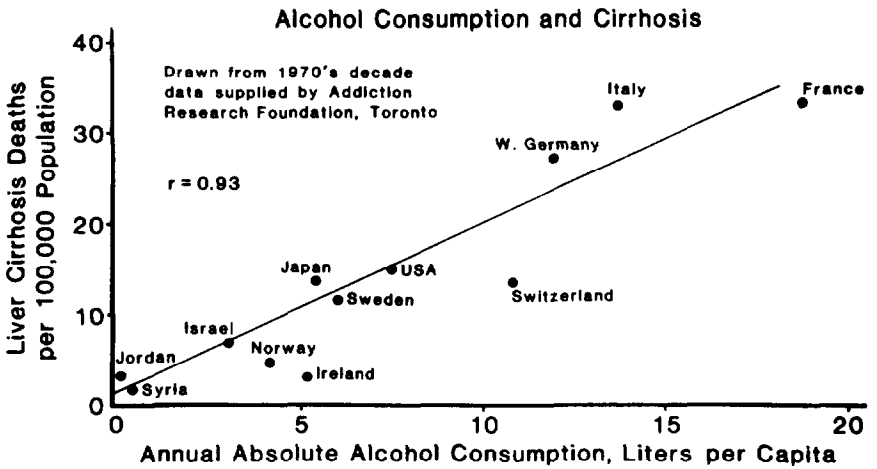

FIGURE 2. *National per capita alcohol consumption and liver cirrhosis* rates

countries gives us some estimate of the relative prevalence of alcoholism in those countries. Figure 2 shows a very strong correlation between cirrhosis as a measure of alcoholism prevalence, and the average per capita consumption of alcohol among countries; apparently, more alcoholics are produced when the population generally consumes more alcohol. Indeed, 86 percent of the national variance in cirrhosis rates shown in figure 2 is accounted for by average per capita consumption values. Wine is available, cheap, and very accepted in France, and both per capita consumption and cirrhosis rates are very high; alcohol use is condemned in Moslem countries, general consumption is low, and alcoholism is uncommon. Greater availability and acceptability of the drug generally in the society increases the risk that any particular individual may become alcoholic.

Prescriptions and Drug Abuse in a Ski Area Availability and acceptance of drug use are relevant to the prevalence of drug problems, even within more circumscribed areas. Some years ago I directed a cocaine treatment clinic at one of Colorado's ski towns. There were some clinical indications of drug diversion, and I obtained information from the Drug Enforcement Administration on ordering of pharmaceutical cocaine. Physicians and dentists in that area, which included 2.3 percent of Colorado's population, had ordered 8.3 percent of the State's pharmaceutical cocaine in the reference year. It

certainly appeared that the drug, even through legal channels, was unusually available there.

At about the same time the Colorado Health Department and Board of Pharmacy had recorded prescriptions for potentially abusable drugs in counties of Colorado (Vernon and Rawlings, unpublished data). Figure 3 shows the number of prescriptions written per thousand residents, statewide and in the county in which our clinic operated. In a ski area, many prescriptions are written for tourists, who are not reflected in population statistics for the county, and so it is not surprising that per capita barbiturate prescriptions (based on the number of permanent residents) were about 50 percent above the State average in our ski county; prescriptions for selected benzodiazepines were more than three times more frequent, which may also be reasonable. But it is striking that per capita prescriptions for various stimulant drugs and selected opiates were more than five times the State average. Oxycodone was 9 times, and methaqualone nearly 17 times, the State average. It certainly appeared that commonly abused drugs were being prescribed with unusual frequency in that area.

Not long before, the Colorado Health Department had assessed abuse of alcohol and other drugs in a statewide survey (Booth 1979). This random population survey classified 6.8 percent of adults in the State as “involved and dysfunctional” drug abusers; but the State Planning Region, which included our ski community, had 24.3 percent of respondents so classified. Statewide, 8.9 percent of respondents were classified as “involved and dysfunctional” alcohol abusers, while 20.3 percent in the ski-community region were so classified. Our experience in this ski community drove home the important relationship between widespread availability and acceptance of drug use on the one hand and the prevalence of clinical substance use disorders on the other.

Tobacco Acceptance, Availability, and Death. A third example concerns the widespread acceptance and availability of tobacco in the United States. Figure 4 roughly estimates annual deaths from various drugs. The tobacco number derives from estimates of the U.S. Surgeon General (1979). The alcohol figure is in the midrange of estimates (50,000 to 200,000) quoted in publications of the National Institute on Alcoholism and Alcohol Abuse. The range probably results from different inclusions by different authors; e.g., is a pedestrian killed by an alcoholic driver a “death from alcoholism”? I arrived at the remaining numbers by rounding off tripled mortality

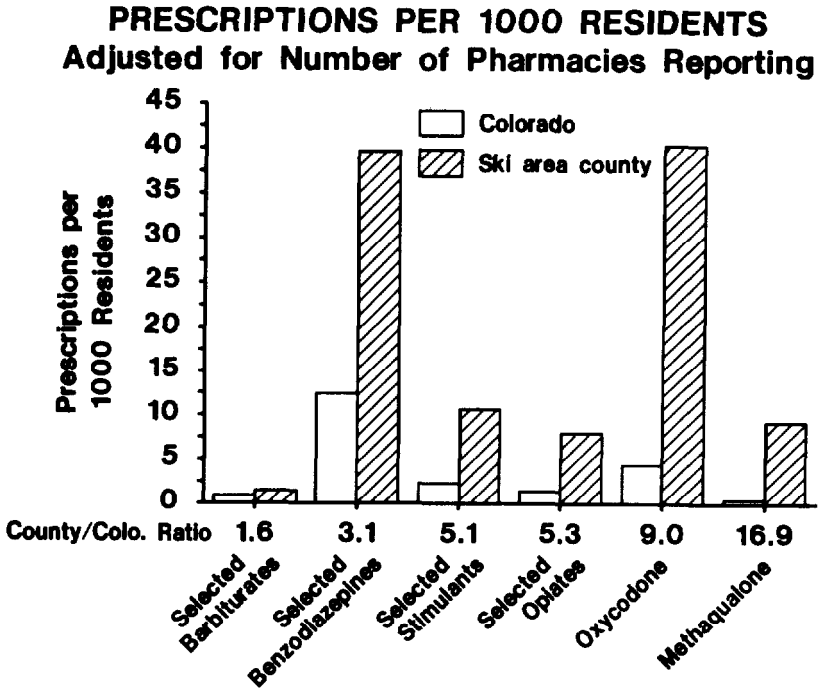

FIGURE 3. *Numbers of prescriptions for potentially abusable drugs*

NOTE: Ratio numbers are the ratio of prescriptions per thousand residents in a ski-area county vs. all of Colorado. See text for data sources.

figures reported in the Drug Abuse Warning Network (National Institute on Drug Abuse 1986), since about one-third of the U.S. population is covered in those reports. Although the figures are derived differently and can only roughly estimate true mortality rates, the disproportionate mortal cost of tobacco remains unarguable.

Consider figure 4 together with the front and back covers of TIME Magazine for March 17.1986. That front cover proclaimed the lead-story title, “Drugs on the Job,” showing a shadowy figure leading a worker astray: the back cover was a full-page color ad for cigarettes. The same media that trumpet against the “lesser killers” of figure 4 sell the “great killer.” Americans accept tobacco, make it eminently available, and die in droves from it.

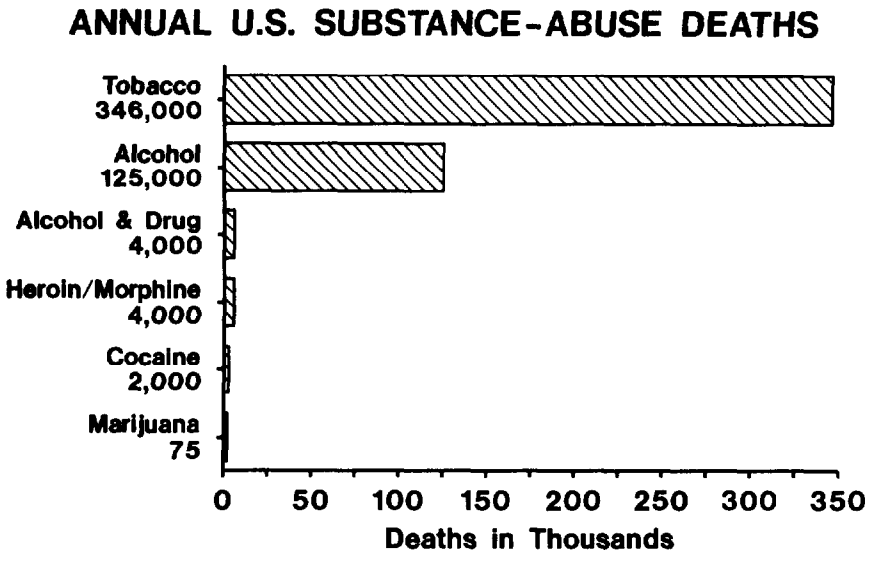

FIGURE *4. Estimated annual U.S. deaths from various drugs*

Animal Research. Even our animal studies seem to underscore the importance of availability and access in the development of drug abuse. One example is the study of high-dose alcoholic-like drinking in monkey social groups (Crowley and Andrews 1987). Lower ranked animals in the group's hierarchy drink less than higher ranked animals. High-ranked monkeys have "priority of access" to favored locations, and the area around our group's drinking spout is a busy, popular place in the animals' pen. We suspect that low-ranked animals avoid that active site to avoid social confrontations, that they accordingly have reduced access to alcohol, and that they are less likely to become "alcoholic" because of their reduced exposure to the drug.

Pharmacologic Reinforcement

Animals self-administer most of the same drugs which are abused by humans (Schuster 1976). This simple fact has profound clinical implications, which are insufficiently understood outside of scientific circles. We tend to think that human beings abuse drugs because of personal psychological problems, social deterioration and anomie, or in response to major life stresses. But to the best of our knowledge, those monkeys and rats which have faithfully self-administered large doses of drugs through many years of laboratory research have not

suffered from borderline personality disorders, were not victims of poverty or racism, and had not undergone recent divorces. Even when housed in social groups in commodious pens, monkeys take drugs (Crowley and Andrews 1987). These animals apparently used drugs because they had the mechanical means to do so, the drugs were available, and because the drugs themselves drove the animals repeated self-injections. In other words, the drugs reinforced drug-taking; the drugs were the animals' reason for taking drugs.

Thus far this paper has discussed (and will discuss further) some nonpharmacologic reasons for drug abuse. But there is growing evidence that drugs exert a biologic effect in the central nervous system that essentially commandeers behavior. The drug drives further self-administration of the drug. A drug that does so is said to be "pharmacologically reinforcing," and the user's behavior comes under the control of that drug. Social and psychologic factors may strengthen or weaken that control, but the animal data make it clear that the drug itself is central to the process.

Earlier psychiatric texts emphasized that "narcotic addiction nearly always results from emotional problems" (Noyes and Kolb 1958). This view led to treatments emphasizing hospital withdrawal and very prolonged psychotherapy, since "these emotional problems are the same anxieties, conflicts, and neuroses as those with which other emotionally unstable persons are confronted" (Noyes and Kolb 1958, p. 568). Drug dependence may occur in emotionally unstable people, but it certainly also occurs in emotionally stable people. The shift in emphasis from "underlying psychopathology" to the behavior-commandeering, or reinforcing, property of the drug has generated newer treatments aimed at reducing drug reinforcement: methadone, naltrexone, and nicotine gum. Many addicts may benefit from psychotherapy (Woody et al. 1986). But animal studies have shown that man's peculiar psychopathologies, complex symbolic thinking, or unique social environment are not essential for a drug to drive repeated drug–taking.

RISK TAKING

Accepting that a prime territory for producing substance abusers is an environment in which a pharmacologically reinforcing drug is widely accepted and available, as we sit on top of Olympus attempting to predict who in the next generation will abuse drugs, how do we choose from all of the youths who live in such environments? Simple logic suggests that if a society even gently

sets rules against the use of a drug, those who risk the breaking of rules will be most likely to experiment with the drug. Of those who experiment with the drug, some will become "hooked" by its reinforcing property, driven repeatedly to self-administer it.

Research indicates that a general tendency to take risks does contribute to the development of drug abuse. Loper et al. (1973) found a group of alcoholics in treatment programs who had taken the Minnesota Multiphasic Personality Inventory (MMPI) as college freshman, many years before receiving alcoholism treatment. in comparison to a randomly selected sample of MMPI's of their classmates, those freshmen destined to become alcoholic showed significantly higher scores on Scales 4 and 9, indicating that the pre-alcoholic freshmen tended to be more rebellious, impulsive, socially aggressive, and expansive, and were less bound by social custom; these are risk-taking characteristics. It is important to note that these differences were not pathological; they were moderate in degree and did not exceed the bounds of normality. But an enhanced risk-taking propensity was apparent and antedated the alcoholism.

Another association of risk taking and substance abuse is found in a recent national survey of over 20,000 adults. Tobacco smokers were significantly more likely than nonsmokers to engage in the risky behavior of not using seat belts (Remington et al. 1985).

In still another example, rule breaking and risk taking are central characteristics of the antisocial personality. If a propensity to break rules and take risks predisposes to substance abuse, then there should be proportionately more people with antisocial personality disorders in substance abuse treatment programs than there are in the general population, and there are (Hesselbrock et al. 1985; Woody et al. 1983; Rounsaville et al. 1983; Khantzian and Treece 1985; Schuckit 1985; Robins et al. 1984).

Prior Drug use

Prior drug use tends to predict further drug use. This is a corollary of the fact that abused drugs are reinforcing; that is, they commandeer behavior in such a way that the user is likely to repeat the drug self-administration.

GeneticFactors

Let us say that, from Olympus, we have now identified a number of young risk takers who (1) live in a society where a reinforcing drug is readily available and widely used and (2) already have had some experience with the drug. What else will predict which of these young people will develop full-blown patterns of drug abuse?

Accumulated data strongly support the view that alcoholism runs in families, and that a genetic propensity to become alcoholic is passed from parent to child (Cloninger et al. 1981). Our clinical experience with a number of cocaine-abusing patients who reported parental alcoholism led us to speculate that the genetically transmitted propensity to abuse alcohol might also predispose to cocaine abuse (Crowley 1987). A recent study does suggest that the offspring of alcoholic parents are at increased risk to abuse other drugs, even when the children are raised apart from their alcoholic parents (Cadoret et al. 1986). So another solid predictor of substance abuse is a family history of alcoholism.

Male Sex

Males generally are more likely to become substance abusers than are females. About 57 percent of cigarette smokers are male, as are over 80 percent of diagnosable alcoholics in the general population (Robins et al. 1984). The reasons for these discrepancies may be environmental or biological; we simply do not know at this time. But, other factors being equal, boys are at greater risk than girls of becoming substance abusers.

Social and Pharmacologic Punishment of Drug Use

One who expects quick, painful, and highly predictable punishment for drug use may seem unlikely to use the drug. This kind of punishment for drinking alcohol is produced pharmacologically by disulfiram (Antabuse). Recent research establishes clearly that when alcoholic patients are provided with either disulfiram or placebo for a l-year study period, the disulfiram-treated patients drink on significantly fewer days than do the placebo-treated patients. So pharmacologically punishing drinking does reduce drinking (Fuller et al. 1986). We use aversive contingency contracting in substance abuse treatment. Drug abusers hire me or my colleagues to establish schedules for urine collection and to apply specific aversive consequences if the patient produces a urine containing drugs, or fails to provide

scheduled urine samples. For example, a physician may write a letter to his licensing board, stating that he is surrendering his license because he is a drug abuser. He deposits the letter with me and directs me in a written contract to mail the letter if subsequent urine samples contain drugs. We find more than a hundredfold reduction in drug use under these conditions of social punishment for relapse (Crowley 1986).

Certainly, if a youth believes that there is a high probability of detection and swift punishment for drug use (by family, school, or friends), that youth will be much less likely to abuse drugs.

Modeling and Social Reinforcement of Drug–Incompatible Behavior

There is evidence that we can reduce drug abuse not only by punishing drug use but also by reinforcing abstinence. Even "derelict" skid row alcoholics significantly decrease their alcohol consumption and arrests for public drunkenness, while increasing their hours of employment, when community agencies provide goods and services contingent upon sobriety (Miller 1975).

A number of recent studies also show reductions in cigarette smoking if patients simply are paid to cut down or stop (Stachnik and Stoffelmayer 1983; Stitzer and Bigelow 1982; Stitzer and Bigelow 1984). We have tried those procedures in patients with Chronic Obstructive Pulmonary Disease-a severe, often fatal, cigarette-induced illness which stops progressing when the patient stops smoking-unfortunately, many severe tobacco addicts with the disease continue smoking. We observe a significant reduction in smoking by these patients if they are paid state lottery tickets for reducing carbon monoxide levels, a measure of smoke intake (Crowley et al., in press). So even severe addicts may reduce their drug use if social reinforcers are made contingent upon greater abstinence.

From Olympus' top, do not bet that a youth will become a drug abuser if that youth strongly wants something and believes that drug abuse will prevent him from getting it. If we provide reinforcers contingent upon abstinence, we probably can reduce drug abuse.

In summary, the youth at highest risk to become a substance abuser would be a male born to alcoholic parents, raised in an area where a highly reinforcing drug is freely available and quite accepted, a boy who generally tends to break rules and take risks, who already has tried the available drug, and whose experience has shown that there

is neither much risk of punishment or loss for using drugs, nor much concrete reward for abstinence. In this volume, Primm[1] describes the tragic outcome in an area where these conditions prevail.

TRANSLATING PRINCIPLES INTO CLINICAL PRACTICE

When a patient seeks treatment, the history of prior drug use, the existence of any genetic predisposition for drug use, and the patient's sex are fixed. The other six factors of figure 1 potentially may be modified, however, and the therapist's job may be conceptualized as changing the balance of factors on that seesaw by: (1) reducing the availability and acceptability of drug use in the patient's environment: (2) reducing pharmacologic reinforcement from the patient's drug: (3) reducing the risk-taking propensity of the patient; (4) maximizing (with the patient's cooperation) social and pharmacological punishment for relapse; and (5) helping the patient develop drug-incompatible behaviors (which earn reinforcers but only when the patient is abstinent).

Two cases treated by the author highlight these approaches. Both cases show a profound reduction in drug use, and one had a very favorable general outcome: after several years the other ended in tragedy, emphasizing the extremely complex problems encountered in substance abuse treatment.

Case I. Jack was a physician, approximately 30 years of age, and his fiancee, Elizabeth, was in her midtwenties (identifying data are obscured to protect confidentiality). Jack was finishing his residency when he was referred to me by his State licensing board. Jack reported that since graduating from medical school he had gradually increased his drug use, which now included daily use of marijuana, about 40 mg per day of amphetamines, about 2,000 mg per day of meperidine, and about 1 pack per day of tobacco. Jack spontaneously commented on the powerful behavior-commandeering effect of meperidine: "It was self-sustaining" (pharmacologic reinforcement). He found that he continued using it and the other drugs despite awareness of major losses. Not only did he fear the loss of his fiancee and his position, but he found his own honesty slipping away. "I was losing my value system, and I would lie about anything."

After an initial evaluation, Jack agreed to a license-surrendering contingency contract, as described above. Indeed, he said that he had specifically sought treatment with me because he understood that I offered such contingency contracts, and he was convinced, based on

numerous previous relapses, that such a contract was essential for him to become abstinent.

Jack described his father as a "workaholic physician" who was both kind and gentle with the patient. Jack had been close to his mother, but she died of cancer when he was 14 years of age. He said, "My mother's use of drugs (for terminal pain) set the stage for my own use" (acceptability). Jack's father remarried 1 year later, and Jack had extensive conflicts with his stepmother. He was a very successful high school student and athlete, dated frequently, obtained good grades, and was a member of the student council. But he contracted a marriage in college which failed quickly.

Jack was in medical school in the 1970s, a time when drug use was widely accpeted and there was considerable risk-taking rebellion against society's proscriptions regarding drugs. He was "curious" about intravenous drugs, and in medical school drugs became physically available. His use of intravenous opiates gradually accelerated, and by 1980 his new fiancee began to find drug paraphernalia around his house. Eventually, he accidentally overdosed and was taken to an emergency room. He then was using meperidine daily, together with the other drugs described above. His drug use was detected at work, and he was referred to the licensing board. The board took several months to act, and, despite his intense concern, Jack continued intermittent use of the drug through those months.

By the time that Jack sought treatment with me he was finishing his residency, and his licensure problems made it difficult to find a position. Jack and Elizabeth married, and he eventually began practice in a small town in a nearby State.

Elizabeth collected the required urines. "I'm real tough. I like him showing me that there is nothing to hide." Under the contingency contract it was clear that there would be a major social punishment (loss of license) for relapse, and Elizabeth unequivocally supported that contingency. Jack said, "I can't say that I haven't thought about drugs, but I remind myself of the consequences." Jack clearly saw the consequences diagrammed on the right side of figure 1-punishment for relapse-and the rewards of practice for abstinence.

Because of the distances involved, meetings with me occurred only once every few months, although urine collection continued frequently. After several months of abstinence Jack said, "I've been

trying to understand what happened. During my residency, I finally had some income, and that's when I used. I was trying to deny that I could be successful. It was like the loss of drive that I felt when I was a high school runner and became successful. Also, when I felt that I could really do it in medical school, I really increased my pot use. Now I'm very successful in a practice, and I really need to be aware of it."

After about 8 months of treatment, a newspaper ran Jack's name as a drug abuser, a reporter had obtained the names of all doctors under probation with the licensing board. Elizabeth said, "Its awful how something can reach out and hurt you when you're doing the best you can." Jack added, "I'm overcalling diagnoses. I have to be perfect, or they will think that I'm using." But the couple survived that trauma, and at the end of 1 year we decreased the frequency of urine examinations. Elizabeth continued to be active in the urine monitoring. We planned that in addition to the scheduled, but now infrequent urines, she would call me if she ever suspected a relapse; Jack then would produce extra urine samples.

Over the next 8 months both members of the couple were very pleased with Elizabeth's role in structuring consequences regarding a relapse. Jack represented his local medical society on a State committee of impaired physicians, and said, "I supported the idea that wives should be involved, even to report the husband if needed."

