Addictive Behavior With and Without Pharmacologic Action: Critical Role of Stimulus Control

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INTRODUCTION

Addictive behavior with respect to drugs often is viewed as the consequence of a biologic action that has its principal origin in the exposure of a subject to the central nervous action of a drug. One objective of this chapter is to refer briefly to evidence that drug abuse is a special case of excessive behavior that typically develops out of, and is sustained by, an antecedent context that can generate a variety of disturbed and excessive sorts of behavior. Drug abuse is often only one feature of this broader picture of behavioral difficulties displayed by an afflicted individual. Conversely then, by this view drug addiction has its major origins and maintaining conditions in environmental antecedents, rather than being the result of specific drug receptor interactive consequences.

A second, more specific aim is to describe a few experiments that begin to clarify how discriminative stimuli (S^Ds) accompanying the occurrence of excessive behavior with respect to one commodity can lead to the persistent selection of an alternative commodity (e.g., a drug) when such S^Ds are presented in proximity to this second commodity, even in the presence of both commodities.

In previous research, several species of animals have been exposed to intermittent schedules of food pellet delivery, resulting in the induction of concurrent, excessive behaviors (Falk 1971, 1981). Although various, noningestive behavioral excesses have been explored (e.g., aggression, escape, hyperactivity), an ingestive alternative, schedule-induced drug intake, has proven useful in evoking chronic, excessive drug-solution drinking, as well as facilitating otherwise weak intravenous (IV) self-injection behavior (Falk 1993; Falk and Tang 1988). In the present experiments, schedule-induced polydipsia was used to provoke chronic and excessive fluid intake upon which drug overindulgence could develop. In a common arrangement used in the author s laboratory, food pellets are delivered to a deprived rat once per minute during daily, 3-hour sessions, which results in a concurrent overdrinking: a polydipsia of about 100 mL. This is in contrast to the regulatory drinking over 3-hours occasioned by the same number of pellets when they are presented all at once at the beginning of the period: about 10 mL. Schedule-induced

polydipsia is, then, a behavioral, not a physiologic, phenomenon (Falk 1969).

In the IV drug self-administration arrangements used in many animal experiments, the baseline IV saline (vehicle) self-injection rate usually is quite low compared to rates occasioned by substituting drugs with reinforcing potential (Johanson and Balster 1978; Schuster and Thompson 1969). In contrast, the schedule-induced oral intake of water (vehicle) is already excessive. Any additional reinforcing effect afforded by the introduction of a drug into the drinking fluid must be detected against this background of behavior that has *already become excessive* owing to the inducing environmental conditions. An assumption underlying the use of this preparation as an arrangement that illuminates the source and persistence of drug abuse is that, owing to an individual s history and current environment, excessive behavior is likely to be occurring prior to the initiation of an abusive interaction with one or more drugs (Kandel et al. 1985; Tarter, this volume). The conspicuous excessiveness of baseline behavior prior to the introduction of a drug presents an analytic challenge. It is necessary to distinguish between the reinforcing efficacy afforded by the inducing environment and the reinforcing efficacy that might derive from the action of an introduced drug. Although the necessity of making this distinction usually does not occur with the use of the IV drug self-injection procedure, nevertheless, when either an intermittent food or a drug self-injection schedule was available to rhesus monkeys, concurrent, adjunctive IV saline self-injection was persistently maintained (Grant and Johanson 1989; Nader and Woolverton 1992). With oral drug self-administration by rats, various methods have been used to determine whether the availability of a drug solution adds a unique controlling feature to behavior that is already present in excess (Falk 1993).

One obvious arrangement was to allow animals to choose between two concurrently presented fluids under a chronic schedule-induction condition: a vehicle and a drug solution, with the relative left-right positions of the fluid reservoirs alternated or randomized across days. Rats overwhelmingly chose the 5 percent ethanol solution in preference either to water or to dilute glucose solutions (Samson and Falk 1974; Tang and Falk 1977). However, under similar conditions, when animals had cocaine solution and water concurrently available, drinking occurred mainly from the fluid presented at a specific location, a so-called side preference (Falk et al. 1990). Although cocaine concentration was systematically varied, there was no evidence of the development of a preference for the drug. Even though cocaine polydipsia occurred every other day, when cocaine was presented on the preferred side, and elevated serum cocaine concentrations of about 200 ng/mL

resulted, preference failed to develop. Only after cocaine had been available in a compound saccharin-glucose (sac-gl) vehicle, and the vehicle was subsequently slowly changed back to water, was there some evidence for the development of a preference for cocaine.