Jack spontaneously discontinued tobacco use without specific treatment. His work often involved lung-cancer patients, and tobacco use simply became unacceptable. He clearly perceived the consequences.

At the end of the second year of treatment Jack commented that "A relapse risk remains. Two years is not a cure."

During the third year of treatment there were very few visits with me, although Elizabeth continued to collect urines. Jack became the president of his county medical society. He commented that he now felt "a very low temptation to use, because other things are on my mind." He was building a very active practice, and he saw continued professional progress as incompatible with relapse.

Contacts with me ended 3 1/2 years after treatment began. At that time, Jack wrote a letter to his licensing board; the letter requested an investigation, stating that Elizabeth believed that Jack had relapsed to drug use. He deposited that letter with his wife, and he

gave her detailed directions of what to do if she suspected a relapse: demand a urine, demand an evaluation by a knowledgeable professional, and mail the letter if Jack failed to follow through. The couple intended to maintain punishment for relapse as a technique to reduce the risk of relapse, or to abort one that might occur.

Case II. Bill was a physician in his forties and his wife, Ann, was about the same age. Bill first consulted me because a patient's husband was threatening suit against him, alleging faulty prescribing of amphetamines. Bill merely wanted information on amphetamine prescribing, he said, but he also stated that he probably would commit suicide if the suit went forward. Despite this, he refused all recommendations regarding treatment and left my office. Some months later he did overdose in a serious suicide attempt. Two months later, Bill's son committed suicide by inhaling carbon monoxide from their automobile in the parking lot of Bill's medical office.

Later that year, Bill had surgery and was found to be very intoxicated in the hospital; at his request, his wife had brought in supplies of ethchlorvynol for him. Bill subsequently was suspended from the hospital staff. Bill's wife clearly was not punishing his drug use. A month later, he argued with his wife saying "Well, I may not be here next week," to which she replied, "Good, I hope you aren't." Bill took another nearly fatal overdose and was referred to me.

Bill reported that his father was an alcoholic who constantly spoke of suicide as Bill grew up. His mother was cold, unloving, and abusive. She frequently sent the children to the barn, telling them to kick through the hay looking for their father's body after arguments in which the father had threatened suicide. After Bill became an adult his father did commit suicide in Bill's apartment.

Bill had first sought psychiatric treatment 25 years before seeing me. His marriage had been extremely stormy; he and Ann sometimes fought with weapons, and she once suffered a multilating, self-inflicted shotgun wound. For many years Bill had abused opiates, barbiturates, amphetamines, and other drugs through indiscriminate self-prescribing (availability).

To regain his hospital privileges, Bill agreed to a program of urine monitoring with regular reports to the hospital. He was now presented with a choice; he could have the reinforcement of drugs or the other reinforcements incumbent in being a practicing physician, but he could not have both. Drug use became incompatible with those other reinforcers.

Bill's adolescent children participated in the evaluation. One son was extremely rebellious, another was quite depressed, and a daughter had been thinking of suicide for several years. Bill also saw an internist for his medical problems after years of being his own doctor. Wiih counseling and urine monitoring, there was steady improvement in Bill's family relationships. He remained abstinent for a number of months and got along better with his wife and his children.

But Bill took a vacation in the sixth treatment month. The urines were suspended, so the punishing consequences for a relapse were gone. Bill quickly intoxicated himself with chlorazepate. Since he was on vacation and not practicing when this slip occurred, there was little concern that his practice privileges would be suspended. The family was in major turmoil when Bill returned to town, and I recommended a change in the urine schedule. Bill said that he definitely would commit suicide, and he was briefly hospitalized. He and I worked out some redefinition of our relationship, and he soon stabilized again. During the next 5 months he showed steady improvement. "Now the motivating force is me, my wife, and my family," he said. "I'm doing better than I ever did before."

His new drug-free life was both attractive and reinforcing. He began investing in stocks. At the end of the first year of treatment, Bill and his wife finally began expressing grief about their son's suicide.

Several months later, Bill underwent more surgery. After undergoing eight hospitalizations and four surgeries in 15 months, he received a prescription for codeine from his surgeon. Drugs again were available.

Bill's investments in penny stocks increased in value tenfold over the next few months. "The two best things I ever did were entering your drug program and buying those stocks," he commented. Throughout the next year the couple was pleased with each other. Urine monitoring continued, and they visited with me about monthly. There was one major argument, after which Bill left home for about 2 days, but there were no drug relapses or suicide threats.

During the fourth year of treatment, Bill experienced increasing pain, had more surgery, and received numerous prescriptions for codeine. His practice was failing financially. He and his wife argued because he wanted her to work at the office more, and she said, “I’m not a slave.” Increasingly they spoke of divorce as these problems worsened, but Bill said he could not afford to leave her because of her employment in the office. The standoff became more unpleasant and Bill’s investment earnings were eroded as his stocks fell in price.

For some time Bill had found an attractive life that was incompatible with relapse to drug use, but now he faced an unattractive life with pain and both marital and financial problems; codeine was available on prescription. At one point it appeared that Bill may have self-prescribed an opiate, although the evidence was uncertain.

At the start of the fifth year of treatment, Bill requested an increase in urine monitoring. He said that urines had been helpful in reducing the desire to use drugs, but now even with increased urines he still had some positive urine samples (always satisfactorily covered by proper prescriptions from his surgeons). Bill underwent additional surgeries during that year, and in the fifth month of the year he determined that he was disabled.

Bill’s family found that he had bought a hose to connect to his car for a carbon monoxide suicide. His wife scolded, “You don’t have a will, and we’ll have to go through probate.” At one point his wife got out a shotgun and threatened to commit suicide if he did so. Finally she said, “Either shut up or do it.”

Bill said, “She killed my tender feelings by saying that I made her a slave.” He added, “Suicide is my divorce.” But at a later visit Bill’s mood had improved. The couple was again talking about going fishing, and he was planning to buy a boat. Then he became very intoxicated on prescription drugs. An argument with his wife followed, and she threatened to call me. He told her, “Show this prescription to Dr. Crowley. You’ll never see me again.” He left home, overdosed, and died.

Both of these doctors had extensive prior experience with drugs, both were male, and one had an alcoholic father (suggesting some genetic predisposition to substance abuse); these were fixed, unalterable characteristics when the doctors sought treatment. Both were also members of a profession which made highly reinforcing drugs easily available, and which honored and accepted drug giving (though not

drug taking). Moreover, the medicating of Jack's dying mother, and the surgeon's prescriptions for Bill's very real medical problems, apparently made drug use more acceptable to these patients.

Bill's wildly chaotic marriage was a saga of risk taking, involving guns and knives, furious midnight drives in cars, one partner bringing dates home while the other partner packed weapons, and so forth. Jack's habits were much more cautious and restrained, except for his drug use.

Effective punishment for substance abuse implies a high probability of rapid, predictable, and adverse consequences that follow almost immediately upon drug use. Slow, ponderous, and legalistic interventions by hospital committees and licensing boards had been ineffective in helping these doctors to abstain. So had the uncertain threats of Jack's well-intentioned, but frightened and confused, fiancee. At times Ann supported Bill's drug use, as shown by her clandestine supplying of drugs to him when he was hospitalized for surgery. Counseling assisted Elizabeth in making clear stands and setting clear consequences for relapse; with counseling, Ann more consistently supported Bill's abstinence.

Before treatment both doctors had been able to carry on with their lives while continuing to use drugs, although Bill had been suspended just prior to seeking treatment. Other rewarding aspects of their lives had not been made incompatible with drug use. Although both were mired in pain and despair, they had not been forced to choose between drugs and life's other rewards. For both doctors, contingency contracts and urine monitoring made practice incompatible with further drug use, by assuring adverse consequences for relapse: drug use stopped. Couples counseling repaired the drug-induced disruptions between Jack and Elizabeth, and they soon settled into a happy marriage. Couples counseling also reduced the turmoil and initially unveiled surprisingly positive feelings between Bill and Ann. Both doctors saw that these improved relationships depended on continued abstinence and that such relationships were incompatible with further drug use. We have extensively discussed elsewhere the conduct of therapy for such patients (Crowley et al. 1987).

Sadly, after several years of happier living, Bill's health and practice deteriorated, and the marriage, fragile at best, was wounded by those strains. Because of Bill's ill health, drugs again became available and acceptable for him. Urine monitoring could not distinguish between prescription codeine taken as directed vs. codeine taken in

intoxicating doses. Thus, the medical need for pain relief again opened the door to abuse. Standing between two generations of suicides (his father's and his son's), watching his health and practice slip away, and no longer finding his marriage rewarding, Bill apparently found little reason to avoid drugs and finally chose death by drugs, the long-used and familiar vehicle.

A PUBLIC POLICY ON DRUG ABUSE

The factors in figure 1 lead not only to treatment approaches, but to considerations for public policy. These considerations probably apply to all drugs of abuse, including tobacco and alcohol. If we w&h to reduce the terrible mortality and morbidity from drug abuse in our society, the following steps may be necessary.

Reduce Drug Availability

Availability of illegal drugs is probably controlled only by police measures. Availability of legal drugs, such as alcohol and tobacco, may be regulated through excise-tax price manipulations, eliminating cigarette vending machines, permitting sales only in specially licensed stores, and punishing sales to minors.

Reduce the Acceptance (or Prevalence) of Drug Use

Each user presents a model of drug use for others, and even non-users' acceptance of drug use by others makes it easier for some to begin using. Making drug use illegal, making it less convenient, limiting places where drugs (such as tobacco) may be used, publicly discouraging drug use, preventing drug advertising, and blocking any public encouragement of drug use (in movies, nightclub acts, concerts, etc.) may all reduce drug use. "Just Say No" is probably a step in the right direction.

Punish Drug Use

The data cited here make it clear that punishing drug use does reduce drug use. But effective punishment requires a high probability of detection with swift (but reasonable) consequences: it does not mean a very low detection rate coupled with ever-harsher jail sentences. Many people see urine monitoring as a threat to individual liberty, but urine monitoring with punitive consequences may save lives by reducing drug use. U.S. military surveys show

dramatic declines in drug use between 1980 and 1985, and about two-thirds of military respondents believe that urine testing contributed to that decline (Bray et al. 1988).

Make Other Desired Reinforcers Contingent Upon Abstinence-Rendering Them Incompatible with Drug Use

We certainly have advanced beyond the days when we planned a youth center in every neighborhood, expecting that youth busy with basketball would be too busy for heroin. If the items of figure 1 are arranged to lead toward drug abuse, youth centers in heroin-infested neighborhoods simply will host basketball games between heroin-intoxicated youths. But if we make desired reinforcers (basketball or whatever) incompatible with heroin intoxication, youths seeking those reinforcers must abstain. The success of contingency contracting does indicate that making the rewards of medical practice incompatible with drug use reduces drug use. It is the opportunity to do both together (to practice and to use) that enables continued use. Some employers, concerned about medical insurance costs, now hire only nonsmokers. Others provide less complete health insurance for smokers. As these practices spread, smokers will be forced to choose between continued tobacco abuse and certain jobs. Forcing that choice may accelerate the decline in smoking prevalence.

CONCLUSION

This simple, four-point public policy probably will reduce substance abuse, but it will not work for everyone. Many people will be exposed to conflicting cues from their environments. They will have spouses, or friends, or tobacconists and other drug dealers who encourage continued use, make drugs available, and (in some cases) actually punish abstinence. And the individual psychopathology of others will impair their judgment or restraint sufficiently that they will plunge into substance abuse regardless of the obvious hazards. Once a drug secures a foothold in society, we probably cannot fully eradicate it, but we can reduce its prevalence of use by a thoughtful and vigorous public policy.

I cannot deny the negativity of the four points in this proposed public policy. But my understanding, based on scientific and clinical experience, is that drugs commandeer the behavior of drug users and that the drug, not the user, controls the continued drug taking. Our fundamental concepts of social liberty assume that the citizen directs his own behavior. In the case of addicting drugs, we may need to

apply more external controls, as outlined above, because the drug more than the citizen comes to control the citizen's behavior.

We are confronted with highly reinforcing drugs that commandeer human behavior and drive continued self-administration. Many of those who are exposed repeatedly to these drugs become dependent upon them. Hundreds of thousands die from them each year. Only powerful public health policies will reduce the mortal cost of substance abuse in our society. Such policies could have saved the one-third of a million Americans who will die this year of tobacco abuse.

Bill might never have been a happy man, but earlier application of these principles might have prevented his death from drugs.

FOOTNOTES

1. Due to the administration's war on drugs, to which Dr. Primm contributed his time, he was unable to prepare his chapter for this monograph.

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The Relationship of Stimulus Control to the Treatment of Substance Abuse

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INTRODUCTION

In the behavior analysis of substance abuse, much concern has been placed on the consequences or reinforcement processes of drug self-administration. An equally important behavioral process that has not received comparable scientific attention is the role of discriminative stimulus control in drug self-administration. A discriminative stimulus refers to a class of stimuli whose presence alters the probability of a class of responses previously reinforced in the presence of that stimulus class. Behavior under the control of a discriminative stimulus is referred to as stimulus-controlled behavior. Our purpose here is to describe how stimulus control might affect substance abuse. The relationship of stimulus control to substance abuse and its treatment will be examined by: (1) briefly reviewing the role of stimulus control in drug self-administration; (2) describing some possible ways that stimulus control may be employed in the treatment of substance abuse; and (3) discussing the ways in which traditional therapeutic modalities may be employing these processes.

STIMULUS CONTROL OF DRUG SELF-ADMINISTRATION

Environmental stimuli can exert considerable control over drug-maintained behavior. Environmental stimuli previously correlated with drug taking engender an increased probability of drug seeking. For example, if the presence of a red light is correlated with the availability of response-dependent drugs and the absence of the light is correlated with the absence of drug, then the probability of drug-seeking behavior is greater in the light's presence. Such control can likewise be exerted by stimuli that are interoceptive, such as the stimulus properties of drugs once taken, or by stimuli that are

exteroceptive, such as events or objects correlated with drug delivery. In this section, we will briefly review some literature showing that both interoceptive and exteroceptive stimuli can set the occasion for drug self-administration (Bickel et al. 1987a).

Interoceptive Discriminative Stimulus Properties of Drugs

Drugs, once ingested, in addition to serving as reinforcers, can also function as stimuli which set the occasion for behavior. For example, a discrimination between two drugs can be trained by reinforcing one response in the presence of the interoceptive effects of a drug and reinforcing a different response following injections of saline or some other drug. The discriminative properties of drugs, which have been extensively studied in the animal laboratory, have also recently been extended to the human laboratory (Bickel et al. 1986b; Chait et al. 1986; Preston et al., in press).

Relatively new in research of the stimulus properties of drugs and germane to the problems of drug abuse has been the ability of passively received drug injections to reinstate previously extinguished drug-seeking behavior. For example, de Wit and Stewart (1981) trained rats to respond for intravenous cocaine. Extinction conditions were introduced so that responding no longer produced cocaine. When responding had decreased to low levels, non-response-contingent cocaine injections restored responding even when the extinction conditions remained in effect. Reinstatement has been demonstrated to be pharmacologically specific to the degree that a range of drugs pharmacologically similar to the drug previously self-administered engenders reinstatement. Reinstatement has been systematically replicated in animal studies using a wide variety of drugs (see Young and Herling (1986) for a review).

This reinstatement effect has also been demonstrated in studies of alcohol self-administration in humans. Bigelow et al. (1977) sup pressed the alcohol consumption of alcoholics living in a research ward by time-out or response-cost procedures. The administration of a single response-independent dose of alcohol engendered reliable increases in ethanol self-administration. Similar results have also been obtained by Funderburk and Allen (1977). Thus, there appears to be generality across human and animal studies, demonstrating that the interoceptive stimulus properties of the drug are sufficient to reinstate drug-seeking behavior (Griffiths et al. 1980).

Reinstatement suggests that a given dose of the drug once taken may set the occasion for the next episode of drug self-administration. This may be related to relapse. Relapse may be initiated by one set of factors, but then maintained by other factors that are distinctly different from those that initiated relapse. Once a relapse episode has been initiated, the interoceptive stimulus properties of the drug may then lead to continued drug taking.

Research on the interoceptive stimulus properties of drugs also suggests that drug stimuli, like exteroceptive stimuli, may have multiple functions. In the above example, the reinforcer (a drug) also sets the occasion for responding for the next drug delivery. Thus, the drug in this instance functions both as a discriminative stimulus as well as a reinforcer. Clearly much work needs to be done to better understand the interoceptive discriminative stimulus properties of drugs, particularly as they relate to reinstatement. For example, research needs to address whether the reinstatement effect persists throughout the duration of action of the priming dose or whether it is restricted to onset or offset of drug action, as well as the effects of drug tolerance and physical dependence on the reinstatement process.

Exteroceptive Stimuli

In addition to interoceptive stimuli, there are various exteroceptive stimuli that can set the occasion for drug self-administration. The effects of some of these stimuli are observed most clearly in the behavior of humans (e.g., modeling and rule-governed behavior).

Conditioned Drug Effects. Conditioned drug effects have been widely known to control drug self-administration since the initial work by Wikler (1965). Basically, conditioned drug effects result from the pairing of pharmacological drug effects or physical withdrawal with exteroceptive stimuli. As a result of this pairing, the environmental stimuli come to elicit withdrawal (and sometimes the agonistic response) which is typically associated with reports of drug craving. For example, if a light is paired with injections of nalorphine (an opioid antagonist) in morphine-dependent monkeys, the presentation of this light will elicit certain signs of the morphine abstinence syndrome and produce large increases in the rates of morphine self-administration (Goldberg et al. 1969; Goldberg and Schuster 1967; Goldberg and Schuster 1970). Thus, conditioned drug effects can be seen as stimuli which set the occasion for drug-seeking behavior. This line of study has been examined extensively and productively

with animals and humans (O'Brien et al. 1988; O'Brien et al., this volume: Siegel, this volume).

Conditioned Reinforcers as Discriminative Stimuli. As noted previously, a reinforcing event (interoceptive drug stimulus) can also function as a discriminative stimulus. The effects of exteroceptive stimuli can function in a similar fashion. For example, stimuli paired with reinforcing events can serve both as conditioned reinforcers and discriminative stimuli. In a study by Hursh (1977), monkeys were responding on the repeated acquisition of behavioral chains procedure, in which every correct response in a chain resulted in the presence of a light which was also present at the end of the chain when food was delivered, but the specific response chain changed and had to be repeatedly learned. The influence of the light stimulus on the acquisition of response chains was examined by removing its presentation after a link in the chain. Acquisition of the link was disrupted by removal of the light. Moreover, the acquisition of the next link was also disrupted. Thus, the stimulus presented after a correct response in the acquisition of the chain functioned as a conditioned reinforcer increasing the probability of the previous response, and also served as a discriminative stimulus engendering the next response. Stimuli paired with drug consumption may also function simutaneously as conditioned reinforcers and as discriminative stimuli, thereby controlling extensive chains of drug-seeking behavior. There have been many demonstrations of the reinforcing efficacy of stimuli paired with drug consumption (Goldberg et al. 1981; Goldberg et al. 1979; Kelleher and Goldberg 1977). If conditioned reinforcement can also set the occasion for behavior, then the discriminative properties of that conditioned reinforcer may play an important role in maintaining drug self-administration (Meyer and Mirin 1979; Levine 1974). Thus, the discriminative functions of stimuli paired with drug consumption are likely to play a critical role in the reinstatement process.

Modeling. Modeling can also affect drug self-administration. The behaviors of models are thought to "serve as discriminative cues for observers in facilitating the expression of previously learned responses" (Bandura 1969, p. 196). Thus, in laboratory situations in which a subject is paired with a confederate, we would expect that the subject's drug consumption would to some extent imitate or match that of the confederate. This result was obtained by Garlington and Dericco (1977). Three college students who were moderate drinkers served as subjects. Each subject was paired with a confederate who, under one condition, consumed alcohol at a high rate (measured in ounces per minute) and, under another condition, consumed alcohol at

a low rate, with the drinking occurring in a naturalistic bar environment. Under these conditions, subjects matched the consumption of the confederates. These discriminative stimulus properties of a model on alcohol consumption have also been demonstrated with alcoholics (Caudill and Lipscomb 1980) and heavy drinkers (Caudill and Marlatt 1975) under laboratory conditions, and with free-ranging normal drinkers in a public tavern (Reid 1978). Similar results were obtained in a study with cigarette smokers by Antonuccio and Lichtenstein, in which the effects of modeling on cigarette smoking were examined (Lichtenstein 1977). One interesting aspect of this study was that the topography of smoking was not influenced by the model; only the initiation of a cigarette. These studies indicate that a model can be a controlling stimulus for human drug self-administration.

Rule-Governed Behavior. Rules or instructions may have a multiplicity of effects with respect to drug self-administration. Rule-governed behavior as initially proposed by Skinner (1969) refers to the control of behavior by instructions. Under some circumstances, rule-governed behavior has been demonstrated to result in human operant behavior that is seemingly insensitive to contingencies of reinforcement. However, rule-governed behavior is itself an operant that can be reinforced, extinguished, or brought under stimulus control. Rules may alter the topography of drug self-administration, the reinforcing efficacy of a drug, or even behavioral responses typically emitted in complex chains of drug-seeking behavior.

One of the first studies on the effects of instructions on drug self-administration (Frederikson and Simon 1978) examined how instructions could modify the topography of cigarette smoking. Subjects were instructed to decrease the number of puffs and puff duration. The effects of these instructions were first documented in a laboratory setting, then a contract was drawn to generalize this change to other settings. The topography did change in these other settings, and changes were maintained at a 6-month followup. The clinical significance of these findings were validated by documenting a decrease in carbon dioxide that indicated decreased biological exposure to cigarette smoke. This study demonstrates that a single instruction can exert powerful effects over drug-taking behavior.

Instruction can also alter the reinforcing efficacy of drugs. Hughes et al. (1985) found that cigarette smokers who were required to stop smoking with the aid of nicotine gum were strongly influenced by verbal instructions about what to expect from the two gums they were offered, these being a nicotine and a placebo gum in every

case. When told the two gums might be any combination: both nicotine, both placebo, or one of each, subjects preferred the nicotine gum. When told both gums were nicotine, but one had fewer side effects, subjects showed no preference for nicotine. When told one gum was nicotine and the other a placebo with worse side effects than nicotine, subjects showed no preference for nicotine. In all these cases, the gums tested were the same, demonstrating that instruction can control whether a drug acts as a reinforcer. Bickel et al. (1986a) have also suggested that providing instructions to methadone maintenance patients about the size of an increase in dose would enhance its reinforcing efficacy compared to the same increase done blindly, that is, without noting it by confirming instruction.

Conditional Stimulus Control. The different controlling stimuli discussed above can be involved in more complex relations. One of these complex relations is the conditional discrimination. A conditional discrimination is a discrimination in which the reinforcement of a response in the presence of a given stimulus depends upon or is conditional upon another stimulus. An example relevant to drug self-administration is provided in a study by Stretch et al. (1971). In that study of reinstatement of drug self-administration via the stimulus properties of drugs, a noise was paired with the availability of amphetamine reinforcement. Behavior was then extinguished by withdrawing amphetamine. After behavior occurred with a low probability, a presession injection of amphetamine reinstated responding only when the noise was present, suggesting that the ability of presession injection of amphetamine to set the occasion for behavior was conditional upon the presence of the noise. Clearly, any of the stimuli that can control behavior discussed earlier may be involved in more complex stimulus interactions. In the treatment of substance abuse, these complex actions may be the rule rather than the exception and may indicate why treatment success or effect transfers with difficulty outside the therapeutic environment. Thus, there may be value in the laboratory study of complex stimulus conditions related to drug self-administration.

Summay

This review suggests that stimulus factors that set the occasion for drug self-administration may be important in both short- and long-term treatment success. The form of the stimuli controlling behavior may vary widely, ranging from interoceptive stimulation to instructions. These stimuli can increase or decrease drug self-administration

and, in the case of instructions, augment or diminish the reinforcing effects of drugs. Research is needed to organize these many effects into a conceptual framework useful for treating and preventing drug abuse. The literature is still limited, and there is a clear need for more research in many of these areas.

ISSUES OF STIMULUS CONTROL IN THE REDUCTION OF DRUG SELF-ADMINISTRATION

The brief review above has demonstrated that discriminative stimuli can influence drug self-administration. There is also good reason to believe that issues of stimulus control can be employed for therapeutic purposes. Three distinct tactics have immediate implications for treatment: (1) changing the function of stimuli already controlling drug self-administration; (2) removing stimuli controlling drug self-administration: and (3) providing stimuli that will successfully compete with the stimuli currently controlling drug self-administration (Schroeder et al. 1986). Each of these tactics will be considered in turn.

Altering the Function of the Stimulus

To alter the function of a stimulus controlling behavior, contingencies of reinforcement are typically employed. Reinforcement contingencies used to successfully alter discriminative stimulus control include punishment, reinforcement, and extinction. For example, punishment procedures typically produce decreases in drug self-administration. Punishment may be viewed as a way to change the function of the discriminative stimuli that set the occasion for drug taking; that is, self-administration is punished in the presence of stimuli that previously set the occasion for that behavior. Thus, with continued exposure to the punishment, discriminative stimuli acquire a different function, which is to set the occasion for behavior other than self-administration. Similar interpretations could be made of reinforcement of behavior incompatible with drug self-administration or extinction procedures with respect to altering stimulus function.

Although changing the function of discriminative stimuli via these methods is usually effective in the short term, long-term success is more doubtful. For example, Wilson et al. (1975) examined the effects of punishment on alcohol self-administration by chronic alcoholics living on a research ward. The punishing event, shock, effectively suppressed alcohol consumption, but drinking subsequently returned to baseline levels after punishment was withdrawn. This and other

findings from similar studies suggest that there may be a difference between reducing a stimulus-response relation in frequency and changing the nature of a stimulus-response relation. Ray (1969) has shown that training a new response to a stimulus with a previously established discriminative function decreases the frequency of the previously controlled response without necessarily altering any properties of the original stimulus control relationship. Thus, under new circumstances, behavior previously controlled by the original stimulus may emerge fully blown. Research by Stoddard and Sidman (1971) has shown, however, that stimulus control can be abolished. Generally, the conditions necessary for the abolishment of stimulus control are not as well understood as the conditions for maintaining or establishing it. Until the conditions which abolish a stimulus-response relation, as distinguished from those which merely reduce its probability of occurring, are separately identified, a zero frequency of behavior will be impossible to interpret. Given the intractability of drug self-administration, it may be a case where the procedures effective in decreasing drug consumption typically do not abolish previously conditioned controlling stimulus-response relationships.

Removing the Stimulus Controlling Drug Self-Administration

If the controlling stimuli for drug self-administration are specific to one stimulus or a small class of stimuli, then one treatment approach could be to remove the stimuli that set the occasion for drug-seeking behavior from the substance abuser's environment (e.g., stop the substance abuser from associating with a particular group of drug-using individuals). However, if the controlling stimuli are numerous and widely distributed, then the treatment might necessitate removing the substance abuser from so many environments as to be impractical. Unfortunately, the latter case is more typical for humans.

An early demonstration of the effects of removing the organism from the environment was examined by Thompson and Ostlund (1965). They established morphine self-administration in rats. After responding was stable, the rats were withdrawn from morphine. Thirty days later, the rats were reexposed to morphine in either the same or different environments. Subjects reexposed in the same environment were readdicted faster than rats reexposed in a novel environment. This is consistent with clinical outcome. Cushman (1974) reported that addicts who were detoxified and then returned to the environment in which the addiction occurred showed a readdiction rate of 90 percent, while other studies found that only a small percentage of Vietnam veterans who began their addiction in Vietnam continued

excessive drug use on returning to the United States (O'Brien et al. 1980; Robins et al. 1974). These studies indicate that drug-associated environments may be an important determinant of drug relapse. Treatment approaches in which patients are taken from environments maintaining significant drug consumption, and placed in other environments in which stimulus control of drug-seeking behavior has not been established, may experience greater success.

Providing Successfully Completing Stimuli

Another stimulus control tactic that could be used to treat substance abuse would entail providing stimuli that engender behavior incompatible with drug seeking.

For humans, one of the most convenient stimuli to employ in this regard is verbal behavior in the form of rules. As previously noted, one of the effects typically encountered with rule-governed behavior is that it renders human performance temporarily insensitive to contingencies of reinforcement. The effectiveness of rules in controlling behavior in spite of sometimes conflicting contingencies has been accounted for in a variety of ways. From our perspective, the most satisfactory account, provided by Hayes and his colleagues (Hayes et al. 1986a; Hayes et al. 1986b; Zettle and Hayes 1982) considers the insensitivity to one set of contingencies to result from additional contingencies brought into play by instructional control. According to this view, insensitivity "is not a reduction in contingency control but rather an effect of competing contingencies, such as the social consequences for rule following" (Hayes et al. 1986b, p. 238). Thus, rule-governed behavior can be considered the introduction of competing stimuli and associated contingencies.

The introduction of stimuli in the form of verbal rules as we have discussed earlier has been demonstrated to alter drug-maintained behavior. As reviewed above, rules can alter the topography of drug self-administration and modify the reinforcing efficacy of drugs of abuse. Rules are most likely an important part of most traditional therapies for substance abuse (Skinner 1953). What must be determined are the functional properties of rules, the conditions under which they will be followed, as well as whether there are different functional categories of rules as some have suggested (e.g., Zettle and Hayes 1983).

IMPACT OF SUBSTANCE ABUSE TREATMENT PROCEDURES ON STIMULUS CONTROL

The relative success of a particular treatment modality in reducing drug consumption depends upon its ability to alter the specific factors controlling drug consumption for any individual. Assuming that the stimulus control dimensions affecting drug-taking behavior vary across individuals seeking treatment, then knowledge of the specific dimensions of stimulus control effectively addressed by the various treatment modalities becomes an important issue. When the effects of traditional therapies on stimulus control are understood, we might begin to develop a strategy for matching a treatment seeker with an appropriate treatment program based on an analysis of stimulus factors controlling that individual's drug use (Thompson 1987).

We have chosen five general categories of drug abuse treatment to discuss in light of these stimulus control considerations: pharmacotherapy, individual therapy, group therapy, behavioral therapy, and hospitalization. Our analysis of the stimulus control dimensions addressed by these treatments is summarized in table 1. Most treatment programs use techniques from one or more of these categories. Our analysis is based on an abstraction of the general procedures employed within a particular category.

Pharmacotherapy

Pharmacotherapy, namely the use of drugs to treat, may disrupt the interoceptive stimulus properties of other drugs by dramatically altering the interoceptive stimulus control over drug seeking. For instance, drug maintenance programs, such as methadone maintenance, provide relatively constant interoceptive stimulus cues. This interferes with the pairing of changes in interoceptive drug stimuli with drug consumption. The relatively constant interoceptive drug condition also alters the consistent pairing of environmental stimuli (e.g., needles, locations where drugs are obtained, etc.) with interoceptive drug stimuli. A contingent relationship is necessary to maintain environmental control over drug-seeking behavior. Maintenance dosing also eliminates the interoceptive cues associated with drug abstinence. Since these interoceptive stimuli control drug-seeking behavior (O'Brien et al. 1986), maintenance dosing eliminates the powerful controlling effects of the drug abstinence syndrome.

Drug antagonists, on the other hand, achieve the same result by blocking the interoceptive stimulus effects of drugs, thereby eliminating the interoceptive stimulus cues altogether. As with maintenance dosing, complete blockade of interoceptive cues destroys the contingent relationship between environmental drug-related events and interoceptive drug cues necessary for maintaining stimulus control of drug-seeking behavior. However, antagonists at a Mocking dose can also produce interoceptive drug abstinence cues that may produce an increase in drug-seeking behavior (Katz and Valentino 1986).

Aversive procedures, such as disulfiram treatment, radically alter the stimulus properties of drugs, thereby altering the discriminative functions of drugs. By blocking further breakdown of a toxic alcohol metabolite, disulfiram causes extreme physical discomfort following alcohol consumption.

Unfortunately for the drug abuser, pharmacological procedures have little direct effect on other stimulus control parameters, such as the discriminative properties of conditioned reinforcers, modeling, rule-governed behavior, and conditional stimulus control. As such, pharmacotherapies may not interact with many dimensions of stimulus control; that is, pharmacotherapies may not control a wide enough range of cues for drug-seeking behavior to have a pervasive or sustained effect.

Some drugs used in pharmacotherapy do not alter the interoceptive stimulus properties of drugs. In fact, some agents have little direct impact on drug-seeking behavior, but may affect it in less direct ways. For example, drug users sometimes emit behaviors characteristic of several clinical psychiatric conditions (e.g., depression). For these individuals, drug use may be seen as secondary to or precipitated by another clinical syndrome. As such, substance abuse may be treated with pharmacotherapeutic agents selected with this other clinical syndrome(s) as the primary focus (e.g., antidepressant medication given to an individual dually diagnosed as depressed and drug abusing). Under these conditions, pharmacotherapeutic agents may be seen as having little impact on the stimulus properties of drugs of abuse. Instead, these agents alter the stimulus dimensions of the primary clinical state, be it depression, mania, schizophrenia, or any other. Clinical states may combine with other environmental variables in a conditional stimulus control relationship. For example, environmental variables may exert powerful control over drug-seeking behavior only when an additional clinical condition is also present.

TABLE 1. *Stimulus control factors influenced in the treatment of substance abuse*

Treatment Type	Interoceptive Stimulus Properties of Drugs	Conditioned Drug Effects	Conditioned Reinforcers	Modeling	Rule-Governed Behavior	Conditional Stimulus Control
Pharmacotherapy						
Drug Maintenance	Yes	Yes	No	No	No	No
Drug Antagonism	Yes	No	No	No	No	No
Aversive Procedures	Yes	No	No	No	No	No
Indirect Drug Treatment	No	No	No	No	No	Yes
Psychotherapy						
Psychoanalytic	No	No	Maybe	No	Yes	No
Insight-oriented	No	No	Maybe	No	Yes	No
Behavioral Therapy						
Contingency Contracting	No	No	No	No	Yes	No
Systematic Desensitization	No	Yes	Yes	No	No	No
Aversion Therapy	Yes	No	No	No	No	No
Group Therapy						
Therapeutic Community	No	No	No	Yes	Yes	No
Alcohol Programs	No	No	Maybe	Yes	Yes	No
Hospital Intervention						
Inpatient Treatment	No	No	No	No	Yes	No
Outpatient Treatment	No	No	Yes	No	No	Yes
Detoxification	No	No	No	No	No	No

Once the clinical condition is treated, environmental variables alone may exert little control over drug-seeking behavior.

Individual Therapy

We consider individual therapy as a procedure in which 8 therapist works with an individual client using verbal behavior as the primary therapeutic tool. Verbal interaction procedures have no impact on the stimulus properties of drugs. Rather, they interact with exteroceptive stimulus control dimensions. More precisely, these procedures alter the control of verbal rules over drug-seeking behavior and provide new rules engendering behavior that is incompatible with drug-seeking behavior. For example, insight-oriented therapists may alter the role of statements of stress such as, “When my wife gets on my case, I find myself in the nearest bar.” A clever therapist may train a client to evaluate those statements occurring early in a drug-seeking chain and after the behavior they control. Ideally, for treatment success, alternative behaviors incompatible with drug-seeking behavior should be placed under the control of these early statements.

Individual therapy procedures can also alter the role of discriminative properties of conditioned reinforcing stimuli that maintain chains of drug-seeking behavior. By conditioning a new response to stimuli early in the chain that leads to drug seeking, the end result can be avoided. However, as described above, conditioning new forms of behavior in the presence of stimuli originally controlling drug-seeking behavior does not guarantee any change in the functional properties of the original stimulus control relationship. A pertinent change in environmental conditions (e.g., termination of therapy) may suddenly reinstate the original stimulus-response relation.

Group Therapy

Group therapies, such as therapeutic communities and Alcoholics Anonymous, provide 8 unique setting for impacting aspects of stimulus control. In addition to restructuring the control that verbal rules exert over drug-seeking behavior (as occurs during individual therapy), groups provide 8 richer mix of socially relevant stimuli, including models of the behavior of individuals who are successfully engaged in treatment. Group therapies enhance the opportunity for conditioning socially appropriate and drug-incompatible behaviors.

Therapeutic groups also provide new functions to old controlling stimuli by conditioning new responses in the presence of stimuli that control drug-seeking behavior via the social reinforcement available from group members. The social reinforcers available in group settings can be used to establish and maintain new stimulus-response relationships (e.g., Alcoholics Anonymous groups haVe clients call their sponsors anytime they feel an urge to drink, as well as provide social reinforcement for sobriety at meetings, etc.).

Therapeutic communities have a unique advantage over other group therapies. By removing individuals from their natural environments during treatment and gradually rebuilding alternative life patterns and social interactions, those stimuli present in the natural environment that controlled drug seeking do not prevent the developing of new behavior. The disadvantage of this procedure, on the other hand, comes when stimuli not present in the therapeutic community are encountered in the natural environment when an individual leaves the therapeutic community. AS we have discussed, changing the functional properties of controlling stimuli in the natural environment is not an easy task.

Behavioral Therapy

Behavioral therapy is 8 procedure that modifies environmental control over behavior during treatment. This modification can include introduction of new contingencies (e.g., contingency contracting), systematic manipulation Of controlling variables (e.g., Systematic desensitization), or controlling the consequences of behavior (e.g., aversion therapy). Behavioral therapies exert varied effects on dimensions of stimulus control. For example, contingency contracting has little impact other than to provide a new set of contingencies governing drug-seeking behavior, while systematic desensitization/ relaxation training makes a strong effort at altering the conditioned drug effects and controlling features of stimulus events associated with chains of drug-seeking behavior. Aversion therapy procedures attempt to alter the interoceptive stimulus properties of drugs through conditioning. If successful, these procedures *can* diminish the probability that any single exposure to drug will result in complete reinstatement of drug use.

Hospital-BasedTreatment

Hospital interventions, such as detoxification and inpatient or outpatient treatments, have one important feature in common. These

procedures are primarily used to treat individuals who consume large amounts of drugs and for whom drug tolerance is a likely condition. As a course of treatment, individuals are withdrawn from drug use, and the interoceptive cues associated with drug abstinence are gradually eliminated while access to additional drugs is denied. However, a consequence of this procedure is that the stimulus properties of drugs may become more discriminable; therefore, the interoceptive stimulus properties of drugs potentially become more powerful controllers of drug-seeking behavior when tolerance is eliminated. To the extent that these procedures are combined with other treatment modalities, other aspects of stimulus control can be addressed.

Summary

This brief review points out important reasons for considering stimulus control in the treatment of substance abuse. Traditional drug abuse treatment procedures appear to manipulate stimulus control factors during treatment whether or not explicitly Stated. In addition, treatment procedures differ in the profile of stimulus control dimensions addressed during treatment and can be differentiated in these terms. Assessment of the relative success of various treatments in modifying aspects of the environmental control of drug taking is beyond the scope of this paper, but analysis of dimensions of stimulus that control an individual's drug-seeking behavior may be 8 critical issue in determining which of the range of available treatment modalities will be most successful.

CONCLUSION

We have reviewed the ways in which stimulus control processes are intimately involved in drug self-administration and thus ought to play a significant role in the treatment of substance abuse. Unfortunately, stimulus control is a behavioral process that has not received a great deal of scientific attention, both in relation to the basic processes involved and the application of that knowledge for the socially important problems of substance abuse. More research on each of these levels needs to be conducted. In particular, a basic understanding of rule-governed behavior and modeling is needed for better application of these processes to therapeutic ends. If we continue to ignore stimulus control processes, our goal of having a behavior analysis of substance abuse will be woefully incomplete.

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Social Learning Approaches to Alcohol Relapse: Selected Illustrations and Implications

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INTRODUCTION

In a recent discussion of how behavioral theories have evolved over the last 20 years, Wilson (1986b) pointed out that social learning theory has the advantage of including respondent learning, operant learning, and certain specified cognitive factors in an integrated theory. Social learning theory has been heuristic both in leading to new research directions and in leading to innovative practical treatment applications. Indeed, its potential to bridge the gap between theory and practice has long been recognized as 8 special advantage of this approach. This has certainly been the case when social learning theory has been applied to the area of alcohol abuse in humans (Wilson 19868). Although it is beyond the scope of this chapter to present the numerous advances made by social learning theorists to understanding and treating alcohol abuse (see Abrams and Niaura (1986) for a review), some of the current applications can be illustrated through examples from our own research.

SOCIAL LEARNING APPROACHES TO RELAPSE

Relapse has long been a serious problem in the outcome of alcoholism treatment programs and therefore has been a major focus of current research. Social learning theory formulations of alcoholic relapse include various features among which are the following (see Mariatt and Gordon (1985) or Abrams et al. (1986) for a more detailed discussion).

Relapses occur in response to certain situations, generally referred to as high-risk situations for relapse. The situations in which alcohol abusers have commonly been found to relapse after treatment include

interpersonal pressure, interpersonal stresses including those leading to anger and frustration, intrapersonal negative affective states such as depression and boredom, and the presence of alcohol or drinking stimuli (Marlatt and Gordon 1985). Alcoholics are presumed to have learned vulnerable, or failed to learn protective, cognitive and behavioral responses to high-risk situations, which will influence the probability of relapse in any given situation. These learned reactions include among others: (1) expectancies (beliefs about the effects of alcohol, beliefs about the probable outcome of one's actions, and beliefs about one's ability to effectively use one's skills); (2) coping skills (cognitive or behavioral skills for dealing with a high-risk situation and with the individual's conditioned reaction to a situation); and (3) classically conditioned reactions to alcohol and drinking stimuli (commonly interpreted by the individual as craving or affect). These factors will be explained in more detail below.

Expectancies

Research concerning expectancies for the effects of alcohol have important implications for the relapse process. One way in which these expectancies have been studied has been with the balanced placebo design in which the expectancy that alcohol is being administered is manipulated independently from actual alcohol administration (Marlatt and Rohsenow 1980, Rohsenow and Marlatt 1981). A review of studies shows that the belief that alcohol was consumed is sufficient to produce changes in a variety of social and emotional behaviors (e.g., social anxiety, perceived sexual arousal especially to deviant stimuli, aggression, and mirth), with actual alcohol consumption having little or no effect at moderate doses in many studies (Marlatt and Rohsenow 1980). Furthermore, four separate studies have found that loss of control or craving in alcoholics after drinking is a function of expectancy, not actual alcohol consumption (Berg et al. 1981; Engle and Williams 1972; Marlatt et al. 1973; Merry 1966). (For further details and discussion of the sources of these expectancies, see Marlatt and Rohsenow (1980)). One possible mechanism underlying these results is that people may attribute responsibility for their behavior to the alcohol, thus allowing themselves to behave in ways that they would normally inhibit (Marlatt and Rohsenow 1980).

To further understand the range and development of alcohol expectancies, research has been conducted with questionnaires. Brown et al.'s (1980) Alcohol Expectancy Questionnaire has been administered to a variety of populations. The studies show that adolescents' expectancies predate their actual experiences with drinking but are

less specific before they drink, and the more heavily a person drinks the more domains of reinforcement he or she expects alcohol to provide, with alcoholics expecting the most reinforcement (see review by Christiansen and Brown (1985)). Using a modification and extension of the scale to distinguish between beliefs about the effects of alcohol on oneself as opposed to on people in general, Rohsenow (1983) found that heavy drinkers most strongly expect to obtain social/physical pleasure and social expressiveness from alcohol and least expect alcohol to enhance their own aggression or sexual pleasure. All drinkers expected to become impaired and careless after drinking, but the heavier drinkers also expected many positive effects from alcohol. The fact that people enter a drinking situation with multiple expectancies, some of which may compete with others, was used to interpret a series of studies which had unexpected results. These studies found that heavy drinkers who believed that they had consumed alcohol were significantly less aggressive after provocation than those led to believe they were drinking only tonic water (Rohsenow and Bachorowski 1984). Of those subjects, 90 percent had expected alcohol to increase their social/physical pleasure more than they expected it to increase their aggression, and this pleasure expectancy may have made them feel less aggressive, since subjects who expected or received alcohol also reported feeling happier. Therefore, if drinkers expect that alcohol can make them feel happier, even after an aversive event, they may be more likely to use alcohol to mitigate the impact of aversive events. This may be why some alcoholics are particularly prone to relapse after aversive intrapersonal or interpersonal events (Marlatt and Gordon 1985).