At this point the issue of whether there may be more involved in the genesis of drug addiction than simply bringing a subject into continued, self-administration contact with an agent possessing a potential for abuse. Although drug solutions have easily discriminable, gustatory effects, additional S^Ds might be required to develop drug preference owing to the generally slower pharmacokinetics of orally self-administered drugs. The success of the ethanol preference experiments may be atypical, since the preference for low concentrations of ethanol to water under a variety of conditions has a gustatory, rather than a pharmacological, explanation. Meisch and his associates (Meisch et al. 1990) were able to transform the preference of rhesus monkeys for an ethanol solution into a preference for cocaine solutions by gradually reducing the ethanol concentration of the solution while increasing the concentration of cocaine, with the position of the drug-solution alternative indicated by a distinctive S^D light. In addition, fluids were made available only contingent upon fixed-ratio (FR) behavior. The following experiment used rats and the schedule-induced polydipsia technique, but incorporated three of the features used by Meisch and colleagues (1990): ethanol preference history, cocaine solution position indicated by an S^D light, and fluid available contingent upon operant responding.

STIMULUS CONTROL AND THE ACQUISITION OF DRUG PREFERENCE

When rats were allowed a history of preferring an ethanol solution to concurrently available water under a schedule-induced polydipsia condition, drug preference was maintained when the solution was gradually changed from ethanol to cocaine (Falk and Lau 1993). In this situation, the animals were given daily 3-hour sessions: concurrent fixed-interval (FI) 1 minute (food), FR6 (water), and FR6 (drug solution). The daily position at which the drug solution was available varied, and its location was indicated by the adjacent presence of a small S^D light. An overwhelming preference for cocaine solution was maintained as was the excessive intake level. Subsequently, caffeine solution was gradually substituted for cocaine solution, and then nicotine solution for caffeine solution. In each case there was a virtually complete preference for the drug solution to water (figure 1). A return to an ethanol preference condition was followed by the gradual substitution of lidocaine solution for ethanol. Lidocaine solution

also was preferred to water (figure 1). Although ethanol, cocaine, caffeine, and nicotine are all known to function as reinforcers, lidocaine has not so functioned, nor is it known to be abused. Except for the initial preference for ethanol solution to water, the likely explanation of the other preferences for drug to water is that they were attributable to the associative history of the S^D with the ethanol solution. After this association, animals continued to choose and ingest the fluid indicated by the S^D, even when that fluid was lidocaine solution. Even more dramatically, in a later stage of the experiment, when the S^D simply indicated an alternative source of water rather than a drug solution, these animals had an almost complete preference for the S^D-indicated source of water compared to the alternative source of water (not shown in figure 1).

PERSISTENCE OF STIMULUS CONTROL OF PREFERENCE WITH AND WITHOUT PHARMACOLOGICAL CONSEQUENCES

The efficacy and durability the S^D had in initiating and continuing to determine the polydipsic choice of several drugs suggested that environmental S^Ds are critical for the development and maintenance of drug abuse. The next experiment was designed to ascertain several features of the S^D control of excessive intakes: (1) the durability of the S^D control of intake when drug content was discontinued, (2) the ability of gustatory properties of a drug solution to serve an S^D function, and (3)-determination of whether a gradual transformation of one S^D controlling condition into another one is a necessary feature in effecting a transfer of how the environment evokes the seeking and taking of drugs, or whether an abrupt S^D change also would permit transfer of control.

Rats from four groups (N = 8 each group) were exposed to a fixed-time (FT) 1-minute food-delivery schedule (FT 1 min) for 3-hour sessions, with one or two sources of fluid freely available (Falk and Lau 1995). For 3 to 4 weeks, a single fluid, 2.5 percent ethanol, was available during the session and was presented at a position to the left or the right of the center position on one panel of a chamber. Drug solution position always was indicated by illuminating an S^D light next to the drinking spout. The FT 1-minute schedule induced a concurrent polydipsia during each session. Two fluids were made available during sessions for the next 2 weeks, 2.5 percent ethanol and water, with the same drug positioning and S^D procedure remaining in effect. Following the establishment of chronic ethanol polydipsia and preference, the composition of the drug solution was altered. Over a 1-month period, its ethanol content was gradually reduced to zero while cocaine concentration was increased to 0.16 mg/mL. This final

cocaine concentration, unadulterated with ethanol, was presented for 16 sessions. The first group of eight rats is shown in figure 2 (top). The leftmost bar shows that 2.5 percent ethanol was preferred to water almost exclusively. The second bar shows the results for the 16-session period for which 0.16 mg/mL cocaine solution and water were concurrently available for ingestion. Cocaine solution was preferred to water almost exclusively. The preference for ethanol to water, and for cocaine solution to water, are features of the remaining groups (figures 2 and 3), which show the results for the other groups. Cocaine milligram per kilogram intakes were similar across the groups and agree with values from the author s previous research presenting this concentration (Falk and Tang 1989; Falk et al. 1990).