To elucidate why alcoholics may choose to continue or resume drinking in spite of the negative consequences they experience, a decision-theory model of relapse was developed by Rohsenow et al. (1978). In this model, the probability of drinking at any time is a function of: (1) the various expected consequences of drinking: (2) the subjective value of each consequence; (3) the subjective expected probability that each consequence will occur; and (4) the subjective expected immediacy of the consequence for the particular individual at a particular time. For a younger alcoholic, the expectancy that alcohol will result in death by liver damage or cancer may exist, may have a very high negative value, but even if seen as 100-percent probable, it will be viewed as an event so far in the future as to be much less salient than the very immediate and highly valued expectancy of enhanced social/physical pleasure. An alcoholic decides to enter treatment when the negative consequences are no longer delayed. When alcoholics are faced with a high-risk situation for drinking, some may

weigh the subjective expected utility of drinking again: the positive expected effects are usually immediate (e.g., intrinsic pleasure, recreation associated with alcohol, reduction of negative affect, socializing with familiar friends), whereas the negative effects are usually again delayed either by some hours (e.g., social censure, hangover) or months/years (e.g., major health loss, job loss). High-risk situations may increase the salience of the positive effects (e.g., by increasing negative affect or social loneliness), leading to an enhanced subjective utility of drinking. This model gives a possible reason why the probability of relapse is so high within the first 6 months after treatment (Marlatt and Gordon 1985). (See Marlatt and Gordon (1985) for more recent elaborations of this model.)

This model suggests several avenues for intervention. One is to teach the alcoholic alternative ways to immediately produce similar positive consequences and thereby build new expectations. However, if the alcoholic acquires the skills but has little belief that he or she can effectively use the skills (low self-efficiancy), then the alcoholic may still view drinking as most effective in producing the desired consequences. A second approach is to increase the subjective probability and immediacy of negative consequences, rather than focusing only on enhancing the negative value of these consequences. Third, by involving family members in treatment and encouraging friendships among other treated alcoholics, the negative social consequences for drinking and the positive social consequences for remaining dry may be made more immediate and probable. Some of these implications will be discussed further below.

A person may have learned adequate skills for coping with a high-risk situation but not use these skills due to expectancies that interfere. First, some alcoholics may believe that they do not have the skill due to learned helplessness or faulty monitoring of their own progress. Second, some alcoholics may believe that they would be ineffective in applying the learned skill (low self-efficacy). Third, some may believe that even competently using the skill would not affect the outcome (low outcome expectancy). If any of these are the case, then treatment approaches for these individuals would be best designed to change the beliefs that interfere with using the skills.

Coping Skills in Alcoholics

Many alcoholics, on the other hand, may simply not have learned cognitive or behavioral skills that would allow them to effectively cope with high-risk situations. Some individuals may simply never

have learned appropriate social skills in general due to inadequate early experiences. These people would need a broad-based social skills training program. Others may be skillful in general but lack the specific skills needed to effectively handle high-risk situations for drinking (such as resisting peer pressure to drink). If this is the case, then treatment should be designed to increase these specific skills (Monti et al. 1986) for a review of theory and practical considerations). One major focus of our clinical research has been to investigate alcoholics' general social skills (those required to deal with social anxiety-provoking situations) vs. their alcohol-specific social skills (those required to deal with high-risk situations for drinking), the extent to which these skills can be modified, and whether skill levels are associated with drinking outcomes after treatment.

First we developed a behavioral instrument for assessing general social skill, called the Simulated Social Interaction Test (SSIT) (Monti et al. 1980). The SSIT consists of eight simulated brief social interactions which sample a broad range of social situations often related to social anxiety. The patient is videotaped while engaging in role plays in these simulated interactions, then the tapes are independently rated by trained raters for dimensions of anxiety and social skill. Excellent interrater reliability has been found in each study, the ratings are stable over time (Wessberg et al. 1982), and ratings do not seem to be influenced by extraneous factors (Corriveau et al. 1981). Both discriminant (between psychiatric and nonpsychiatric groups) and convergent (other measures of social functioning) validity have been demonstrated on the SSIT (Curran et al. 1980; Wessberg et al. 1981; Monti 1983; Monti et al. 1982). Since skills specific to drinking-related situations may be more relevant to treatment outcome, we next developed an Alcohol-Specific Role Play Test (ASRPT), based on the 10 categories resulting from our behavior analytic study of 600 drinking situations reported by alcoholic inpatients (Abrams et al., in press). Half the categories were based on interpersonal situations (such as using alcohol to facilitate business transactions or to escape from interactions with significant others) and the other half on situations not directly involving others (such as using alcohol to avoid hangover or withdrawal). Behavioral measures for the ASRPT include observers' ratings of subjects' skills and anxiety. Self-report measures after each role play include such measures as skill, anxiety, realism, difficulty, and urge to drink. Interrater reliability has been found to be excellent for the ASRPT (Cronbach alphas range from . 90 to .96).

Alcoholics' skills in responding to both the general and the alcohol-specific situations were compared to a group of nonalcoholic control subjects (Abrams et al., in press). There were no differences found between groups in general social skills or anxiety on the SSIT. However, on the ASRPT the alcoholics were seen as being lower in social skill and higher in anxiety than the nonalcoholics. Also, the alcoholics rated themselves as being more anxious and less skillful than did the nonalcoholics. An additional finding was that the alcoholics reported stronger urges to drink during the ASRPT and reported that these situations were very likely to happen to them. Thus, the alcoholics appear to have more difficulty coping with particular high-risk situations than nonalcoholics, whereas these groups do not differ on general social situations.

Are the alcoholics' skills in responding to drinking-related situations associated with their drinking rates after treatment? We recently completed a treatment outcome study which addresses this issue. In this study, three experimental forms of group treatment were compared: Individual Social Skills Training (ISST), Family Social Skills Training (FSST), and Cognitive/Behavioral Mood Management Training (CBMMT). The social skills training (SST) offered in this study was a modification of the SST package that we have developed over a period of years in our social learning treatment programs with psychiatric patients (Monti et al. 1979; Monti et al. 1980). The program was modified to target the special deficits of many alcoholic patients. The ISST was designed to help the alcoholic learn to cope with those drinking-related situations which involve any interpersonal features, with considerable emphasis on communication skills, and the FSST was the same but with a significant other (preferably a close family member) present. The CBMMT was designed to help the alcoholic cope with intrapersonal negative emotional states such as anxiety. All were added to the standard inpatient alcohol abuse treatment program at the Veterans Administration Medical Center, Providence, RI. Preliminary outcome results are now available.

The alcoholics were indeed able to improve their skills in coping with drinking-related situations: patients in all three groups showed improvements in the behavioral social skill ratings in the ASRPT. The effectiveness of their responses and the speed with which they responded improved, along with their self-reported anxiety, urge to drink, and perception of their own skill in the ASRPT, with the most improvement in skill and effectiveness shown by patients in the ISST group. During the 6 months following treatment, alcoholics who received either the ISST or the FSST drank significantly less than

patients who received CBMMT. Furthermore, skill in the ASRPT at posttest predicted drinking rates during the &month followup interval. Higher behavioral skill ratings, shorter latency to response, lower anxiety, and less urge to drink during the ASRPT were all associated with significantly less drinking during the followup interval.

The results are consistent with several other studies which included attention-placebo control groups or standard-treatment-alone groups. Chaney et al. (1978) developed a skills training program based on the interpersonal and intrapersonal situations which had been found to be most commonly associated with relapse (Marlatt and Gordon 1985). The alcoholics who received the skills training drank significantly less during the next year than those who received the standard alcoholism treatment or standard treatment plus placebo treatment, with shorter latency to respond on an alcohol skills role play at posttest predicting better treatment outcomes. Eriksen et al. (1966) compared social skills training groups to discussion control groups for inpatient alcoholics in Norway; those receiving social skills training were sober and at work twice as many days, although they drank much more on days when they did drink. Skills training possibly helped them be more socially appropriate about when and where they drank. Oei and Jackson (1980) compared group and individual social skills training to traditional supportive therapy and found that both forms of social skills training resulted in significantly better drinking outcomes than did supportive therapy during the next year.

Thus, although alcoholics have not been found to have less skill than nonalcoholics in general social situations (Monti et al. 1981; Twentyman et al. 1982; Abrams et al., in press), their ability to handle alcohol-related situations is less than that of nonalcoholics. Further, individual differences in skills on the ASRPT at posttreatment are predictive of drinking outcomes after treatment. These abilities can improve with behavioral training, and skills training results in more improvement in drinking rates 6 months after treatment than does placebo therapy, supportive therapy, or mood management training.

Cue Reactivity in Alcoholics

In most skills training programs, all the role plays are conducted without any actual alcohol present, even in scenes in which the alcoholics practice refusing a drink. However, following treatment, alcoholics return to an environment that includes actual alcohol and

is replete with drinking stimuli not used in skills training. Thus, they have to be able to employ their new skills while being confronted with the full range of sights and smells associated with drinking. Studies by several investigators suggest that reactivity to such cues may be particularly acute among alcoholics.

Alcoholics are likely to have developed classically conditioned responses to the presence of stimuli which have repeatedly been associated with the effects of alcohol, and these responses may increase the probability of relapse. Siegel's model (this volume) seems to provide the most explanatory power in describing these responses; alcoholics may have developed a classically conditioned compensatory response that is opposite in effect to the pharmacologic effects of alcohol and is associated with any stimuli which have frequently been paired with alcohol ingestion. In humans, this response would probably be uncomfortable and may be interpreted by the alcoholic as craving. The person may as a result be motivated to reduce this aversive state by drinking. Therefore, returning to an environment which contains many stimuli associated with drinking is likely to produce this conditioned response that skills training has not addressed and may lead to rapid relapse.

Until recently, little work existed on cue reactivity in alcoholics, although its role in drug addiction has been studied more thoroughly (O'Brien et al., this volume; Meyer, this volume). Recent research on the effects of exposure to stimuli associated with drinking has indicated that conditioned responses to alcohol (e.g., changes in heart rate, galvanic skin response, and affect) do exist and can be elicited and measured (Kaplan et al. 1983; Cooney et al. 1984).

For example, Pomerleau et al. (1983) showed that holding and sniffing alcohol resulted in greater electromyogram-measured swallowing rates (which were correlated with salivation) and self-reported desire to drink for people with a history of chronic excessive drinking than for people with a history of moderate drinking.

A recent series of studies in our laboratory compared cue reactivity in alcoholics to nonalcoholics using salivation as the primary measure of reactivity (Monti et al., 1987). Both alcoholics and nonalcoholics were presented with the sight and smell of their usual alcoholic beverage and a nonalcoholic control beverage (water). Subjects were instructed to hold and sniff each beverage for a 3-minute exposure interval. In addition to salivation, dependent measures included self-reported urge to drink alcohol and water during the exposure trials.

In a preliminary study in which order of beverage presentation was counterbalanced across subjects, we found that nonalcoholics tended to salivate less on the second of two trials regardless of whether alcohol had been presented in the first or second trial. Since the alcohol/water sequence appeared to mask between-group differences in reactivity, a second study was conducted using only the water/alcohol sequence (sequence 2) (figure 1). A significant interaction effect was found for group by beverage indicating that alcoholics were more reactive to alcohol than nonalcoholics in terms of salivation but not in terms of urge to drink alcohol. Both groups reported greater urges to drink alcohol in the presence of alcohol. Although social drinkers as well as alcoholics may have conditioned reactions to alcohol cues, the larger doses experienced by alcoholics may lead to stronger conditioned reactions.

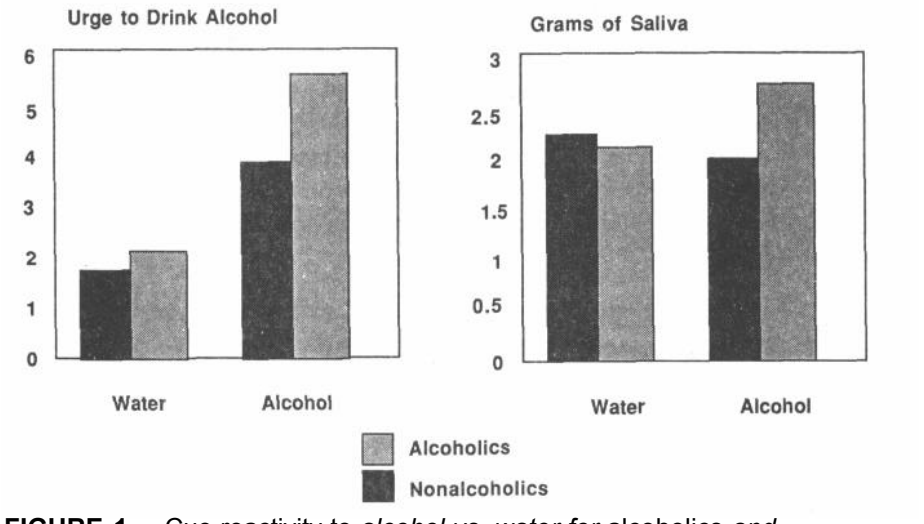

FIGURE 1. Cue reactivity to *alcohol vs. water for* alcoholics *and nonalcoholic controls (sequence 2 only)*

Does Cue Reactivity Influence Behavior? Findings regarding cue reactivity led us to consider wheather the presence of an alcohol-related stimuli might disrupt alcoholics' use of coping skills and whether adding alcohol-related stimuli to treatment might enhance the generalization of skill training. The first question was, "Does the presence of alcohol cues affect an alcoholic while refusing a drink?" If cue reactivity is one important determinant of relapse, then we

would expect behavioral as well as physiological, affective, and cognitive effects of cue exposure. We have recently completed a study (Binkoff et al., submitted for publication) of 50 inpatient alcoholics that involves within-subject comparisons of drink refusal skills with and without the presence of the alcoholics' typical alcoholic beverage. Alcoholics reported feeling more anxious during drink refusal when the alcoholic beverage was used as a prop than when alcohol was not used.

We then investigated (Binkoff et al., submitted for publication) a related second question, "Does an individual's cue reactivity (salivation) predict the extent to which alcohol presence impairs drink refusal skills?" We assessed alcoholics' cue reactivity during a pretest, then conducted two drink refusal role plays, one with and one without alcohol as a prop. Results indicated that greater salivary reactivity to alcohol cues was associated with less behavioral skill in the subsequent role play when alcohol was present than when alcohol was absent. Self-reported anxiety during the cue reactivity assessment was also predictive of impaired behavioral skill during the subsequent alcohol-present role play. These results suggest that individuals with greater cue reactivity as indicated by increased salivation and anxiety in response to the sight and smell of alcoholic beverages may indeed be at greater risk of relapse because their skills are disrupted in the presence of alcohol.

A third question was, "Does cue reactivity predict drinking after treatment?" Two earlier studies suggest that cue reactivity may be predictive of early relapse from alcoholism treatment. In an analogue study, Kaplan et al. (1963) found that alcoholics with greater cue reactivity, as measured by psychogalvanic response to the sight of beer, chose beer more often than a lottery ticket on a subsequent operant task. In a more direct test of this question, Kennedy (1971) found that alcoholics who, just prior to discharge, continued to respond to the smell of their preferred alcoholic beverage with pupillary dilation were more likely to relapse than were alcoholics who no longer showed this response. In our study of 50 inpatient alcoholics, cue reactivity as measured by behavioral ratings of craving and anxiety during the alcohol-present drink refusal scenes was significantly related to drinking rates during the 6 months after treatment (Binkoff et al. 1966; Binkoff et al., submitted for publication). Thus, cue reactivity at the end of treatment can identify at least some individuals who are at the greatest risk for relapse: highly reactive alcoholics are more likely to succumb to temptation to drink.

IMPLICATIONS AND FUTURE DIRECTIONS

Findings from the above series of studies are consistent with various aspects of the social learning theory model of alcohol relapse and have important clinical implications as well. According to social learning theory, differential reactivity to alcohol cues may be part of the cognitive, behavioral, and physiological response to a high-risk situation. The conditioned response is hypothesized to put a strain on existing coping resources and may disrupt the ability to employ effective social skills to cope with a high-risk situation, which in turn results in low self-efficacy and even lower probability of using the skills. The conditioned response, experienced as unpleasant, may also enhance the expected reinforcing effects of alcohol in the situation. A combination of disrupted skills, low self-efficacy, and enhanced positive expectancies for the immediate effects of drinking may ultimately result in a relapse episode. Therefore, interventions designed to extinguish cue reactivity or to decrease the disruptive effects of cue reactivity on social skills would be likely to decrease the probability or delay the onset of relapse.

The results of our cue reactivity studies are supportive of classical conditioning models of substance abuse (Pomerleau 1981; Siegel, this volume; Wikler 1965), but particularly with Siegel's model of a classically conditioned compensatory response. The results showing increased salivation in response to alcohol cues may be predicted as a compensatory response. Alcohol ingestion appears to result in dehydration (Flynn 1958) leading to an inhibited rate of salivation (Massler 1979) and increased thirst resulting in a dipsogenic effect (Lawson 1977). To the extent that a direct drug effect of alcohol is reduced salivation, then a conditioned compensatory response would be increased salivation. The increases in plasma insulin in response to alcohol stimuli reported by Meyer (this volume) are similarly consistent with this model. On the other hand, Martin and Pangborn (1971) did not find alcohol ingestion to result in decreased salivation, but instead found a positive relationship between alcohol dose and salivation, which would make our results consistent with a direct conditioning effect (Wikler 1965) rather than a conditioned compensatory response. Until the effect of alcohol ingestion on salivation is clarified, it will not be apparent which of the theoretical conditioning models has the most explanatory power for our results. Even without knowing which model will be supported, the clinical implication is that a network of learned responses to alcohol cues does exist, and this could result in relapse for some problem drinkers, suggesting

that interventions designed to alter these learned responses hold promise for preventing or postponing relapse.

It now appears that alcoholics who react more strongly to the presence of alcohol cues at the end of treatment are likely to drink more after treatment. Furthermore, some findings show that alcohol cues result in increased anxiety while refusing the offer of a drink, and that salivary reactivii to alcohol cues in one situation is associated with impaired behavioral skill in a very different situation; these results suggest that practice in using skills in the presence of alcohol cues may be an important area for future treatment programs to address. It may be that a form of state-dependent learning operates; that is, the state of cue reactivity is normally associated with impaired drink-refusal skills in alcoholics and with drinking as the predominant learned response to their reactions. Effective treatment may require having patients practice using coping skills while in this aroused state.

The degree of stimulus specificity for reactivity to alcohol-associated cues needs further exploration. Is the conditioned response elicited more by gustatory-related stimuli than by visual stimuli, or more by a larger number of cues associated with high-risk environments than by just the one or two most alcohol-relevant features? Aspects of the wnditioned response need further exploration, including the relationship among different responses necessary within the sympathetic nervous system, such as pupillary dilation, electrodermal activity, heart rate, and salivation. The relationship among various responses is not necessarily synchronous (Lang 1969) and may be complicated by other factors such as stress/anxiety reactions (Abrams 1963). Sympathomimetic stimulation from anxiety would result in inhibition of salivation, and alcoholics in treatment who are exposed to alcohol may experience more anxiety than nonalcoholics, or alcoholics who have not sought treatment. Thus, the fact that alcoholics in our studies salivated more to alcohol cues is even more interesting, since the effects of anxiety and alcohol cues on salivation are expected to be in the opposite direction. This underscores the importance of using multiple response measures in assessment. These complex interactions among responses, anxiety, and alcohol cues must be carefully explored in future studies in order to explain why physiological and/or cognitive data (i.e., self-report) may be inconsistent with each other.

The motivational status of the subjects studied (alcoholics in treatment vs. those not in treatment) raises the interesting issue of the

role of expectations in response to cues in the laboratory. In our studies, alcoholics were given the clear message that no consumption would be permitted. Given this instruction and the overall set that our assessment was embedded in an alcohol treatment program, it is likely that the strength of the alcoholics' cue reactivity was moderated. If alcoholics were given the instructional set that they could consume the beverage, one might expect the cue reactivity phenomenon to be enhanced. Indeed, in a recent study reported by Meyer (this volume), this was found to be the case. While our protocol was probably more face valid for alcoholics in treatment (who would not be expecting to drink), there can be little question that giving alcoholics the expectancy that they can consume the beverage is more like the real world and therefore more generalizable. A good post-treatment test might be to include alcohol in a drink-refusal role play with instructions that the patients can drink the drink if they so choose. Those who then drink may be considered to be at high risk for relapse. While drinking under such circumstances necessitates further treatment, this might avert an otherwise rapid relapse for individuals who are more susceptible to the effects of alcohol cues.

Finally, it would be useful to know whether strategies that alter cue reactivity can improve treatment outcome in problem-drinking populations or in the subgroup of alcoholics who have greater cue reactivity. Some preliminary studies based on applying cue exposure with response prevention similar to those done with obsessive-compulsives and individuals with phobic disorders (Rachman and Hodgson 1980) have suggested that these methods may have utility with alcoholics (Blakey and Baker 1980; Hodgson and Rankin 1976; Rankin et al. 1983). In order to develop the most effective method of using cue exposure, a number of questions will need answering, including the effects of medications on cue reactivity, gender differences, the best parameters for presenting stimuli in cue exposure treatment, and whether cue exposure alone is sufficient to improve outcome or whether skills training needs to be done in the presence of alcohol cues in order to provide the alcoholic with adequate inoculation against the disruptive effect of alcohol stimuli on coping skills.

Since alcoholics need to be able to apply coping skills in the presence of drinking-related stimuli after discharge from treatment, the strongest intervention is likely to be one which allows coping-skills practice in the presence of such stimuli as extinction and can occur at the same time as the alcoholics are learning to apply skills in a more generalizable situation. Drinking-related stimuli need not be

limited to the sight and smell of alcoholic beverages but may include a living room or bar room setting, the presence of certain friends, anger or frustration, or other stimuli which are commonly associated with drinking for each individual.

CONCLUSIONS

In summary, social learning models of relapse have resulted in significant advances in understanding factors that contribute to relapse and advances in developing treatment interventions. Common high-risk situations for alcohol relapse have been identified, including negative affect (interpersonal and intrapersonal in origin), social pressure, celebration, and stimulus-related cravings. The nature of expectancies about alcohol's effects has been clarified; these include beliefs that alcohol enhances social pleasure, expressiveness, aggression, sexuality, tension reduction, cognitive and motor impairment, and irresponsibility. Furthermore, expectancies have been shown to have a powerful effect on behavior after drinking, independent of drink content, such that the belief that alcohol has been administered is sufficient to produce changes in measures of social and emotional constructs such as anxiety, aggression, sexual arousal, and mirth. These expectancies are likely to contribute to a decision to drink. Alcoholics have been found to be deficient in the coping skills needed to handle situations that put them at risk for drinking (as measured by behavioral ratings of skill and effectiveness in the Alcohol-Specific Role Play Test), and their skill level is related to drinking after treatment. Alcoholics were able to improve these skills when given specific training, resulting in less drinking after treatment. Alcoholics also appear to have classically conditioned reactions to alcohol cues (such as increased salivation and urges to drink). These reactions can disrupt the use of coping skills, and those with stronger reactions (particularly urge to drink in alcohol-relevant role plays) have been found to be at greater risk for relapse. Implications from the work reviewed in this paper suggest the addition of cue-exposure-based approaches to treatment.

This discussion has focused on some of the learning factors that we have studied. However, biological predisposing factors may also play a role. Children of alcoholics may show different reactions than children of nonalcoholics, which could be a determinant of their heightened risk status for alcoholism. For example, children of alcoholics may have greater genetic sensitivity to the reinforcing effects of alcohol, which would lead both to greater expected reinforcement from alcohol and to a larger conditioned compensatory response to

alcohol cues. This heightened response, if experienced as dysphoric and appraised as craving, would raise the probability of seeking alcohol for instant relief. Genetic predisposition may also account, in part, for other forms of heightened reactivity to alcohol. Future work should focus on the integration of learning and biological factors.

Research by ourselves and others is beginning to map out the parameters involved in a social learning analysis of relapse. The analysis presented here starts with high-risk situations to which alcoholics have physiological and cognitive reactions. These reactions include: (1) a conditioned compensatory response if the stimuli were associated with drinking, a stress response otherwise; and (2) cognitive appraisals of their physiological reactions, the expected positive and negative consequences of drinking, their available skills for coping with the situation, and the expected consequences of trying to use those skills. These appraisals in turn may lead first to modifications of the physiological and cognitive reactions and then to behavioral responses (e.g., coping or drinking). Further understanding of the physiological, cognitive, and behavioral reactions of the alcoholic to environmental demands should prove important in developing comprehensive treatment programs for alcoholics.

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Conditioning Phenomena and the Problem of Relapse in Opioid Addicts and Alcoholics

Roger E. Meyer

INTRODUCTION

Like many psychiatrists and psychologists of my generation, my own research interests in addictive disorders were strongly influenced by the seminal work and theories of Abraham Wikler. in 1948, Wikler first proposed using a conditioning model to understand drug addiction (Wikler 1948). In 1952, he described the effects of morphine self-administration in a single individual over a 120-day period of observation (Wikler 1952). Wikler concluded that morphine's initial attractiveness to his subject was based upon its ability to diminish the primary drives such as hunger and sex. Once physical dependence supervened, drug administration served to reduce the "drive" associated with abstinence symptoms. At this stage, Wikler postulated that physical dependence functioned like one of the "primary drives," and that opiate reinforcement was related to drive reduction. These notions of conditioning, physical dependence, and drive-related motivation formed the basis of Wikler's theoretical approach to addictive disorders.

Based on studies of addicts at Lexington and experiments in animal models of addictive behavior, Wikler developed a theory of relapse behavior which proposed that a previously opioiddependent individual would become readdicted to opiates in an environment in which he had previously experienced withdrawal symptoms (Wikler et al. 1963; Wikler and Pescor 1967; Wikler et al. 1971). The symptoms had been paired to environmental cues (conditioned abstinence) as a consequence of repeated episodes of pharmacological withdrawal (Wikler 1965). Subsequently, he postulated that environmental stimuli could elicit "counter adaptive" interoceptive responses; mirror opposites of the effects of opioids as individuals anticipated the

administration of heroin (Wikler 1974). O'Brien et al. (this volume) were able to demonstrate the conditioning of narcotic abstinence symptoms in human subjects; while Siegel (this volume) demonstrated a role for opponent process conditioning in the development of tolerance to some effects of morphine. With Ludwig, Wikler extended his theoretical approach in an effort to explain relapse to alcohol addiction (Ludwig and Wikler 1974). Ludwig (1975) linked craving for alcohol by alcoholics to these conditioning phenomena. Finally, Wikler postulated that classically conditioned withdrawal symptoms and operant responding for heroin would be extinguished if addicts were maintained on a narcotic antagonist that would prevent them from experiencing the pharmacological reinforcement associated with heroin self-administration (Wikler 1971). With the introduction of potentially useful narcotic antagonists, the time seemed right, in 1972 to 1973, to examine some of Wikler's theories about the role of conditioning factors in opioid addiction.

STUDIES IN OPIOID ADDICTS

Over a 4-year period, my colleagues and I were involved in a multivariate study of opiate reinforcement in a population of heroin-addicted volunteer subjects. This work was best summarized by Meyer and Mirin (1979). Because narcotic antagonists in appropriate dosage should block pharmacological reinforcement (while not affecting conditioned reinforcement), these drugs appeared useful in studies designed to elucidate the nature of opiate reinforcement. This work proposed to: (1) define the multivariate nature of opioid reinforcement through an interdisciplinary study of the effects of blocked and unblocked heroin consumption upon catecholamine metabolism, endocrine homeostasis, operant work output for heroin, subjective effects, and gross behavior; and (2) assess the effects of narcotic antagonists upon heroin self-administration in a research ward setting and at followup in the community. The multivariate biobehavioral design in which addicts could work on an operant device to earn points toward the purchase of heroin was based on similar studies in alcoholic subjects conducted by Mendelson and Mello (1966).

The following questions were asked in the context of an operant research paradigm: (1) What is the effect of narcotic antagonist administration on the level of craving for opiates and on drug seeking behavior? (2) Under what circumstances will heroin consumption persist despite narcotic antagonist treatment? (3) Is there evidence for extinction of classically conditioned autonomic responses

to heroin and/or operantly conditioned drug self-administration behavior in the presence of a narcotic antagonist; or does the individual behave as though heroin were unavailable?

Two general research designs were employed: (1) Studies involving nonblind administration of the narcotic antagonist and (2) studies

TABLE 1. *Schedule of phases-experiment 1*

Period	Description
A	7 days drug-free after detoxification elsewhere
B	10 days with access to heroin
C	7 days of methadone-assisted detoxification
D	10 days without drug
E	2 days with antagonist alone
F	10 days of antagonist administration while patient has access to heroin
G	14 days with antagonist alone-patient on ward preparing for aftercare
H	1 year of aftercare using narcotic antagonist

SOURCE: Meyer and Mirin 1979, Copyright 1979, Plenum Publishing Corporation,

involving double-blind administration of the narcotic antagonist (naltrexone) vs. placebo. Tables 1 and 2 contrast these two designs.

There was a strong correlation between self-reports of craving for heroin and actual heroin self-administration behavior. Figure 1 contrasts heroin consumption by some blocked and unblocked subjects. Figure 2 describes self-reports of craving over the course of the nonblind studies. When heroin was not available, craving was not substantial. When craving was high, during the period of unblocked heroin consumption, each heroin injection did not result in a

TABLE 2. *Experimental design of double-blind studies*

Antagonist-treated subjects	Placebo-treated subjects
Drug-free– 10 days	Drug-free– 10 days
Narcotic antagonist alone– 2 days	Placebo alone– 2 days
Narcotic antagonist plus heroin– 10 days	Placebo plus heroin– 10 days
Narcotic antagonist alone– 20 days	Methadone-administered detoxification– 5 days
	Drug-free– 10 days
	Narcotic antagonist alone– 5 days
Aftercare on narcotic antagonist– 1 year	Aftercare on antagonist –1 year

SOURCE: Meyer and Mirln 1979, Copyright 1979, Plenum Publishing Corporation.

substantial decline in craving. Figure 3 describes subjective reports of craving by all subjects involved in the double-blind studies. Prior to the period of actual heroin self-administration, while subjects received either the narcotic antagonist or placebo, subjects did not differ in self-reports of craving. Once heroin administration began, craving in unblocked subjects rose and remained elevated throughout the period of heroin availability. Blocked subjects consumed much less heroin over the 10-day period than did unblocked subjects; some blocked subjects, however, stopped self-administering heroin early on during the 10-day period of heroin availability, whereas other subjects continued to challenge narcotic blockade.

The data on craving, operant work output, and actual heroin consumption did not appear to be consistent with models of operant extinction described in the animal literature. One would have

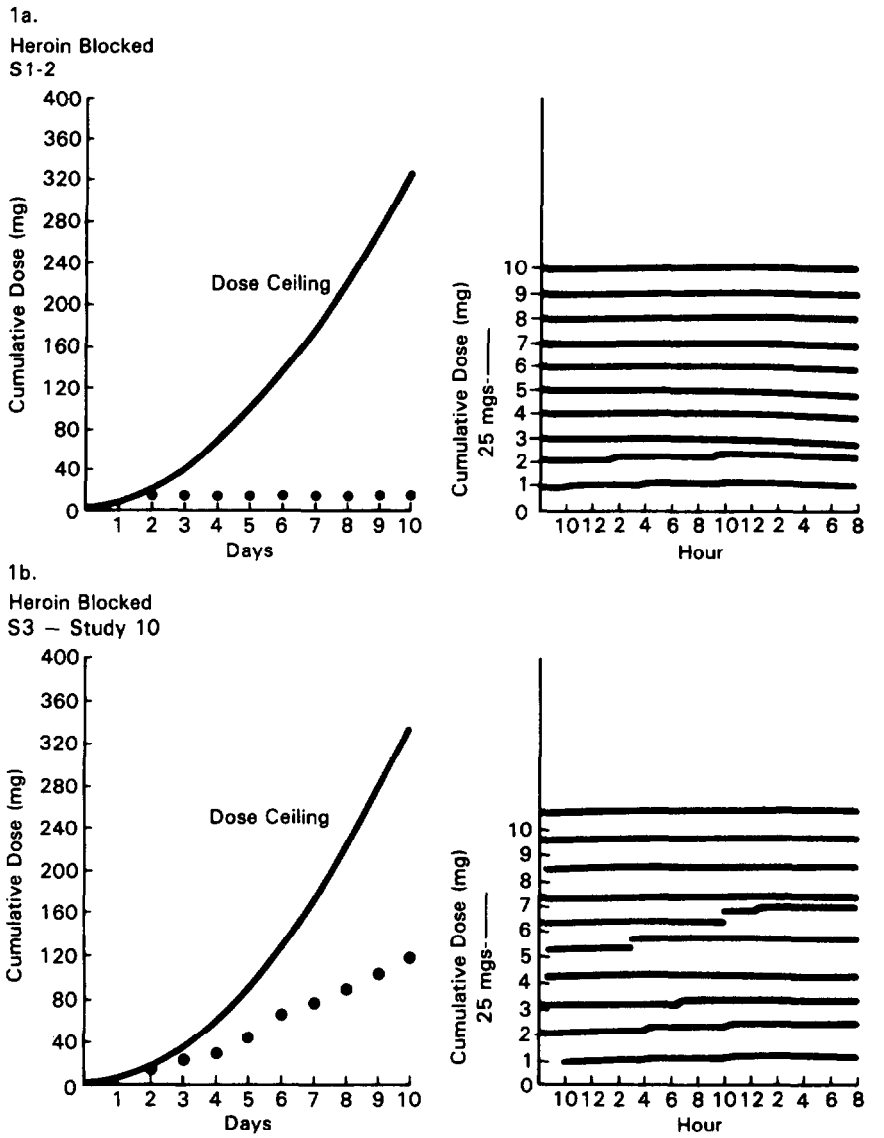

FIGURE 1. *Samples of heroin self-administration patterns in the presence of naltrexone*

NOTE: The dose ceiling represents the maximum dose of heroin available over 10 days. With one exception, all "unblocked" subjects took the maximum dose of heroin available. These two subjects are representative of subjects who stopped heroin challenges (while on naltrexone) after a few (a) or many (b) challenges. Both subjects took much less heroin than unblocked subjects.

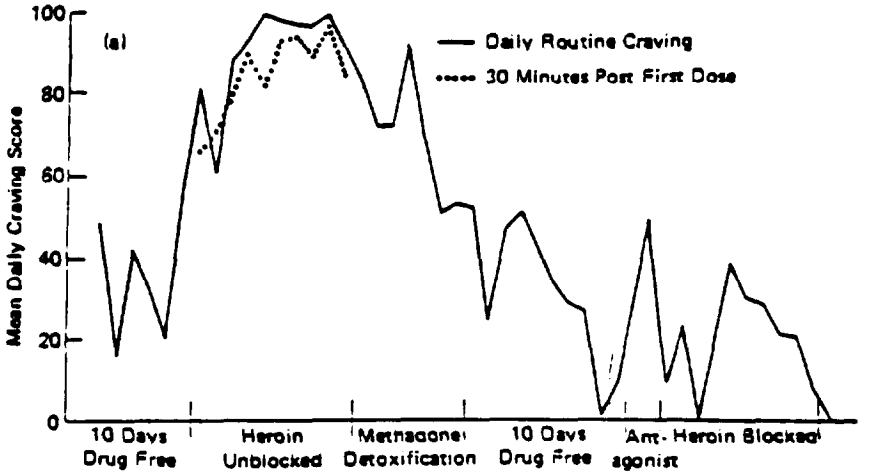

FIGURE 2. *Self-reported assessment of craving by phase of study (nonblind studies)*

SOURCE: Meyer and Mitin 1979 Copyright 1979, Plenum Publishing Corporation.

predicted an increase in craving, operant work output, and actual heroin consumption in all blocked subjects followed by a gradual decline. This pattern was not observed in any of the blocked subjects. Forty-three subjects were studied in the double-blind paradigm; 22 subjects received naltrexone and 21 received placebo. Those subjects receiving the narcotic antagonist could be divided retrospectively by a median split into individuals who repeatedly challenged narcotic blockade and those who did not. Table 3 contrasts the 22 "blocked" subjects with the 21 "unblocked" subjects prior to the first dose of heroin. Table 4 describes craving before and after the first dose of heroin, and operant work output in the first 24-hour period. Those subjects receiving naltrexone who continued to challenge narcotic blockade ("high-frequency" subjects) could not be differentiated in terms of operant work output from those subjects who received unblocked heroin. In contrast, subjects who did not repeatedly challenge narcotic blockade ("low-frequency" subjects) showed little operant work for heroin after the first dose and also showed a dramatic drop in self-reports of craving.

One question that comes to mind concerns the effects that "high-frequency" blocked subjects received from heroin that resulted in their continuing to challenge narcotic blockade. When we compared

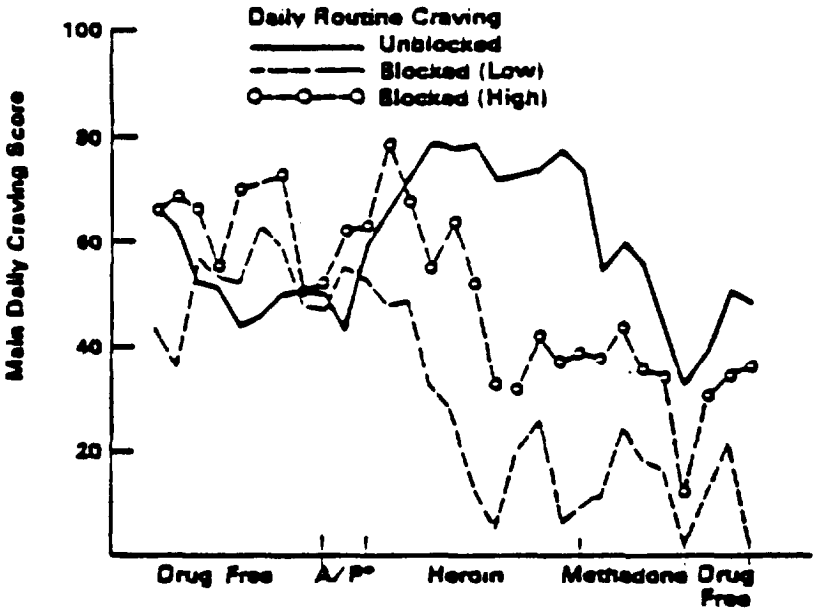

FIGURE 3. *Subject assessment of craving by phase of study (double-blind studies)*

SOURCE: Meyer and Mirlin 1979, Copyright 1979 Plenum Publishing Corporation.

changes in respiration before and after the first three doses of heroin with changes observed after the last three doses self-administered by the "high-frequency" subjects, we observed a statistically significant decrease in respiration for the first three doses in the subjects and no change as a consequence of the last three heroin challenges. "High-frequency" subjects also showed statistically significant pupillary constriction associated with the first three heroin injections and no change associated with the last three doses of heroin. The data suggest that these subjects were getting some autonomic effects from their first blocked heroin injections, but that there was extinction of these conditioned heroin-like effects. The persistence of heroin administration in these subjects (X=1 5.9 doses over 10 days vs. 4.3 doses for "low-frequency" subjects) provides suggestive evidence of conditioned reinforcement in these subjects, associated with the conditioned autonomic effects. Indeed, these subjects reported feeling significantly more relaxed ($p<.006$) and

even felt intoxicated ($p<.10$) after each of the first three doses of blocked heroin, but not after the last three doses. It was of interest that these subjects reported no dysphoric moods associated with the last three heroin injections. For all blocked subjects, the operant behavior was consistent with discrimination learning in which individuals learned that under the naltrexone condition, heroin was "unavailable" (SA). This learning took longer in some subjects (the "high-frequency" subjects) than in others.

TABLE 3. *Effects of the narcotic antagonist*

	number	$\bar{X}$ craving score before first dose	2-hour operant work output before first dose
Blocked subjects			
All	**22**	**79.64**	**13,200 points**
High-frequency	**11**	**77.82**	**13,200 points**
Low-frequency	**11**	**79.60**	**13,300 points**
Unblocked subjects	**21**	**77.86**	**13,600 points**

SOURCE: Meyer and Mirlin 1979, Copyright 1979, Plenum Publishing Corporation.

Overall, in both the nonblind and the double-blind studies, we found that the best predictor of the frequency of heroin consumption by "unblocked" subjects on this four-bed research unit was the frequency of heroin consumption by other subjects on the unit at the same time. In contrast, the frequency of heroin self-administration by subjects receiving naltrexone was not influenced by the pattern of self-administration of heroin by other subjects on the unit at the same time (including subjects who were receiving unblocked heroin). Indeed, the best predictor of "high-frequency" heroin challenges in the presence of naltrexone was a history of intense alcohol use by these subjects. In our animal studies we found a relationship between length of addiction and the persistence of intravenous

TABLE *4.* *Craving before and after the first dose of heroin and operant work output after first dose of heroin in blocked and unblocked subjects*

	number	X number of heroin doses over 10 days	X craving first dose Before	After	P	Operan to work output in 24 hours after first dose
Blocked subjects						
All	**22**	**10.09**	**79.64**	**63.95**	**<.032**	**14,000**
High-frequency	**11**	**15.91**	**77.82**	**76.82**	**NS**	**22,000**
Low-frequency	**11**	**4.27**	**79.60**	**49.80**	**<.03**	**5,900**
Unblocked subjects	**21**	**54.14**	**77.86**	**67.91**	**<.077**	**26,400**

SOURCE: Meyer and Mirin 1979, Copyright 1979. Plenum Publishing Corporation.

morphine selfa dministration in rats treated with a narcotic antagonist (Carnathan et al. 1977).

Summary of Opioid Studies

In summary, we found a remarkable correlation between the availability of heroin, the subjective sense of craving, and associated heroin acquisition and self-administration behavior. Craving increased in our research ward environment just prior to the heroin period. For subjects on naltrexone, craving fell when heroin injections failed to produce the expected physiological and subjective effects. We proposed that craving results when the addict feels that heroin is "available." In the community, the addict attributes great power to heroin availability and may challenge his own "moral fiber" by repeatedly appearing in environments associated with prior heroin use. His visceral response to "the heroin stimulus" (i.e., availability) challenges the insight and learning that may have occurred in a treatment program. Our operant methodology, which did not restrict mobility in the research ward setting, did not permit a precise determination of physiological responses associated with the craving associated with "the heroin stimulus." Nevertheless, our subjects did not report feelings of sickness (withdrawal-like symptoms) prior to their first heroin injection; nor did they manifest the physiological signs associated with opioid withdrawal (pupillary dilatation, increased pulse and respiratory rates). Among unblocked subjects, some anxiety was reported prior to heroin injection, with tension relief associated with self-administration in the first days of heroin consumption. In the latter part of the 10-day period of heroin use, subjects reported more dysphoric feelings associated with chronic intoxication.

We hypothesized that the drug-free addict in a heroin-available environment experiences a dysphoric response (craving) that may include classically conditioned abstinence symptoms, but almost certainly includes anxiety and tension associated with an approach/avoidance conflict. The conflict is a consequence of a history of euphoric "highs" associated with heroin use, as well as previous encounters with the aversive consequences and guilt associated with drug use.

STUDIES IN ALCOHOLICS

Our studies of alcoholic subjects have focused on subjective and biological responses to alcohol-related stimuli in individuals who have been alcohol-free for 7 to 14 days. These subjects also participated

in a 21-day inpatient alcohol rehabilitation program that was designed to help individuals maintain an abstinent lifestyle after discharge. Our research was based on the premise that an alcoholic's craving for alcohol is a multidimensional response involving the interrelationship of cognitive, physiological, and biochemical events that result in increased probability of drinking. Our methodology involved comparison of alcoholic and nonalcoholic subjects along a variety of dimensions. Prior to the start of these laboratory-based studies, assessments were made of cognitive functioning, drinking history, and severity of alcohol dependence. These measures enabled us to contrast the biological, subjective, and behavioral responses of alcoholics compared to nonalcoholics in the presence of an ethanol stimulus.

In our first alcohol stimulus-control study, we reported the following observations.