After this preference for cocaine solution to water had been maintained for 16 sessions, the groups were then given different treatments, although

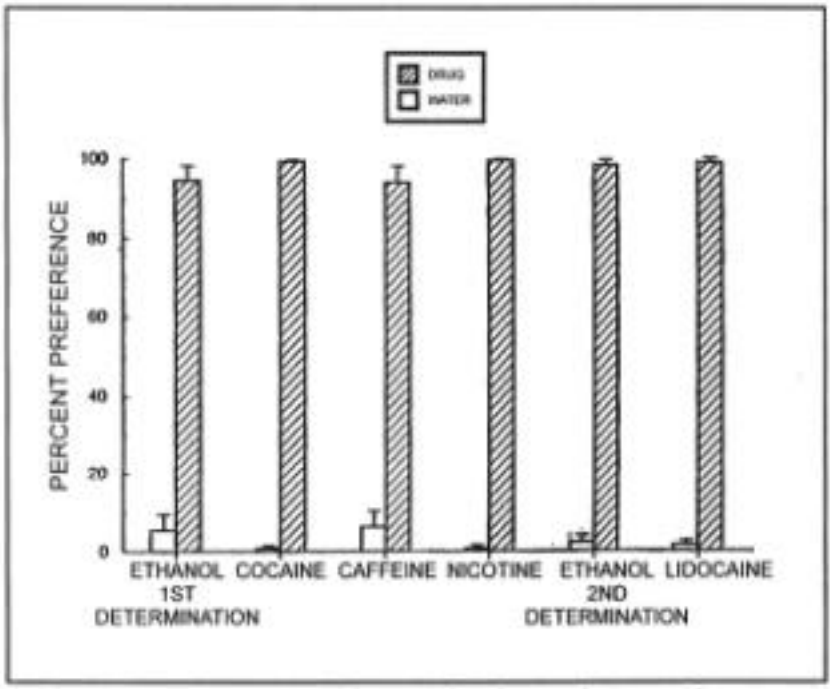

FIGURE 1. *Percentage preference for drug solution and water (concurrent FR6 schedules of 30-s access) under a schedule-induced polydipsia condition (FI 1-min food-delivery schedule). N = 7 animals. Ethanol = 2 percent (v/v); cocaine = 0.16 mg/mL; caffeine = 0.1 mg/mL; nicotine = 0.01 mg/mL; lidocaine = 0.11 mg/mL.*

all continued to receive FT 1-minute schedule-induced polydipsia sessions daily. For the S^D-fade group shown in figure 2 (top), the same fluid choices were continued, but the intensity of the S^D light associated with cocaine was gradually reduced over a 4-week period from full intensity (visual fader setting = 10) to off (fader setting = 0), and then remained off for an additional 4 weeks. Most of the animals continued to show a strong preference for cocaine solution during S^D fading, and the preference remained high for the 4-week exposure period after the completion of S^D fading. (One animal developed a fluid position preference at and beyond fader setting 8.0.) The oral self-administered dose of cocaine is shown by the filled circles and the scale on the right-hand ordinate.

For the cocaine-fade group (figure 2, bottom), the S^D light remained at full intensity, but the cocaine concentration was gradually reduced over a 4-week period from 0.16 to 0 mg/mL, and remained at zero for an additional 4 weeks. The cocaine-fade group continued to prefer the cocaine solution (which was proximate to the daily position of the S^D light) during solution concentration fading, and preference for the S^D-proximate fluid remained at its high-level for the 4-week exposure period after the cocaine concentration had been reduced to zero.

Neither group showed extinction of its preference, nor did the polydipsic intakes of either group decrease. The S^D-fade results demonstrated that a stable, chronic preference for cocaine solution can be maintained in the
absence of the visual S^D if the S^D is gradually faded. The cocaine-fade results indicate that a stable, chronic choice of a water source, which has become associated with the S^D light for cocaine, can be maintained when the cocaine content associated with the S^D is faded gradually.

In figure 3 (top), the center block of five bars indicates the preference for cocaine solution in successive 6-session blocks after the visual S^D was abruptly removed rather than gradually faded. Upon S^D removal, cocaine preference immediately fell precipitously, and out of the group of eight, the number of animals retaining an 80 percent or greater preference for the cocaine solution across the five successive 6-day blocks was: 2, 3, 3, 3, and 3. As a final 10-day control condition, both fluids offered were water, and all animals showed a position preference for the water that was offered in the right-hand position (rightmost bar).

Upon cocaine removal (figure 3, bottom, see the center five 6-session blocks), preference for the S^D-proximate water source fell gradually, and the number of animals retaining an 80 percent or greater preference for the S^D-proximate fluid source across the 5 blocks was: 6, 4, 5, 3, and 2-out of 8. As a final 10-day control condition, the S^D was removed, and all animals showed a position preference for the water that was offered in the right-hand position (rightmost bar).