(1) Alcoholics showed greater autonomic reactivity during *exposure* to an alcoholic beverage than did nonalcoholics. This was positively related to both increased desire to drink and measures of severity of withdrawal symptoms in the 30 days prior to admission (Kaplan et al. 1933).

(2) Immediately following consumption of a nonalcoholic malt beverage (the placebo), alcoholics (compared with nonalcoholics) were more likely to believe they had consumed a real beer. (The beer and placebo administration was double blind.)

(3) Among alcoholics, the immediate perception of having consumed alcohol following the consumption of either an alcoholic or placebo drink was more related to the autonomic response prior to consumption than the actual alcohol content of the drink (Kaplan et al. 1984).

(4) The prediction of an alcoholic's choice to drink an optional drink could be made using a multivariate model including a measure of alcohol dependence, and the physiological and subjective reactivity to the beverage stimulus prior to consumption (Kaplan et al. 1983). The alcohol content of the beverage (i.e., real beer vs. placebo) was not significant.

In our initial study, the option to consume a beverage was an important part of the stimulus presentation, since we postulated that the cognitive perception of the "availability" of alcohol was a critical

dimension to “craving.” The administration of placebo to half the subjects presented the opportunity to examine conditioned drug effects that we had previously observed in heroin addicts on naltrexone. At the time of these studies, no alcohol antagonist was available. One recent report suggests that some drugs that alter the effects of alcohol on the chloride ion channel associated with the bentodiazepine gamma-aminobutyric acid (GABA) receptor of cell membranes may block the intoxicating effects of alcohol (Suzdak et al. 1986).

In another study by our group, alcoholics experienced craving in the context of simple exposure to an open bottle of their favorite beverage, even in the absence of opportunity to drink. Alcoholics experienced significantly more craving and a higher swallowing rate (an index of salivary response) than nonalcoholics in the presence of their favorite beverage (Pomerleau et al. 1988); the salivary response was highly correlated with positive expectations concerning the behavioral and cognitive effects of drinking (Cooney et al. 1984).

Because of the potential clinical diagnostic usefulness of physiological assessments associated with simple cue exposure (without beverage consumption), we conducted a third stimulus-control study of autonomic and subjective responses to alcohol-related cues in 59 hospitalized alcoholic subjects (25 of them were women) and 26 nonproblem drinkers (11 of these were women). We found skin conductance levels (electrodermal level) and heart rates during alcohol cue exposure significantly higher in alcoholics than in nonalcoholics. The results were similar to our experiments involving actual beverage consumption. Again, self-reported desire to drink and skin conductance levels during alcohol exposure were correlated for alcoholic, but not for nonalcoholic, subjects. This relationship was strongest for the most severely dependent alcoholics (Kaplan et al. 1985). Data from this study failed to replicate changes in swallowing rates that differentiated alcoholic subjects from controls in the second study (Pomerleau et al. 1983).

While alcoholic subjects in both studies showed similar increases in swallowing rates during alcohol cue exposure, the nonalcoholic sub jects in the third study behaved more like alcoholic subjects with respect to swallowing rate. From these observations we concluded that nonalcoholic subjects in the third study were heavier drinkers than nonproblem drinkers in the second study. Further, in the third study, the time of experiment (early evening) was more consistent with the “real life” drinking behavior of nonalcoholic subjects than in

the second study (midafternoon). This may explain why nonalcoholic subjects in the third study were more likely to show an increase in swallowing rate when allowed to hold and sniff their favorite beverage.

Findings from the cue exposure paradigm, in which subjective (desire to drink) and autonomic (skin conductance and heart rate) measures are simultaneously recorded in both alcoholic and nonalcoholic subjects, have established a concordance of these responses in alcohol-dependent individuals. Indeed, the concordance of cognitive, physiological, and behavioral responses supports the conception of craving as a multidimensional response. We have reanalyzed the data for implication since this was written and the findings are less clearcut.

In an effort to define more precise biological correlates of the alcohol dependence syndrome (particularly "craving" and diminished control of alcohol intake), we conducted studies of endocrine responses to an ethanol stimulus followed by beverage (placebo) consumption in alcoholic and nonalcoholic subjects (Dolinsky et al. 1987). Alcoholics, when compared to nonalcoholics, demonstrated significantly larger and more rapid insulin and glucose responses following the consumption of a placebo beer, which they believed contained alcohol (Dolinksy et al. 1987). Associations between peak neuroendocrine response, desire to drink, anxiety, and psychophysiological reactivity in alcoholics reinforced the notion of a multivariate craving response. Alterations in endocrine activity that regulate energy metabolism and food intake could serve as discriminative stimuli for craving and other subjective measures often associated with excessive alcohol consumption.

Another application of a neuroendocrine strategy to studies of alcohol dependence involves the potential delineation of the conditioning process. In our study, alcoholics, but not controls, showed a mean percent decrease in plasma testosterone and luteinizing hormone (LH) concentrations during an initial period of exposure to an ethanol stimulus. LH levels continued to decrease during and after placebo beverage consumption, while testosterone levels returned to baseline after placebo consumption. The initial decrease in testosterone and LH in response to the presentation of the ethanol stimulus is consistent with the recent report that alcoholics experience cognitions associated with the taste and feel of ethanol as they anticipate actual beverage consumption (Ludwig 1985). In other words, the discriminative state associated with the anticipation of

beverage consumption “feels” like the effects of alcohol. The results seem to conform to a traditional Pavlovian model of conditioning, not a compensatory response model-at least in the context of these data on reproductive hormone response to ethanol cue exposure.

DISCUSSION

The results reported in this paper should be seen as a progress report rather than a definitive statement. Results from our stimulus-control studies to date suggest a symmetry among subjective, psychophysiological, and neuroendocrine responses in alcohol-dependent subjects at least 2 weeks postwithdrawal. The data can be used to support the notion that conditioning processes are associated with the development of alcohol dependence; but this interpretation needs to be viewed with caution. Is the enhanced cue responsiveness of alcohol-dependent subjects principally a function of conditioning phenomena, or is it also related to the subacute symptoms of withdrawal described in the central nervous systems of alcoholics within 2 weeks postwithdrawal (Pojesz and Begleiter 1985)? To what extent can the observed responses be attributed to stress reactions (an approach/avoidance conflict) in alcoholic subjects? Since alcohol dependence accounted for only a portion of the variance in the response we observed, are there other stimulus conditions that consistently elicit concordant physiological and subjective responses in alcoholic subjects? O’Brien et al. (this volume) report on the relationship between certain negative affective states and desire for heroin. Can this also be demonstrated in abstinent alcoholics? Monti and colleagues (this volume) have employed similar stimulus-control paradigms to predict treatment outcome suggesting a relationship between laboratory responses to alcohol-related stimuli and behavior in the community.

At least since the writings of Benjamin Rush, in 1790, physicians have observed the persistence of relapse tendency in detoxified alcoholics and the inability of alcoholic individuals to moderate their drinking behavior. Persistence of relapse tendency is also a problem in detoxified opioid addicts, who continue drug consumption despite the negative consequences associated with use. Wikler (1965) postulated a relationship between the compulsion to continue chronic heroin use associated with the development of physical dependence, and the persistence of relapse tendencies in the detoxified addict. His theories were developed at a time when drive reduction was viewed as a source of motivation, i.e., when behavior was seen to serve homeostatic functions. His view that opioid abstinence

symptoms could be conditioned to environmental stimuli has been demonstrated in the laboratory (O'Brien et al. 1977; Wikler and Pescor 1967). However, Wikler's hypothesis that development of withdrawal symptoms was central to an explanation of drug- or alcohol-consuming behavior remains unproved. With the discovery of centers of reinforcement in the brain (Olds and Milner 1954) and the development of methods for the study of intravenous self-administration of drugs in animal models (Weeks 1963; Schuster and Thompson 1969) researchers have been able to separate the reinforcing properties of opiates from characteristics of these drugs associated with the relief of abstinence symptoms and signs (Shuster and Villareal 1968; Bozarth and Wise 1983).

Craving for heroin in the community does not appear to be associated with the presence of conditioned (or other) withdrawal symptoms for the majority of addicts (O'Brien et al., this volume). Craving for alcohol is greater after alcohol consumption in a bar-like setting than after placebo consumption in a laboratory-like setting (Ludwig 1981). While we have observed a concordance between craving and autonomic arousal (suggestive of classical conditioning of withdrawal-like signs) in alcohol-dependent individuals, the same physiological signs have been observed in subjects exposed to alcohol cues after "successful" aversion therapy (Elkins 1980). Indeed, in our alcohol studies (as in the heroin studies), craving was highest at times when subjects expected to receive their preferred drug and remained elevated (or increased) after drug consumption (figures 2 and 3). This "priming" effect has been observed by other investigators in studies of alcoholics (Stockwell et al. 1982) and in animal models of drug self-administration (DeWit and Stewart 1981; Dewit and Stewart 1983). In a recent review article, Stewart et al. (1984) point out that while there is evidence that conditioned physiological responses can be demonstrated that oppose the direct action of drugs, these responses may be invoked only to explain learned tolerance and/or conditioned withdrawal. However, these responses fail to account for the motivational issues underlying drug self-administration or to explain the data (above) that links craving to drug availability. Stewart and colleagues postulate that conditioned drug effects that mimic unconditioned drug effects are elicited by environments in which drug taking has previously occurred (or settings in which the individual expects to receive the drug). These environmental stimuli (through conditioning) arouse reinforcing areas of the brain that serve to increase the effectiveness of drug-related stimuli. Under these circumstances, there is an increase in drug-related thoughts and actions.

This view of conditioning, based on a positive incentive view of drug use, stands in contrast to Wikler's drive reduction model of relapse. It is a view that seems to explain much of the data that we have reported, while also accounting for the observation that many detoxified addicts and alcoholics will regularly return to places which they associate with past drug (or alcohol) use. For the alcoholic, cognitive impairment (and/or personality factors) and an inability to discriminate blood alcohol levels (Ludwig 1981) may influence the behavioral response to environmental stimuli and actual alcohol consumption-leading to relapse. The heightened insulin response that we observed after beverage consumption could theoretically serve as a mediating variable in this progression from "first drink" after a period of abstinence to impaired control of alcohol intake. At this writing, the theory and experimental methodologies have become far more sophisticated than when Wikler began his work. The challenge remains to apply our growing knowledge base to the improved assessment and treatment of patients.

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The Use of Second-Order Schedules To Study the Influence of Environmental Stimuli on Drug-Seeking Behavior

Charles W. Schindler, Jonathan L. Katz, end Steven R. Goldberg

INTRODUCTION

The problem of drug abuse has recently received renewed interest both in the popular press (Castro 1986) and from policy makers in the Federal Government (Pollin 1987). The reason for this increase in attention can be traced to a number of highly publicized deaths due to cocaine overdose and to the clear increases in the abuse of cocaine and other drugs over the last decade. Surveys by the National Institute on Drug Abuse (NIDA) indicate that nearly 37 million Americans used one or more illicit drugs during 1985, and, while the abuse of most drugs has remained fairly constant over recent years, there was a 36 percent increase in the abuse of cocaine between 1982 and 1985 (Pollin 1987). Proposals to deal with the problem of drug abuse typically focus on one or more of three separate issues: (1) prevention of drug abuse; (2) interdiction in the supply of illegal drugs into this country: and (3) treatment for the drug-abusing population.

While prevention programs are still in their infancy, a wide range of treatment programs are available to drug abusers. These programs range from extensive inpatient care at private hospitals to methadone outpatient treatment available in urban areas of the nation. While many of these programs claim a high success rate, most have success rates far below 50 percent. In addition, the cost of many of these treatment programs places them far beyond the reach of the majority of the drug-abusing population. To be a lasting part of any national program to solve the drug abuse problem, a treatment program must be both effective and relatively inexpensive. In devising such programs, a thorough understanding of the acquisition, maintenance,

and extinction processes involved in drug-taking behavior is a necessary prerequisite.

A Hypothetical Case History

By way of example, consider the following hypothetical case history. An inner-city youth is introduced to heroin by a friend. Wiihin 6 months, the youth and his friend are making regular trips to a nearby street comer, just across from a bakery, to purchase their heroin. They then return to the friend's home and head directly to the attic where they have hidden the paraphernalia they need to inject the drug. They are soon quite "high." They then leave the house and head for the local youth center where they meet and socialize with a number of their friends. Inevitably, the drug's effect begins to wear off while the youth is at the center, and he soon begins to feel the effects of withdrawal. Within 6 months, the youth is arrested and sent to a youth detention center for 3 months. While at the detention center, the youth is withdrawn from heroin completely and no longer experiences the urges to use heroin or the withdrawal symptoms he had been experiencing frequently while using heroin. Soon after release from the detention center, the youth walks home past the bakery where he had previously bought the heroin along with his friend. The smell coming from the bakery is like one he had experienced many times before, and he begins to experience the same pleasurable feeling he had initially when he was taking heroin. From the bakery, the youth goes to the youth center where he meets his old friends. While at the youth center, he begins to experience the withdrawal symptoms he had while using heroin frequently. He soon finds himself back at the street corner by the bakery, along with his friend, buying heroin and beginning a repeat of the process which had made him addicted to heroin.

What are the behavioral processes which lead to this not uncommon sequence of addiction and relapse? What causes the urges to use drugs and why do addicts relapse months or even years after detoxification? Are these processes unique to the human drug abuse situation, or, are they typical for any organism administering drugs to itself? Are these processes unique to the administration of a drug, or might similar processes be involved in the acquisition of any positive reinforcer, such as food, money, sex, etc.? To understand fully the process of drug abuse, it will be necessary to understand all the behavioral and pharmacological processes involved in the development of drug-taking behavior.

Great advances have recently been made in understanding the pharmacology of abused drugs. Although knowing which drugs can serve as positive reinforcers (i.e., which drugs will be abused) and how they act pharmacologically is certainly useful information, to understand fully the process of drug abuse and to design effective treatment and prevention programs, we must also understand the behavioral processes involved in drug abuse. For example, Wikler has argued on a number of occasions that conditioning processes are intimately involved in the development and maintenance of drug-seeking behavior (Wikler 1973). In the example given above, a number of conditioning processes important to drug abuse are enumerated. For example, the young addict always uses the drug in the same environment (the attic of his friend's house). Thus, the environment may come to elicit the same feeling as the drug itself, through the behavioral process of Pavlovian conditioning. The same sequence of behaviors also typically precede the use of the drug (going to the street corner by the bakery). Each of these behaviors and their associated stimuli (the smell from the bakery) may also become associated with the effects of the drug through the process of second-order conditioning. In addition, the experience of withdrawal also typically occurs within the same environment (the youth center), thus that environment may come to elicit withdrawal symptoms independently from the drug, also as a result of Pavlovian conditioning. Finally, the drug abuse occurs within a social situation that may contribute to both the acquisition and maintenance of drug abuse.

While the example of the youth given above may appear exaggerated, there is ample evidence within the clinical literature to support the importance of conditioning in maintaining drug-seeking behavior. For example, Vaillant reports that "a previous history of active addiction [can condition an] addict to respond to repeated injections of a placebo as if he were addicted" (Vaillant 1969, p.352). The stimuli in the environment that in the past have been associated with drug injection can come to maintain drug-seeking behavior oven in the absence of the drug itself. Just as stimuli in the environment can maintain drug-seeking behavior, environmental stimuli can also elicit the symptoms of withdrawal. Vaillant also reports that on "the research ward, men who have been abstinent for months can experience acute craving and withdrawal symptoms while watching another addict receive an injection of narcotics" (Vaillant 1969, p.353). Thus, it should not be surprising that a detoxified addict who returns to an environment where drug-taking behavior has occurred in the past will relapse.

An Animal Model of Human Drug Abuse

While conditioning processes clearly influence human drug-taking behavior, it is very difficult to study these processes in humans because the appropriate behavioral control procedures to unequivocally attribute drug-taking behavior to a particular behavioral process are often impossible to employ. Basic animal research would appear to hold great promise in the design of effective and inexpensive drug abuse treatment programs, because it is possible to manipulate with relatively precise control the large number of factors thought to be important in the acquisition, maintenance, and extinction of drug-taking behavior. These factors include both pharmacological and environmental influences. However, for animal research to be applicable to the human drug abuse problem, it is necessary to devise procedures that closely approximate the human drug abuse situation.

A typical characteristic of the human drug abuse situation, which is not typically a part of animal models of drug abuse, is the amount of behavior produced to obtain the drug of choice. In the typical animal model, a rat or monkey will emit a small number of responses on a lever to receive a low dose of an abused drug. For the human, however, a long sequence of behaviors is typically emitted prior to the administration of a dose of an abused drug. This behavioral sequence includes raising money to purchase the drug, purchase of the drug, preparation of the drug for administration, and administration of the drug itself. A procedure used in animals, which more closely approximates this long sequence of behavior, is a second-order schedule of drug injection (Goldberg and Gardner 1961; Kelleher 1966a; Kelleher 1966b). Under a second-order schedule, animals can be trained to emit thousands of responses to receive a single injection of a drug. For example, animals can be trained to respond for a drug injection given after a fixed interval of 1 hour (FI 1-hr) where every 30th response (fixed ratio, FR 30) is followed by a stimulus (brief light) that has been paired with the drug injection. This schedule is designated as an FI l-hour (FR 30:s) where the “S” denotes the presentation of the stimulus following every 30th response. Analogous to the example given above, the brief light paired with the drug injection may come to elicit drug-like responses through Pavlovian conditioning. In addition, both the behavior and stimuli associated with the earlier portions of the FI may be associated with the drug through the process of second-order conditioning. Thus, this type of schedule may be more useful in enumerating the behavioral processes involved with the human drug abuse situation. We review here a number of experiments using second-order schedules

that indicate the importance of environmental stimuli in maintaining drug-seeking behavior, a finding which we feel has great implications for drug abuse prevention and treatment programs.

STIMULUS EFFECTS ON THE ACQUISITION OF DRUG-SEEKING BEHAVIOR

Stimuli which are paired with reinforcement can acquire the ability to produce effects similar to those of the reinforcer itself, through Pavlovian conditioning, and also to serve as reinforcers for the behaviors that produce them, through the process of second-order conditioning (Rescoria 1980). Thus, if a stimulus that has been paired with a drug injection is presented following an operant response, the frequency of that response would be expected to increase. If these stimuli are presented early in an animal's drug-taking history, they would also be expected to enhance the acquisition of the drug-taking behavior. Figure 1 presents the results of an experiment that shows the effect of presenting stimuli paired with a drug reinforcement early in the animal's experimental history (Kelleher 1975). In this experiment, lever presses by a rhesus monkey produced IV injections of 30g/kg cocaine under a fixed interval 10 minutes (FI 10 minutes) schedule. On this schedule, the first response emitted after 10 minutes produced a drug injection which was paired with a 2-second illumination of amber stimulus lights (a brief stimulus). The top panel of figure 1 shows a cumulative record of responding under this schedule. Rate of responding is low, and no clear indication of the positively accelerated patterning of responding, characteristic of FI schedules, was yet evident. The second panel from the top shows the effects of changing from the FI 10-minute schedule to a second-order FI 10-minute schedule of fixed ratio (FR) components. Initially, every 10th response, and later every 3rd response, produced the same brief stimulus that had been previously paired with cocaine injections. For the second-order schedule, the first FR component completion after 10 minutes had elapsed produced both the brief stimulus and the cocaine injection. During the first session under the second-order schedule, rate of responding increased slightly when the FR requirement was 10 and increased markedly when the requirement was reduced to 3. Subsequently, rates of responding in excess of one response per second were maintained with either the FR 3 (third panel), or FR 10 (bottom panel) requirement. Thus, the presentation of stimuli associated with drug injection early in the fixed-interval period markedly increased responding during acquisition. This experiment demonstrates the potential importance of second-order conditioning in influencing the acquisition of drug-seeking behavior.

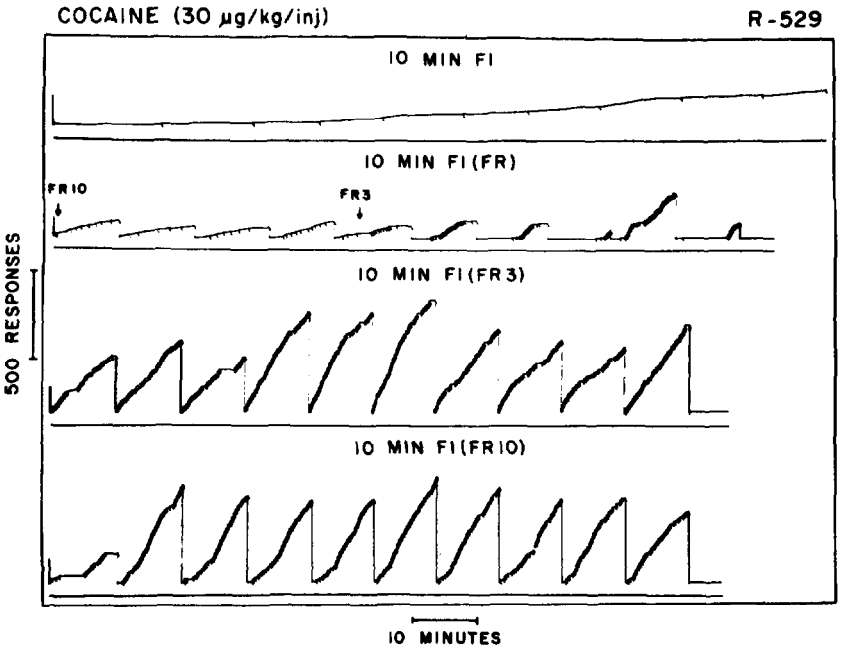

FIGURE 1. *Increases in responding* after transition from a 10-minute *fixed-interval schedule of cocaine injection to a second-order schedule of* cocaine *injection with fixed-ratio components*

NOTE: Abscissae: time. Ordinates: cumulative responses. First panel: performance under a 10-minute fixed-interval schedule of cocaine Injections. Each diagonal stroke on the record indicates a 2-second presentation of amber lights accompanied by an IV injection of 30 ug/kg cocaine hydrochbride. Second panel: first session under a second-order schedule. Completion of each 10-response (FR 10) or 3-response (FR 3) Fixed-ratio schedule component produced a 2-second illumination of amber lights, Indicated by a short deflection on the response pen. The first FR componant completed after a fixed interval of 10 minutes elapsed produced the amber lights and an injection of 30 ug/kg cocaine, indicated by the rasetting of the pen to the bottom of the record. Third panel: second session under a second-order schedule with FR 3 components; recording as in the second panel. Fourth panel: subsequent performance under a second-order schedule with FR 10 components; recording as in the second panel.