To summarize, although this experiment demonstrated that, under an S^D condition indicating drug location, a preference for cocaine solution to water could be substituted for a previous preference for ethanol to water, the gradual fading of either the S^D intensity to zero, or the cocaine concentration to zero, left intact a strong preference for the unchanged stimulus condition, either the cocaine solution without the S^D, or the water associated with the S^D. The strong and stable preference, as well as the persistent, excessive level of intake in both cases, indicates that the maintenance of addictive behavior may be attributable as much to the S^D determination of self-administration behavior as it is to past or present pharmacological consequences. In both cases, the stimulus that remained unchanged after the other one was gradually faded (either the S^D light or the cocaine concentration), came to serve strong S^D functions with respect to ingestive preference. Whether the S^D-fade group, which continued to prefer cocaine solution, also continued this preference owing to a reinforcing effect of cocaine cannot be derived from this experiment, although previous evidence from this laboratory is consistent with such an interpretation (Seidman et al. 1992). The rate and amount of 0.16 mg/mL cocaine solution taken in the present

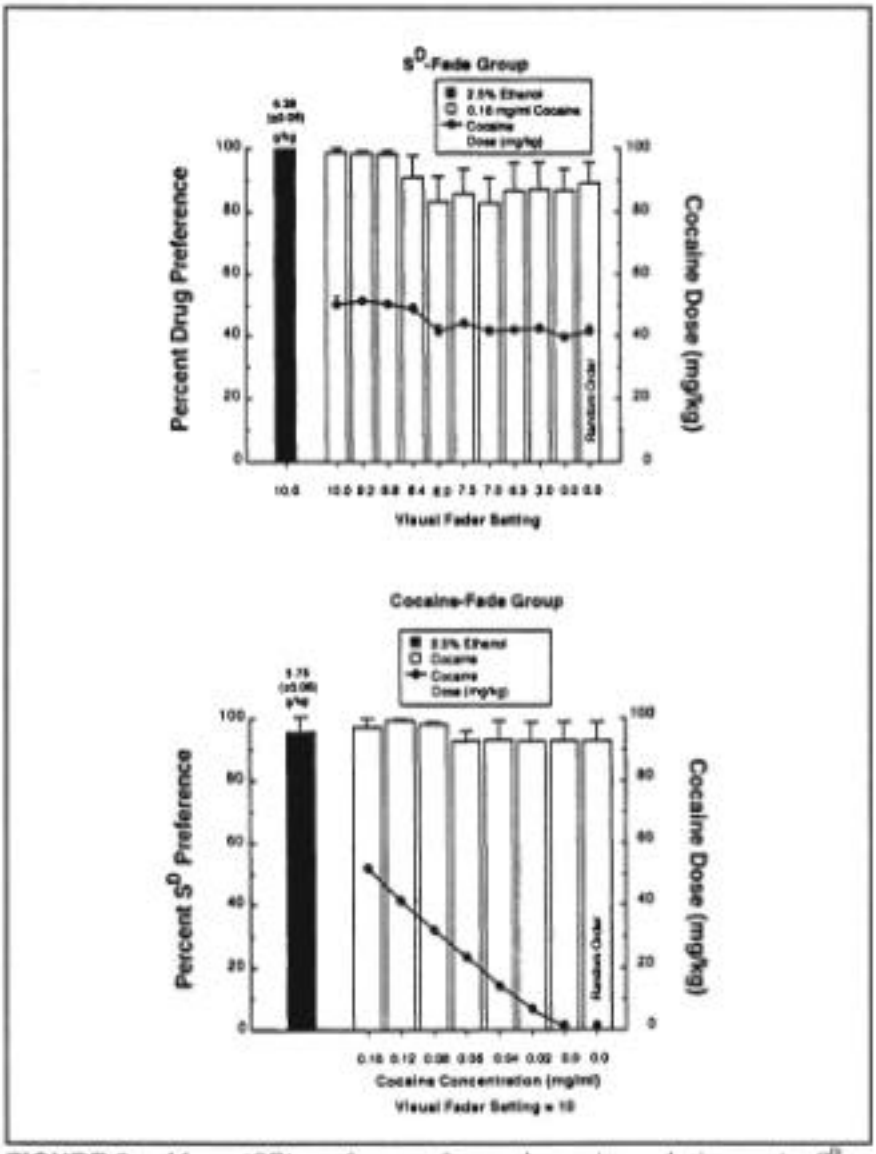

FIGURE 2. *Mean (SE) preference for oral cocaine solution as its S^D was gradually decreased in intensity over 4 weeks from 10 to 0 (top), and preference for S^D-indicated solution as its cocaine concentration was gradually decreased over 4 weeks from 0.16 to 0 mg/mL (bottom). Last two bars (right, top, and bottom) represent an additional 4 weeks for which the terminal condition was maintained. Daily session length = 3 h. N = 8 each group. Concurrent alternative fluid offered was always water. (Visual fader settings are values on linear 10-turn potentiometer.)*