SOURCE: Kelleher 1975, Copyright 1976, Amercan Society for Pharmacology and Experimental Therapeutics.

STIMULUS EFFECTS ON THE MAINTENANCE OF DRUG-SEEKING BEHAVIOR

Just as the presentation of the brief stimulus paired with drug injection enhances the acquisition process, the continued presentation of the paired stimulus maintains the response rate at a high level. Figure 2 presents the results of an experiment where a different brief stimulus, not paired with reinforcement, is substituted for the paired brief stimulus (Goldberg et al. 1979). The top panels of the figure show performance of two squirrel monkeys under the second-order schedules where the paired brief stimulus is presented following completion of each FR component. For the monkey receiving cocaine, the FI requirement was 10 minutes, for the monkey receiving morphine, the FI requirement was 60 minutes. For both reinforcers a high level of responding was maintained. When a different stimulus, which had not been paired with reinforcement (i.e., unpaired), was substituted for the paired stimulus during the 10- or 60-minute intervals, the rates of responding under the second-order schedules decreased considerably. When the brief stimulus during the fixed intervals was removed entirely (bottom panels), response rates decreased even further. Under all these conditions, a brief amber light continued to be paired with drug injection at the end of each interval. Figure 3 presents the results of this experiment in a quantitative manner, where the mean of the last three sessions in a condition is presented for both overall and local rates of responding. As in the cumulative records presented in figure 2, it is clear that substituting an unpaired brief stimulus for the paired stimulus reduces both overall and local response rates, whereas completely removing the brief stimulus reduces response rates even further. The results of this experiment point to the importance of pairing the brief stimulus with drug injection. While any stimulus may serve some discriminative function which enhances responding on the second-order schedule (compare the no-stimulus and unpaired stimulus conditions), the paired stimulus is clearly more effective in maintaining responding (compare the unpaired and paired stimulus conditions).

STIMULUS EFFECTS ON EXTINCTION OF DRUG-SEEKING BEHAVIOR

It is in their effects on the extinction of drug-seeking behavior that stimuli that have been paired with drug injections can have their most profound effects on behavior. The importance of considering the effects of second-order stimuli in extinction is illustrated in

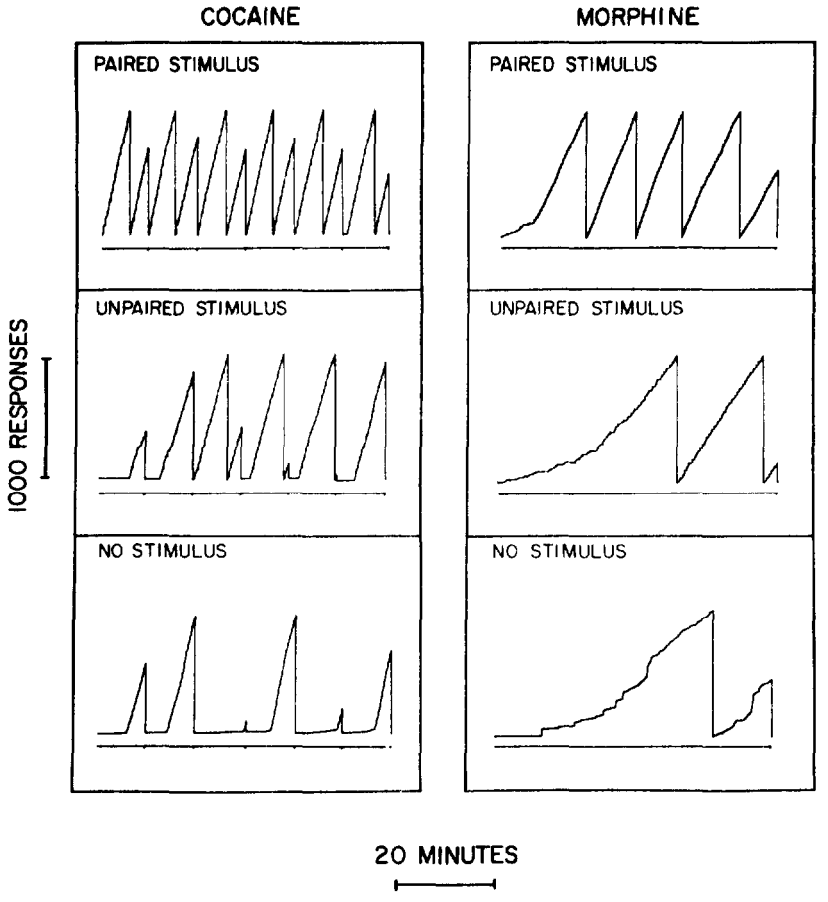

FIGURE 2. *Representative cumulative records of responding under second-order schedules*

NOTE: Abscissae: time. Ordinates: cumulative responses. Records of IV cocaine or morphine injection when the completion of every Rued-ratio component during the fixed interval produced either a paired (amber light) or a nonpaired (blue light) brief stimulus or when the brief stimulus was omitted. Under all conditions an amber light was paired with injection of drug at the end of the interval. Short diagonal deflections of the response pen indicate brief stimulus presentation; downward deflection of the horizontal event lines indicate Injection of drug. Left panels show responding during portions of the session under the second-order schedule of cocaine injection [FI 5-minute (FR 100)]. Right panels show responding during the entire session under the second-order schedule of morphine injectlon [FI 60-minute (FR 30)].

SOURCE: Goldberg et al. 1979, Copyright 1979, Pergamon Journals.

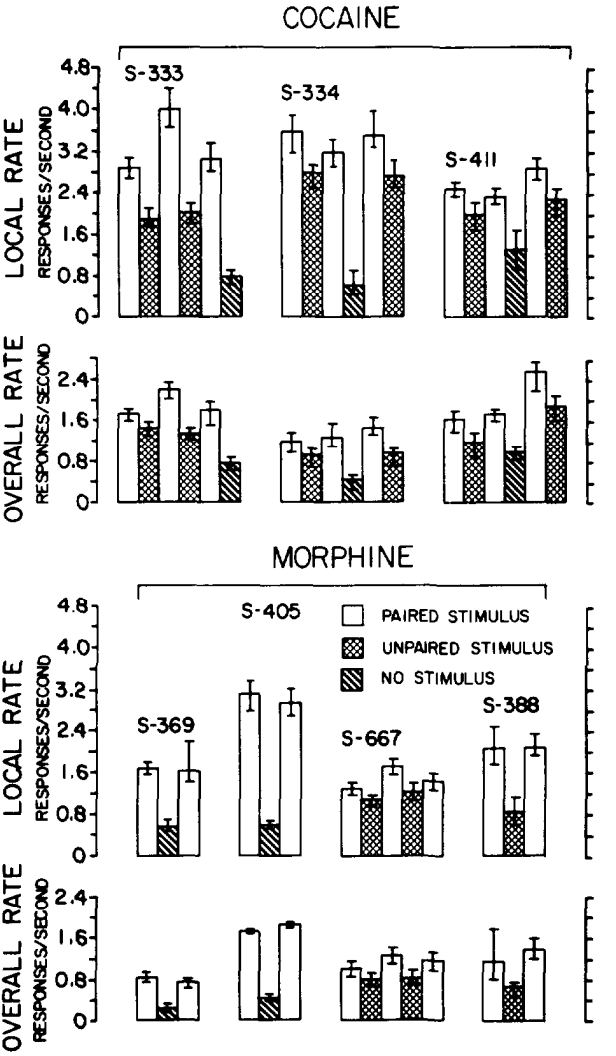

FIGURE 3. *Local and overall rates of responding (responses/second) under the second-order schedule*

NOTE: Local rate is a measure of responding where the time following the completion of each fixed-ratio component until the next response Is excluded from the calculation. Overall rate includes these time periods. A large difference between local and overall rate would indicate a typical fixed-ratio patterning. Bars show average rates of responding during the last three sessions of each successive condition for individual monkeys; brackets show ranges. Each condition was studied for 5 to 20 consecutive sessions,

SOURCE: Goldberg et al. 1979, Copyright 1979, Pergamon Journals.

figure 4. Here, a squirrel monkey was trained to respond on a second-order schedule where completion of 10 FI 5minute units was followed by reinforcement, i.e., FR 10 (FI 5-min:S) schedule (Kelleher and Goldberg 1977). In figure 4, the first 10 points (unfilled circles) represent responding on the schedule after saline was substituted for 300 ug/kg cocaine and the brief stimulus was removed following the FI components. Under these conditions response rates decreased to a lower level. Simply reinstating the stimulus that had been paired with cocaine injections (filled circles) clearly increased response rate. The presence of the brief stimuli also reinstated the pattern of responding characteristic of FI schedules, as indicated by the quarter-life. Quarter-life measures the pattern of responding on FI schedules, where 25 percent equals no patterning and greater than 25 percent indicates patterning that is typical for an FI. Removing the stimulus led again to a decrease in response rate and quarter-life, with a subsequent reinstatement of the brief stimulus again increasing response rate and quarter-life.

Figure 5 presents a similar result for an FI 3-hour (FR 30:S) second-order schedule (Goldberg et al. 1981). On this schedule, every 30th response was followed by a brief stimulus which was also paired with reinforcement, and the first FR 30 unit completed after 3 hours was followed by the brief stimulus and drug injection. In this experiment, responding by squirrel monkeys was maintained by cocaine (0.75 mg/kg). The top panel presents a cumulative record from a baseline session when responding produced both the brief stimulus and cocaine injection. The second panel presents the effects of substituting saline for cocaine and removing the brief stimulus. Response rate is clearly decreased under this condition. The third panel presents the effects of reinstating the brief stimulus. As in the last experiment, response rate is dramatically increased when the brief stimulus is again presented following the second-order component schedules, even though saline continued to be injected.

A recent study by Goldberg et al. (1987) also points to the importance of stimuli paired with drug injection in maintaining behavior in extinction. Squirrel monkeys were trained on a second-order schedule of morphine administration where the first FR completed after 1 hour was followed by drug injection paired with an amber stimulus light. During the 1-hour daily session, every 30th response produced the amber light alone. Thus, the subjects were trained on a FI 60-minute (FR 30:S) second-order schedule. On this schedule, animals will respond at high rates often approaching 1,000 responses per hour for morphine (1 mg/kg). When saline was substituted for

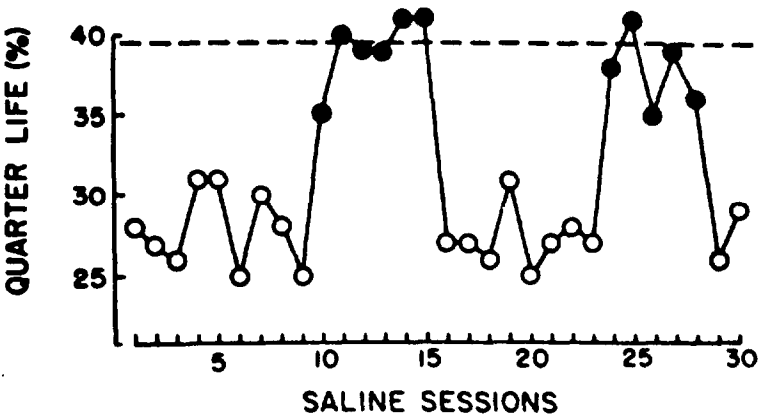

FIGURE 4. *Effects of a brief stimulus paired with cocaine on mean rates of responding and quarter-life values*

NOTE: Unfilled points: no stimulus; filled points: stimulus. Successive daily sessions after saline was substituted for cocaine on a FR 10 (FI 5-min) second-order schedule. Mean response-rate and quarter-life values from the last four sessions under the second-order schedule of cocaine injections are indicated by dashed lines in the upper and lower graphs.

SOURCE: Keleher and Goldberg 1977, Copyright 1977. Society for the Experimental Analysis of Behavior, Inc.

morphine, two of three animals showed virtually no change in their rate of responding, and the third animal showed only a modest decrease in response rate. These high rates of responding were

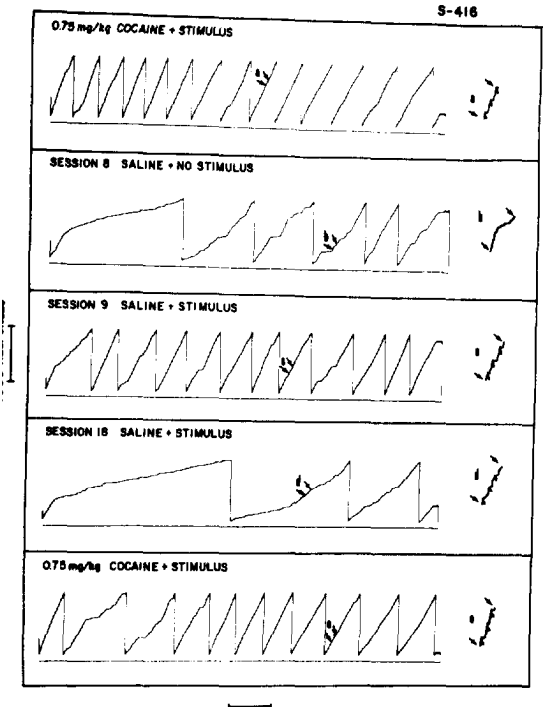

FIGURE 5. *Effect of reinstating brief stimulus presentations during* saline *substitution* after *an intervening number of sessions of* saline *substitution* in *which the stimuli were not presented*

NOTE: Abscissae: time. Ordinates: cumulative responses. Diagonal deflections of the response pen indicate brief stimulus presentations. The response pen reset to the bottom of the record after 1,100 responses and at the end of the session. The event pen was displaced downward during the pedod of time in which repeated injectlons of cocaine hydrochloride (total dose of 0.75 mg/kg) or injections of saline were given. Components were 30-response ftxed-ratio schedules; the overall schedule was a 180-minute fixed-interval. Component completions produced a P-second presentation of the amber light brief stimulus in all records except the one shown in the second panel In which no brief stimuli were presented. The top panel shows responding under the second-order schedule of cocaine injection. Saline was then substituted for cocaine and the brief stimuli were omitted for the next eight sessions; the eighth session is shown in the second panel. Next, the brief stimuli were reinstated, but saline continued to be injected; the first and last sessions under these conditions are shown in the next two panels. The last panel shows reinstatement of cocaine injections.

SOURCE: Goldberg et al. 1981, Copyright 1981, American Society for Pharmacology and Experimental Therapeutics.

maintained for 9 additional days of saline extinction. On the next session, the second-order brief stimulus was no longer presented following every 30th response. Under these conditions, responding decreased to a very low level and remained at that low level when the presentation of the brief stimulus following every 30th response was reinstated. Saline was still injected at the end of the session. Following this condition, morphine was again injected, and the animal's response rates increased to the high level characteristic for this schedule. Subsequent to this initial sequence of conditions, however, substituting saline for morphine did lead to a reduction in responding, even in the presence of the brief stimulus.

These experiments point to the dramatic effects environmental stimuli paired with drug injection can have on drug-seeking behavior, even in the absence of drug injections. This effect of increased responding with the presentation of the brief stimulus holds clear implications for the treatment of drug abuse as it relates to relapse. The treatment of drug abusers outside the environment where the abuse has taken place must necessarily be expected to have a low success rate if the patient is allowed to return to the same environment and be exposed to the same stimuli that have in the past been paired with drug injection.

CONCLUSION

While the above analysis of the effects of stimuli paired with drug injections points to the importance of environmental influences on drug-taking behavior, the breadth of that analysis must necessarily be increased if we are to fully understand the phenomenon of drug abuse and apply that knowledge successfully to drug abuse treatment and prevention programs. This analysis should be directed at both the acquisition process and the maintenance and extinction processes, as they relate to prevention and treatment, respectively. In this analysis we might take our lead from the study of Pavlovian second-order conditioning in the field of basic animal learning. Rescorla's (1977) assessment of the influence of second-order conditioning in basic animal learning may have parallels to studies described above and, therefore, to the treatment of drug abuse. Rescorla states:

> We might expect that to the degree that second-order Pavlovian incentive motivation is responsible for motivating the instrumental performance, that performance should be relatively insensitive to changes in the organism's evaluation of the goal event. So we should not be startled

> by instances in which performance continues relatively unaffected even though the evaluation of the goal has been drastically altered. (Rescorla 1977, p. 147)

To the degree that drug-seeking behavior is also controlled by second-order conditioning, we must also expect it to be relatively insensitive to quantitative or qualitative changes in the effectiveness of the reinforcer. Simply put, substituting placebo for drug (e.g., drug antagonist treatment), or even establishing the drug as aversive (e.g., Antabuse treatment), should not necessarily be expected to reduce a subject's drug-taking behavior. We must also consider the influence of stimuli that in the past have been paired with reinforcement or are a part of the sequence of behaviors that in the past have led to reinforcement. If we leave the conditioned effects of those stimuli intact, then we must expect that the drug-taking behavior will also remain intact.

Given these facts, what might be the best course to take in developing a drug abuse treatment program? The importance of environmental stimuli, paired with a drug of abuse or the drug-abusing situation, to maintenance of drug-seeking behavior is clear. Therefore, the influence of those stimuli must be taken into account. One would expect that the most effective approach to treatment would be to remove all stimuli associated with drug abuse from an individual's environment. That is, move the individual to a different environment and never allow them to return. This is essentially the course of treatment taken with servicemen who became addicted to heroin in Vietnam (Jaffe 1987). Addicts were identified in Vietnam, withdrawn from heroin in Vietnam, and returned to the States, where they had not previously used heroin. Remarkably, only 5 percent of those heroin addicts relapsed to heroin use back in the United States.

Of course, such a radical treatment for the inner-city drug abuser may not be practical. Nevertheless, a number of steps may be taken which could help in treatment. First, it is necessary to identify those stimuli that, in the past, have been associated with drug use or relapse. Once identified, steps should be taken to minimize an individual's contact with those stimuli. In our example of the inner-city youth, if he spends a great deal of time at the youth center because he is unemployed, then finding that youth a job may do much to decrease the probability of relapse, because it will keep him out of the youth center. Barring removal of those stimuli, it will then be necessary to extinguish the conditioned response to those stimuli by presenting those stimuli in the absence of drug. This would be most

effectively done within the total complex of the environment in which they occur; simply exposing the youth to the smell of the bakery away from the street comer on which he had previously experienced that smell may not be effective. This will necessarily be a long process with second-order stimuli as they tend to be relatively resistant to extinction. Once these steps have been taken, one must also recognize that only the probability of relapse has been reduced, while other factors, such as the social component, must also be considered.

Knowledge of the environmental influence on drug abuse may also be important to any prevention programs. Early recognition and removal of stimulus factors contributing to the acquisition of drug-taking behavior may prove to be the most effective method of treatment.

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Human Drug Taking Under Controlled Laboratory Conditions

Marian W. Fischman, Richard W. Foltin, and Joseph V. Brady

INTRODUCTION

Great strides have been made during the past 10 to 15 years in developing procedures for studying drug self-administration under carefully controlled laboratory conditions. Much of this methodology, however, has focused on responding maintained by contingent delivery of drug to nonhuman laboratory subjects. It has been found that animals will work for drugs delivered via the oral, intravenous, smoked, and intramuscular routes of administration under a broad range of experimental conditions. However, research into human drug taking has received less attention until fairly recently. Clearly, some laboratories (Johanson and Uhlenhuth 1980; Griffiths et al. 1980; Bigelow et al. 1976; Mendelson et al. 1976) have pioneered in the study of drug taking in humans under carefully controlled conditions, but, in general, much of what we know about drug taking in humans is derived from anecdotal and observational data.

Drug self-administration in the United States has become an increasingly formidable problem. Efforts to date have not been as successful as one might like in either dissuading young users from experimenting with drugs or in helping established users stop their drug taking. Prevention programs can best be designed only with a better understanding of the variables controlling drug taking in humans. In order to understand these variables, we must study the behavior in question (i.e., drug self-administration behavior), in context, under controlled laboratory conditions. A substantial amount of data exist delineating some of the variables controlling drug self-administration in nonhuman laboratory animals. It is logical, therefore, to utilize some of those procedures, noting where the data converge or diverge. Based on the results of these studies,

cross-species comparisons can be made and data unique to human drug taking highlighted.

The data presented in this paper were collected on human volunteer research subjects in two laboratories: a traditional behavioral pharmacology laboratory, utilizing nonhuman laboratory methodology to extend the self-administration data base to humans; and the other, a laboratory in which subjects reside under naturalistic conditions for periods of several weeks. It is in the residential laboratory that we can best focus on the broad spectrum of stimulus conditions that play a role in drug taking. Continuous, long-term residence provides for control over extraneous influences unrelated to the experimental manipulations. Under these circumstances, the effects on drug self-administration of systematic manipulation of a range of variables, as well as the effects of the drugs being self-administered, can both be studied under conditions closely approximating those in which these drugs are generally self-administered outside of the laboratory. Ideally, It should therefore be possible to investigate variables parametrically in the structured, highly controlled behavioral pharmacology laboratory environment, and then to examine the generality of those Rndings under conditions of continuous residence, where fewer stimulus conditions are controlled and where the influence of interacting contextual factors and behavioral contingencies can be analyzed experimentally.

LABORATORY STUDIES OF DRUG SELF-ADMINISIRATION IN HUMAN SUBJECTS

Cocaine Self-Administration

Cocaine, clearly a drug of abuse and one that has become a major public health problem, has been carefully examined under controlled laboratory conditions (Fischman 1984). Laboratory animals, including rats, cats, dogs, monkeys, and baboons, will self-administer this drug via a number of different routes and over a broad range of experimental conditions (see Johanson (1984) for a review), as will humans outside of the laboratory. A self-administration procedure found useful for the study of drug taking in nonhumans has been developed to investigate the reinforcing properties of cocaine and related compounds under carefully controlled conditions in humans. Data from studies such as these can provide information about the effects of the drug when it is taken in patterns approximating those seen “on the street.” In addition, it is possible to manipulate variables (e.g., dose, cost, route of administration) and evaluate the

effects of such manipulations on drug taking. Such data are clearly of utmost importance in designing treatment and prevention programs.