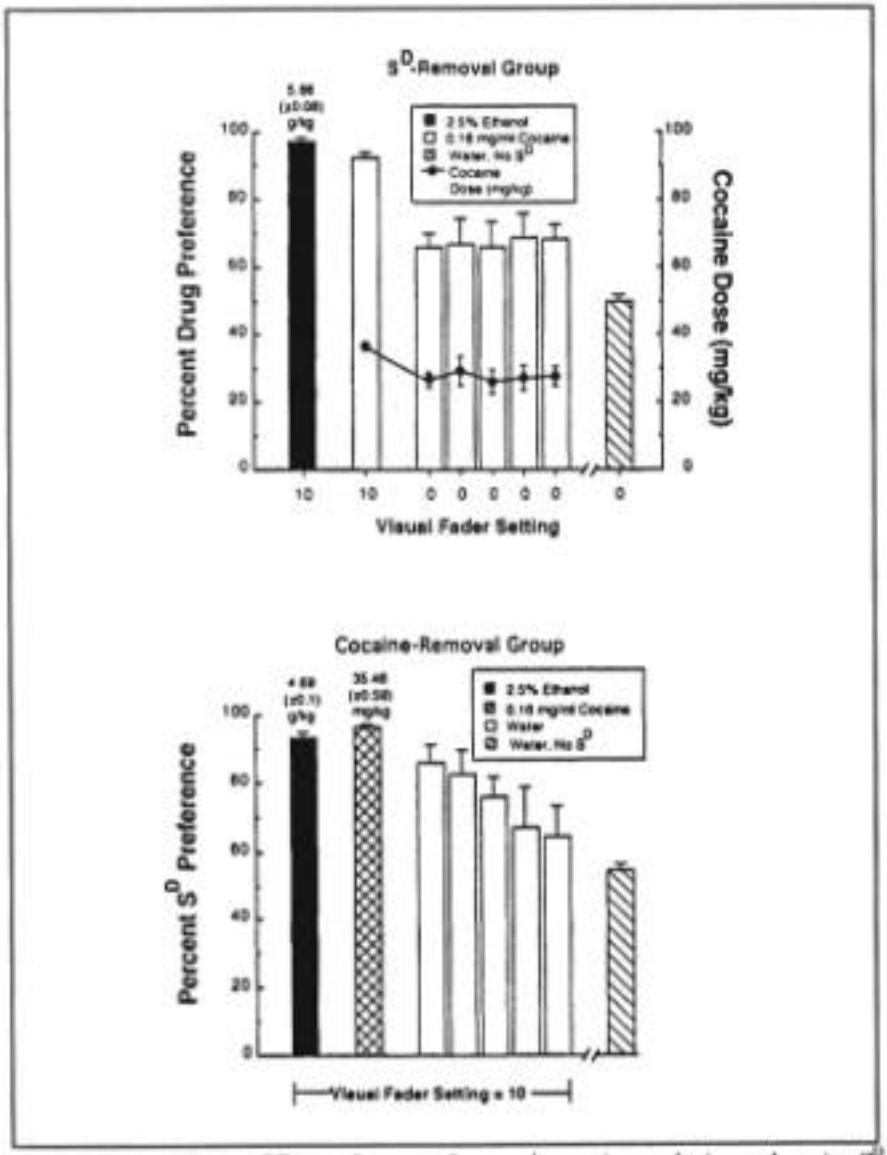

FIGURE 3. *Mean (SE) preference for oral cocaine solution when its S^D was abruptly decreased in intensity from 10 to 0, with middle 5-bar block composed of five consecutive 6-session means (top), and preference for S^D-indicated solution as its cocaine concentration was abruptly decreased from 0.16 mg/mL to water, with middle 5-bar block composed of 5 consecutive 6-session means (bottom). In both top and bottom, the rightmost bar shows final control condition offering water concurrently at both positions without the S^D. Daily session length = 3 h. N = 8 each group.*

experiments produced rat serum cocaine levels comparable to levels observed in humans chewing coca leaves, and was a level sufficient to reinforce behavior in rats as measured by the place-preference method (Seidman et al. 1992).

Within the groups for which the manipulated stimulus was changed abruptly, rather than gradually, individuals were much less likely to come under the enduring S^D control of the unchanged stimulus. The cocaine-removal condition actually left preference behavior more intact than did the S^D-removal condition, which produced a precipitous decrease in the preference for cocaine solution. The combined conditions for the abrupt-removal groups may be analogous to conditions faced by human drug abusers, for whom an abrupt discontinuation of the drug, along with a change in environmental S^Ds, leads to a dramatic and enduring decrease in drug addiction. This phenomenon was documented in the classic epidemiologic study by Lee Robins which found a rapid, unassisted recovery from heroin addiction by the great majority of addicted Vietnam veterans upon their return to the United States of America (Robins 1993).

PRODUCTION OF DRUG PREFERENCE BY AN S^D WITH A NONDRUG HISTORY

Up to this point, the efficacy of the S^D light for determining subsequent drug preferences had been instituted by first associating the S^D with the daily location of a preferred ethanol solution. The question arose as to whether the subsequent drug preferences were instances of animals acquiring polydrug abuse, or if the efficacy of the S^D to determine drug preference could be instituted by associating the S^D with the ingestion of nondrug fluids known to possess reinforcing efficacy in similar experi-mental contexts. The schedule-induced overdrinking of water itself had, some time ago, been demonstrated to be a reinforcing activity (Falk 1966). Rats receiving food pellets under a variable-interval 1-minute schedule of reinforcement developed polydipsia when the water, rather than being made freely available, was provided in small portions contingent upon completions of fixed ratios of lever pressing. Thus, under this schedule-induction condition, the opportunity to engage in water polydipsia was a reinforcing activity sufficient to sustain fixed-ratio behavior. The following experiment was performed to determine whether fluid polydipsia itself, if paired with the S^D light, would be a sufficient condition for instituting a preference for cocaine solution if the S^D was subsequently paired with the location of the cocaine solution.

Two groups of 80 percent body weight rats were given food pellets on an FT 1-minute schedule during 3-hour daily sessions. A

cocaine group (N-= 11) had one fluid, 0.16 mg/mL cocaine solution, available during each session. The daily left-right position of this solution was determined by a quasi-random sequence, and its position was indicated by an adjacent S^D light. A water group (N = 9) was treated similarly except that the available fluid was water. After 27 sessions, animals in both groups were then given a choice between two fluids for 21 sessions, with fluid position varied according to the same quasi-random sequence. The cocaine group was allowed to choose between drinking the 0.16 mg/mL cocaine solution, the position of which was still indicated by the S^D, and water. The water group was allowed to choose between drinking water, which was still indicated by the S^D, and another source of water.

The initial aim of the experiment was to determine if the opportunity to engage in schedule-induced polydipsia under S^D control was an activity with adequate strength as a reinforcer so that the S^D would acquire directive properties sufficient to determine a subsequent polydipsic fluid preference when two fluid sources became available. The results pertinent to this question are shown in figure 4 in the first pair of bars. For both groups, about one-half of the animals came under the control of the S^D light so that 80 percent or more of their polydipsic fluid intake was taken from the source indicated by the S^D. Thus, five animals from the cocaine group drank S^D-indicated cocaine solution in preference to water, and six animals from the water group drank from the S^D-indicated water in preference to the other water source. (These chambers had a moderate asymmetry so that one fluid source was a shorter distance from the pellet receptacle location than was the other one. This feature probably accounted for the position bias (side preference) observed for the other half of the animals. In a replication using an additional water group and symmetrically constructed chambers, all of the animals preferred the water source that was indicated by the S^D to the nonindicated water in the choice phase.)

An unpublished control study had shown that the above provision of a history of a few weeks of polydipsia from a single S^D-indicated water source was crucial for instituting preference for the S^D-indicated source as revealed by the subsequent fluid-choice condition. Naive animals were exposed to a schedule-induced polydipsia condition and a concurrent choice between an S^D-indicated source of water and water not so indicated. Daily fluid position was varied quasi-randomly, but without the initial history pairing polydipsia with the S^D under the single-fluid condition no preference for the S^D-indicated water occurred. Stated plainly, animals had no innate propensity to choose an S^D-indicated water source in preference to one without an S^D. It can be concluded, then, that daily pairing of the S^D with either a cocaine-solution

polydipsia or a water polydipsia is sufficient to endow the S^D with the capacity to determine that the S^D-indicated fluid will be ingested preferentially in a subsequent polydipsic fluid choice situation.

The next phase of this experiment ascertained whether the efficacy of this S^D to control fluid choice was capable of initiating a drug preference. In the present context, this was a question of whether the current power of the S^D, which controlled the choice of water source for six animals in the water group, could come to initiate a cocaine preference for these animals. Figure 4 (second set of bars) shows that when these water-history animals were presented with a choice between an S^D-indicated cocaine solution and water for 10 days, five of the six preferred 0.16 mg/mL cocaine solution to water. The animals in the cocaine group were exposed to an increased concentration of cocaine (0.24 mg/mL) and maintained their preference for cocaine solution to water (second set of bars).