Subjects in these cocaine self-administration studies were carefully screened volunteers, each with a history of cocaine use. Each subject resided on a Clinical Research Unit for the duration of his or her 2-week study and were tested daily in experimental sessions lasting up to 4 hours. Subjects were allowed to choose between an intravenous injection of two different solutions: saline vs. drug or two doses of drug. On the first day of each 2-week study, the subjects were told that the right-hand response button and light were associated with a specific drug solution, and the left-hand response button and light were associated with another specific drug solution. Subjects were required to press a response button a fixed number of times in order to receive an intravenous injection. The first response was an irreversible choice, and the light over the unselected button was turned off. Each intravenous injection was 60 seconds in duration, during which time an additional injection was not available. During each session, a number of physiological measures, including heart rate and blood pressure, were monitored continuously. Prior to each injection, and immediately after a drug choice, a blood sample was withdrawn for cocaine blood level assay, and a series of questionnaires designed to evaluate self-reported moods, sensations, etc., was completed.

In these studies, cocaine was compared to saline, and high doses were compared to lower ones. The positions associated with the sampled solutions remained the same on any one day, but were reversed frequently so that position preferences would not influence the results. Cocaine was consistently chosen over saline, and higher doses were generally selected over lower ones.

Figure 1 summarizes the data collected during a l-hour session for subject 53, who was given a choice between 16 and 32 mg intravenous cocaine. Drug was requested seven times over the hour in a fairly evenly spaced fashion. (Longer studies, in which subjects regularly seld-administered cocaine for several hours with similar paced administration, have been carried out.) Although most choices by this subject were for the 32-mg dose of cocaine, there was one 16-mg injection on this day. Blood levels showed predictable increases with each cocaine injection. Heart rate showed a large initial increase, which plateaued after the initial two to three injections of cocaine, and then began to show a downward trend

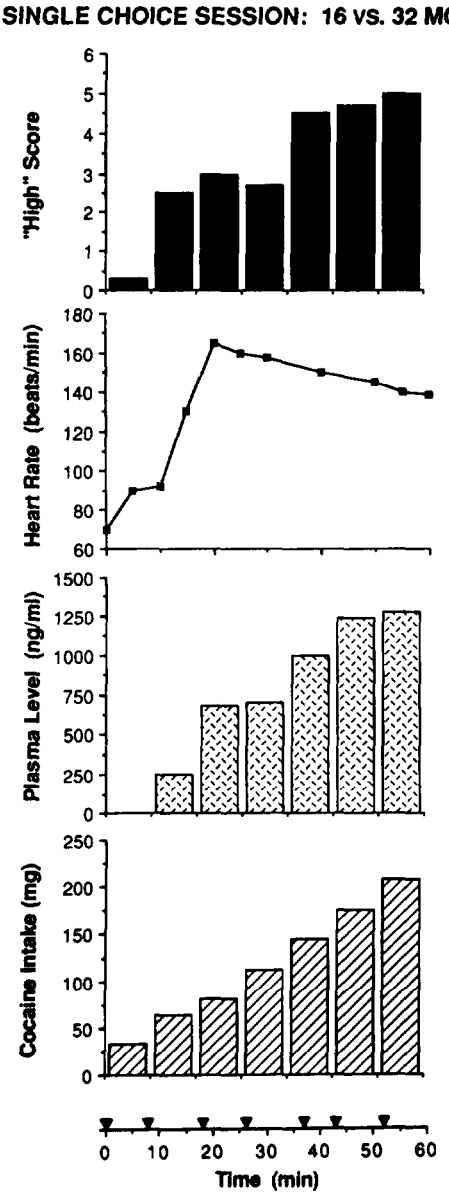

FIGURE 1. *Selected data collected during a 1-hour cocaine-choice session*

NOTE: Doses of 16 and 32 mg intravenous cocaine were available, and drug choices are indicated by arrows.

toward baseline. Subjective reports differed, depending on the measure, but in all cases, the maximal effects were seen after the initial infusions of 32 mg. For example, self-ratings of "high" (as measured on a visual analog scale) essentially leveled off after the first four infusions, despite the fact that a ceiling (of 10) had not been reached. These data indicate that subjects report diminishing effects following repeated administration of a single dose of cocaine. If cocaine taking is controlled, at least in part, by its subjective effects, cocaine users would be required to increase their doses to maintain these effects during a binge, thereby exposing themselves to potentially more toxic dose ranges.

The pharmacological profile of cocaine's action describes a drug with substantial direct reinforcing properties. Clearly, however, it is not only a drug's pharmacological properties which control its use. A variety of environmental conditions, including stimulus cues, consequences of use, period of availability, etc., play a role in controlling drug taking in humans. Investigation of these variables can more readily be carried out under the conditions occurring in a relatively more naturalistic laboratory environment.

The Programmed Environment Residential Laboratory

The Programmed Environment is a residential laboratory designed for continuous observation of human behavior over extended periods of time (see Brady et al. (1974) for a complete description). The laboratory, diagrammed in figure 2, consists of five rooms connected by a wmmon corridor. The three identical private rooms are similar to small efficiency apartments with kitchen (stove, refrigerator, sink, and preparation area); bathroom facilities: a bed, desk, and chair; and other typical furnishings. The social area is equipped with tables, chairs, sofa beds, storage cabinets, and a complete kitchen facility. The workshop contains benches, stools, storage cabinets, tools, exercise and recreation equipment, and a clothes washer and dryer. A wmmon bath serves the workshop and social area. Access to the exterior walls of the laboratory is provided by a corridor which encircles the environment between the residential chambers and the exterior building shell. This permits transfer of supplies and materials through storage facilities (drawers and cabinets) accessible from both sides of the inner walls. Thus, experimenters can introduce or remove supplies and material as required. Access to supplies, activities, or areas can be carefully controlled by the experimenters. Each room of the laboratory has one door which

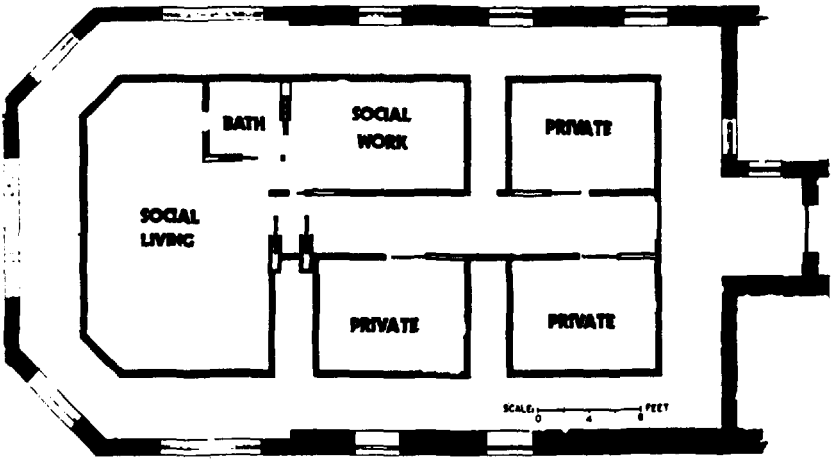

FIGURE 2. *Diagrammatic representation of the floor* plan of the *programmed environment and its arrangement within the external building shell*

remains unlocked at all times in case of emergency or subject termination of participation.

An experimental control room, containing computers and audiovisual equipment for monitoring, programming, recording, and data analysis, is linked to a video display terminal in each of the private and social rooms, allowing for communication between the experimenter and each subject. The communication system in each apartment can also include a telephone intercom system for exchanges among all subjects when this is appropriate. Audio and video equipment in each room of the programmed environment permit continuous monitoring of each subject's activities during the experiment. Except for when they occupy the private space around the bed and bathroom areas, subjects are under continuous observation from the control room. A sophisticated computerized observation program provides the structure for continuous recording and categorization of each subject's behavior (Bernstein and Livingston 1982).

Marijuana Self-Administration

Laboratory research on drug self-administration has often been subject to the criticism that the conditions are not those most commonly in effect when a drug is ingested under "natural" conditions. Marijuana, in particular, is frequently smoked within a social context, and the interaction of the marijuana smoker with his or her extended environment must therefore be considered.

In the laboratory, the drug is most frequently administered to the subject under conditions in which there is typically a minimum of conversation between the experimenter and subject or, under more social conditions, between subjects. When marijuana is smoked socially outside the laboratory, individuals often pass the cigarette from one to another, with no restrictions on communication. Interactions within the group can clearly modify the behavior of the individual under such conditions. Experimental studies under these more "natural" conditions, in which a natural flow of behavior occurs, might well yield results different from those obtained in relative isolation. The few studies investigating this suggest that differential effects are likely to occur under private and social conditions.

Drugs are self-administered under a variety of conditions and according to a broad range of patterns. The behavioral contingencies in effect at the time no doubt determine, to some extent, the amount and patterning of the self-administration. It is also possible that, under conditions where subjects are allowed to control the pattern of their drug self-administration (i.e., frequency and timing), different effects will emerge. For example, perhaps a drug will not be self-administered when productive and efficient performance is required, but will be when no consequences are attached to behavioral output.

Marijuana self-administration was studied under the relatively natural but highly controlled conditions made possible in the Programmed Environment residential laboratory and under conditions in which it could be smoked privately as well as in a social situation. The subjects in this study were healthy, adult male volunteers ranging in age from 23 to 34. They passed extensive medical and psychiatric examinations prior to research participation and signed consent forms following a detailed explanation of the experimental procedure.

Subjects were awakened at 9 a.m. and each received a box containing a wide variety of snack and breakfast items which were available all day and evening. The experimental day began at 9:45 a.m. and was divided into two equal parts: a 7-hour private work day and a 7-hour social access evening period. Between 9:45 a.m. and 4:45 p.m. (16:45), subjects were required to remain in their private rooms and engage in one of four work tasks. These were: a computerized vigilance task, a computerized digit-symbol substitution task, a manual latchet-rug-hooking task, and a manual word-alphabetizing task. Subjects had the option of performing any of the four available tasks, although they were required to perform one of them at all times other than during a required 30-minute break when lunch items could be requested. Between 5:00 (17:00) and 11:45 p.m. (23:45), subjects could remain in their rooms and engage in a variety of individual activities, including reading, writing, artwork, etc., or they could move to the social areas where interactive group activities and games were available. Frozen dinners were available during this period, and no limit was placed on the number that could be obtained. The experimental day ended at midnight with lights out. (Structuring the day and providing appropriate contingencies are important for keeping volunteers in studies in which they are expected to maintain continuous residence in the laboratory for periods of several weeks. This standardization of session lengths facilitates experimental observation and data interpretation.)

Each behavioral activity was monitored continuously with the computerized behavioral observation system, and, for each subject, time spent in each of the work activities was measured during a 4-day baseline period. A time-based activity hierarchy was determined for each subject and provided the basis for contingency conditions. A ratio of time spent in the most preferred work activity to time spent in the least preferred activity was calculated, providing a basis for a contingency ratio (Premack 1965). The ratio was used to determine how much time the subject would have to spend engaged in his least preferred activity in order to have time to spend doing his most preferred activity. The contingency required that subjects engage in four times the amount of their least preferred baseline activity (the instrumental activity), in order to maintain baseline levels of their most preferred activity (the contingent activity). Subjects were told that they did not have to engage in either of the two designated activities, but if they did, they would have to earn time to do the most preferred activity by engaging in the least preferred activity. Subjects did not have to use the time immediately. They could accumulate time in a bank account and use

it later, as long as they used it within the several-day contingency period. During contingency periods, nonavailability of the contingent task was indicated by illumination of a red light in each subject's room.

Food intake was also monitored throughout the course of these studies. Subjects sent a message via the networked computer system whenever they ate or drank anything, and time and amount of all food consumption were recorded. These data were verified through observation. Previous research in this facility has shown that this message sending does not disrupt eating patterns and gives accurate information on pattern of caloric intake during the day (Foltin et al. 1966).

Standard 1-gm active (1.84-percent THC concentration) marijuana cigarettes, provided by the National Institute on Drug Abuse, were smoked in accordance with an experimenter-controlled uniform puff procedure, which allowed for five puffs per cigarette (Foltin et al. 1986). After lighting the cigarette, subjects responded to colored stimulus lights signaling, in sequence, a 5-second "ready" period, a 5-Second inhalation period, a 10-second period to hold the smoke in the lungs, and a 46-second period to exhale and await the next puff. Subjects were told that they could request and smoke a marijuana cigarette at any time during the day. Cigarettes could be smoked in the private rooms (9:45 to 23:45) or in the social room during the social access period (17:00 to 23:45). A maximum of five cigarettes would be available each day. They did, however, have to smoke them in accordance with the experimenter-controlled puff procedure. The study was divided into three 4-day periods, with no work contingencies in the first and third periods and a work contingency present during the middle 4-day period (days 5 to 8). Active marijuana cigarettes were available on the middle 2 days of each period. Thus, marijuana could be smoked on days 2, 3, 6, 7, 10, and 11. There was a work contingency in effect during days 6 and 7 of the marijuana availability schedule.

Despite the fact that no clocks or other indicators of time were available, subjects generally smoked the maximum number of cigarettes available, In a regularly spaced pattern (see figure 3). With few exceptions, three cigarettes were smoked during the social access period and two during the private period.

Subjects 1 and 2 always smoked their social period cigarettes in each other's presence, and marijuana availability and consumption

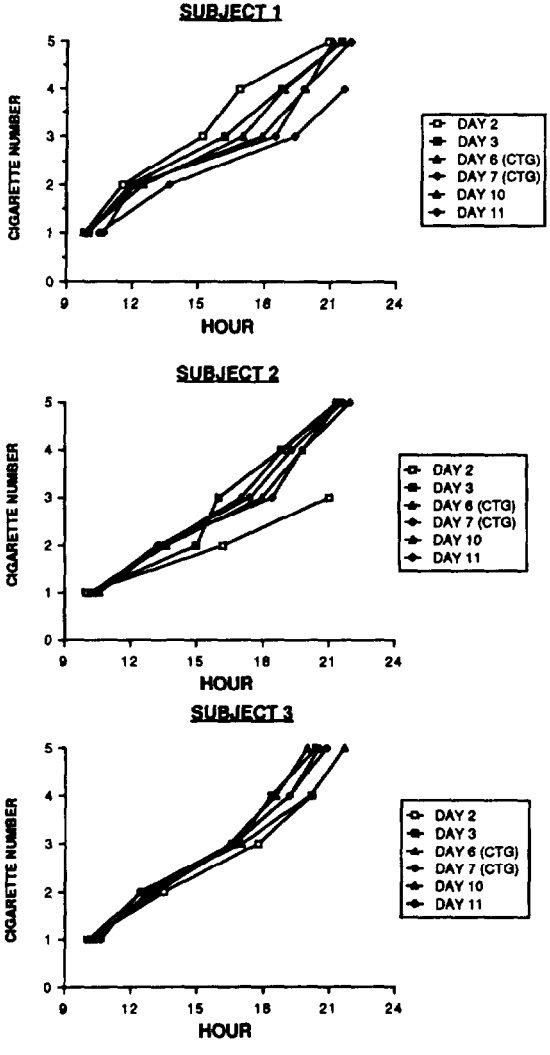

FIGURE 3. *Marijuana cigarette self-administration as a function of time of day over 6 days of active marijuana cigarette availability*

were associated with substantial increases in time spent in social interaction. Under conditions of no marijuana availability, these subjects spent an average of 48 minutes +4 minutes) interacting, while during periods of marijuana availability, these two subjects increased their social interaction time to an average of 225 minutes

(±5 minutes) or 3 3/4 hours. The third subject smoked all marijuana cigarettes in his own room and rarely interacted with the other two subjects.

Self-administered marijuana also had an effect on food consumption, as has been indicated in numerous anecdotal reports, for two of the three subjects, with increases for one subject from 3,000 to 4,200 Kcal (a 40-percent increase), and from 3,400 to 4,500 Kcal for the other subject (a 32-percent increase). Therefore, self-administration of one substance, marijuana cigarettes, had an effect on the self-administration of a second substance, food (Foltin et al. 1986).

These data indicate that, when marijuana is made available under relatively naturalistic living conditions, subjects will self-administer it in a regular pattern which does not change significantly over days despite changing behavioral contingencies. Thus, like cocaine self-administration, marijuana self-administration, measured under carefully controlled, limited-access conditions, was regular and consistent from day to day. The pattern of use, however, was correlated with changes in experimental conditions and suggested that time of day, passage of time, or perhaps THC blood level could affect drug intake. For two subjects, social interaction was increased by marijuana smoking, but this was not a necessary consequence for all subjects (Foltin et al. 1986). Subjects went about their daily activities appropriately, following the rules for work behaviors as indicated in their protocols whether or not they smoked marijuana.

When drug dose is manipulated in laboratory animals self-administering that drug, animals generally compensate by increasing or decreasing their intake. Although such studies can be carried out under conditions comparable to the one just described, we have not yet done so. We have, however, investigated the regulation in intake of another substance-food (Foltin et al. 1988). The procedure and results are interesting, and point to the utility of the design for parametric manipulation of drug doses in self-administration studies with humans.

Three healthy, non-drug-using male volunteers participated in a 15 day study in which the same basic daily schedule as described above was in effect. Two different food conditions were used. On days 1 to 5 and 12 to 15, a box of food in which no caloric manipulations were made was given to each subject every morning. This box contained snack items such as cookies, candies, chips, etc.: breakfast items such as cereal and fruit; lunch items such as sandwich foods,

frozen small meals, etc.: dinner items such as frozen dinners, and accompaniments such as salad, pudding, bread, etc.; and beverages such as juices, sodas, and milk. Days 6 to 11 were reduced-calorie days, and substitutions were made in about 33 percent of the items such that comparable reduced-calorie items were substituted for higher calorie items. For example, a regular-calorie frozen spaghetti and meat sauce item was replaced with a reduced-calorie frozen spaghetti and meat sauce item, from the same manufacturer and in exactly the same packaging, but containing 60 percent of the calories in the regular meal. Diet soda was substituted for regular soda, reduced-calorie pudding for regular-calorie pudding, diet cheese for regular cheese, etc. Subjects were not told of the calorie manipulation until the termination of the study, and no subject reported noticing any differences in the food over the course of the study. Data from days 1 and 2 were not included in the analyses. Two of the three subjects compensated for this calorie manipulation and, in general, the compensation occurred during the social access period (figure 4).

The foods for which calories were manipulated are shown by the open portions of the bars. For subjects 1 and 2, baseline shifted over the course of the study, but there was a clear increase in the amount of regular-calorie food consumed on days when calories were manipulated. The increase is less clear for subject 3. For all subjects, the increased food intake occurred during the evening social access period when behavioral requirements were less structured. This is the same period during which the majority of marijuana cigarettes were smoked in the study described for marijuana self-administration above. Even this limited degree of generality suggests the importance of examining the cues for substance use during this time period and under these stimulus conditions.

The food intake data were collected under conditions in which sub jects were engaged in a variety of activities and were neither food deprived nor informed of the caloric manipulations. Despite this, food intake was both remarkably consistent over days and sensitive to the experimental manipulations. The stimulus cues for eating were variable and no doubt changed over the course of the day and the environmental conditions. Although the procedures of this study do not permit a partitioning of the multiple potential determinants of substance use, the design does, however, approximate conditions in the natural environment, and future studies might address potential determinants with greater precision.

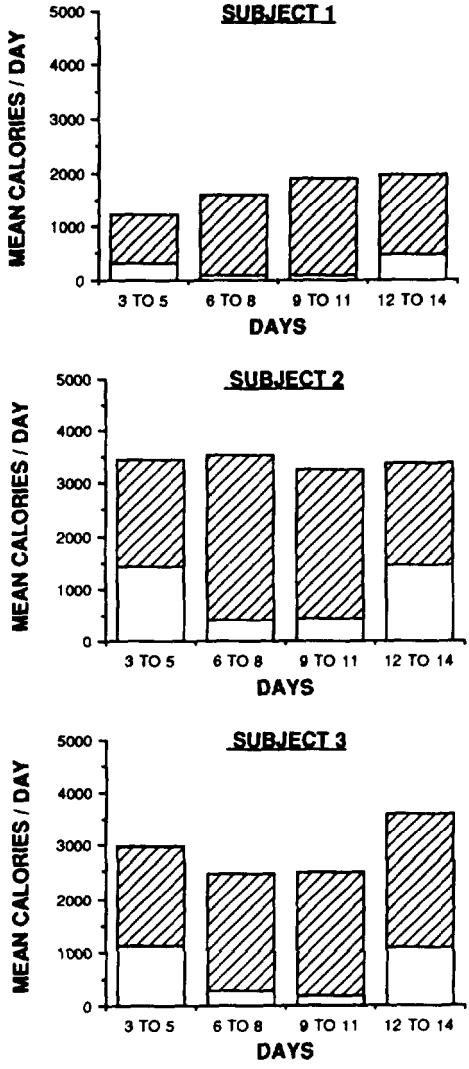

FIGURE 4. *Mean daily caloric intake from calorie-manipulated* (open bars) and regular (hatched bars) *foods* as a function of period of the study

NOTE: Reduced-calorie foods were substituted on days 6 to 11.

SUMMARY

The data presented point to the importance of studying drug effects under the conditions in which those drugs are taken outside of the laboratory. Interactions between the reinforcing and other direct effects of these drugs, as well as their interactions with ongoing environmental events, can only be evaluated under such conditions. Tolerance to cocaine's effects which can lead to a potential for increased toxicity, the regularity of both cocaine and marijuana self-administration under both stable and varying environmental conditions, and the regulation of caloric content of food all are important factors in understanding (and therefore being able to manipulate) substance use and abuse. These data also support the utility of a residential research facility for the investigation of substance use under conditions that approximate those in which people live outside of the laboratory. Thii unique laboratory, designed for continuous observation of human behavior over extended periods of time, provides a carefully controlled research environment with flexibility for establishing a range of subject behaviors and recording both individual and social behavior patterns. We can study regulation both within a day and over days, assessing the effects of experimental manipulations on the patterning of self-edministration behavior. The design of such studies is a logical extension of those reported in the animal laboratory as well as those carried out in a more traditional human behavioral pharmacology laboratory.

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