To summarize, at this juncture in the experiment, without the necessity of providing a history of ethanol drinking, about one-half of all the animals had come under S^D control so that they preferred cocaine solution to water. It was then of interest to determine whether exposing all the animals to an association between the S^D and cocaine solution made with a vehicle of greater acceptability than water would increase the subsequent control possessed by the S^D. Given such a history, and then returned to the previous choice between cocaine (in water vehicle) versus water, more of the animals might prefer cocaine solution to water. From this point on, experimental treatments were the same for both groups. Animals were presented with a choice between a 0.24 mg/mL cocaine solution and water, but for 10 days the vehicle for cocaine was a compound solution consisting of 0.08 percent saccharin and 1.5 percent glucose. The effect on preference is shown in figure 4 (third set of bars). Except for one animal, all preferred the cocaine solution, which was indicated by the S^D light as well. Then, over a 32-day period, the compound vehicle solution (sac-gl) gradually was reduced in concen-tration to 0.004 percent saccharin and 0.075 percent glucose, where it

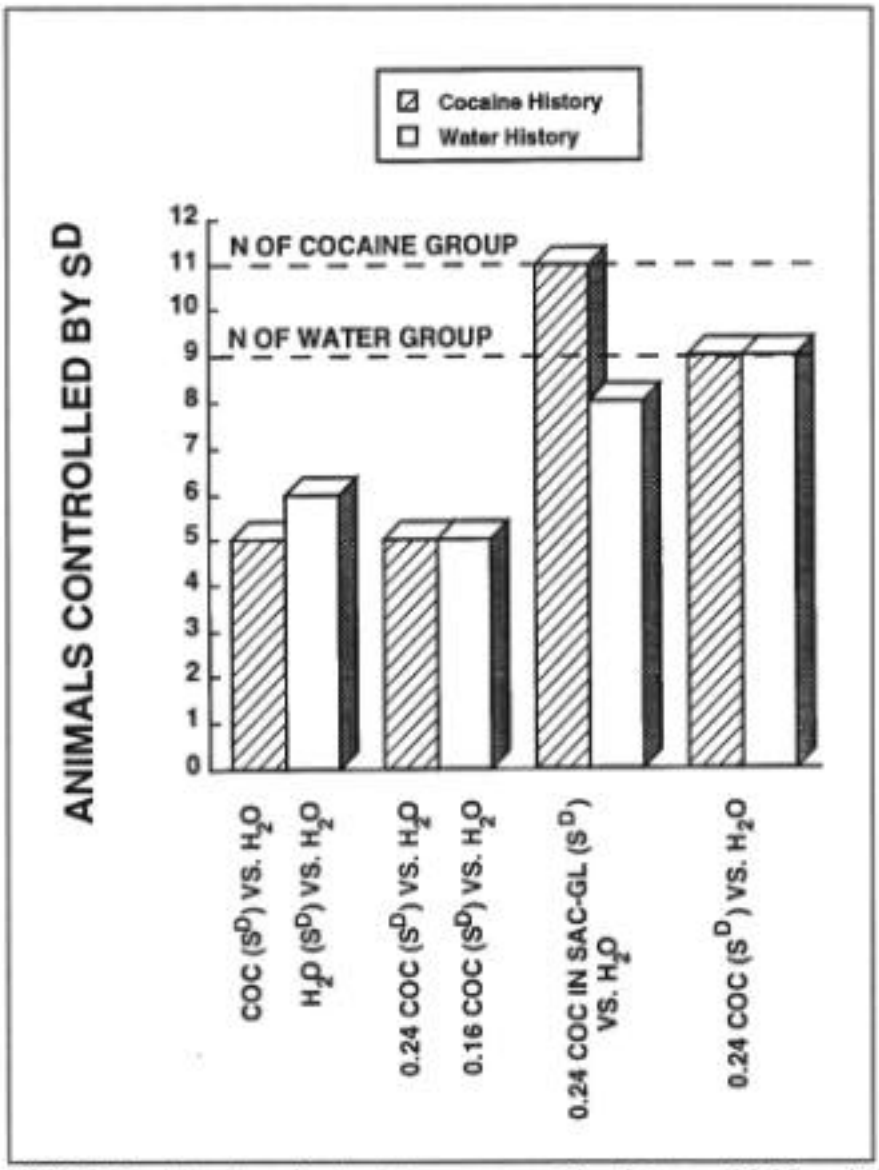

FIGURE 4. *Number of animals in a group with a history of 0.16 mg/mL cocaine solution (with light S^D) polydipsia (N = 11) and in a group with a history of water (with light S^D) polydipsia (N = 9) whose subsequent fluid polydipsia preferential choices were controlled by the S^D.*

remained for 4 days. In the next step, the vehicle became water once again and the 0.24 mg/mL cocaine $+S^D$ versus water choice was presented for 12 days. The rightmost set of bars in figure 4 shows that all except two animals continued to prefer the cocaine solution. Thus, interposing a history of pairing the cocaine plus S^D with a sac-gl vehicle led to an enhanced number of animals choosing cocaine solution polydipsia (compare the second and fourth sets of bars).

In order to determine whether the presence of the S^D was contributing to the strong preference for 0.24 mg/mL cocaine solution to water, the S^D was turned off for 6 days. (The first set of bars in figure 5 is the same as the last set in figure 4, and is presented again to facilitate comparisons.) The removal of the S^D produced a moderate reduction in the number of animals choosing cocaine polydipsia (second set of bars). A further moderate reduction occurred when the S^D was next made to indicate the water source, rather than the cocaine source, for 10 days (S^D reversal, third set of bars). When the S^D was restored for 8 days, so that it now indicated the cocaine solution, there was an increase in the number of animals preferring cocaine, but the total number of cocaine-preferring animals did not attain the previous level (see figure 5, first and last sets of bars). Owing to its recent history of removal and reversal, the S^D might have lost some of its efficacy for determining choice. Indeed, the second and fourth set of bars are almost identical.

The next series of manipulations was designed to combine the 0.24 mg/mL cocaine solution with a dilute sac-gl vehicle in order to enhance the reinforcing value of cocaine solution, while also removing, restoring, and reversing the S^D in blocks of days so as to weaken the efficacy of the S^D in controlling fluid preference. The vehicle for the cocaine solution was 0.032 percent saccharin and 0.6 percent glucose solution for 8 days, which was reduced to 0.024 percent saccharin 0.45 percent glucose (6-days), and then to 0.016 percent sac-0.3 percent gl for a series of S^D manipulations. Figure 6 (first set of bars) shows that with the combi-nation of cocaine, the final dilute sac-gl vehicle, and S^D, all except one of the animals preferred the cocaine solution. Then, for blocks of 4 days each, the S^D was removed, restored, reversed and restored. None of those S^D manipulations affected the preference for the cocaine solution.

The sac-gl vehicle concentration was gradually (8 days) reduced to zero and again all except one animal showed a preference for cocaine solution (figure 7, first set of bars). Upon S^D reversal (10 days), only two of the cocaine-preferring animals lost their preferences (second set of bars). Thus, after the history of combining cocaine with the sac-gl vehicle along with the series of S^D manipulations shown in figure 6, S^D reversal

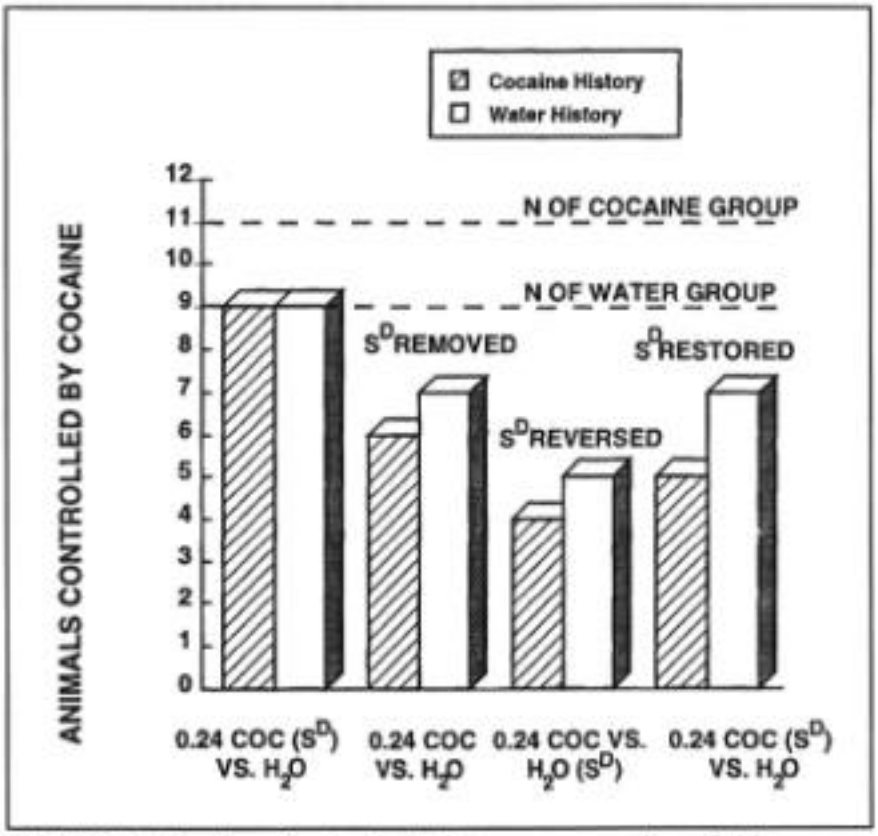

FIGURE 5. *Number of animals in the two groups whose fluid polydipsia preferential choices were controlled by cocaine (0.24 mg/mL) as S^D was manipulated.*

now had very little effect on cocaine preference. The S^D had lost most of its power to control fluid preference. Upon the removal of cocaine (12-days), only one animal s fluid preference was determined by the S^D (third set of bars). Finally, the restoration of a 0.24 mg/mL cocaine fluid source to the situation, together with S^D removal (10 days), resulted in a recovery of cocaine preference, but not for quite as many animals as previously (see figure 5, second set of bars and figure 7, last set of bars).

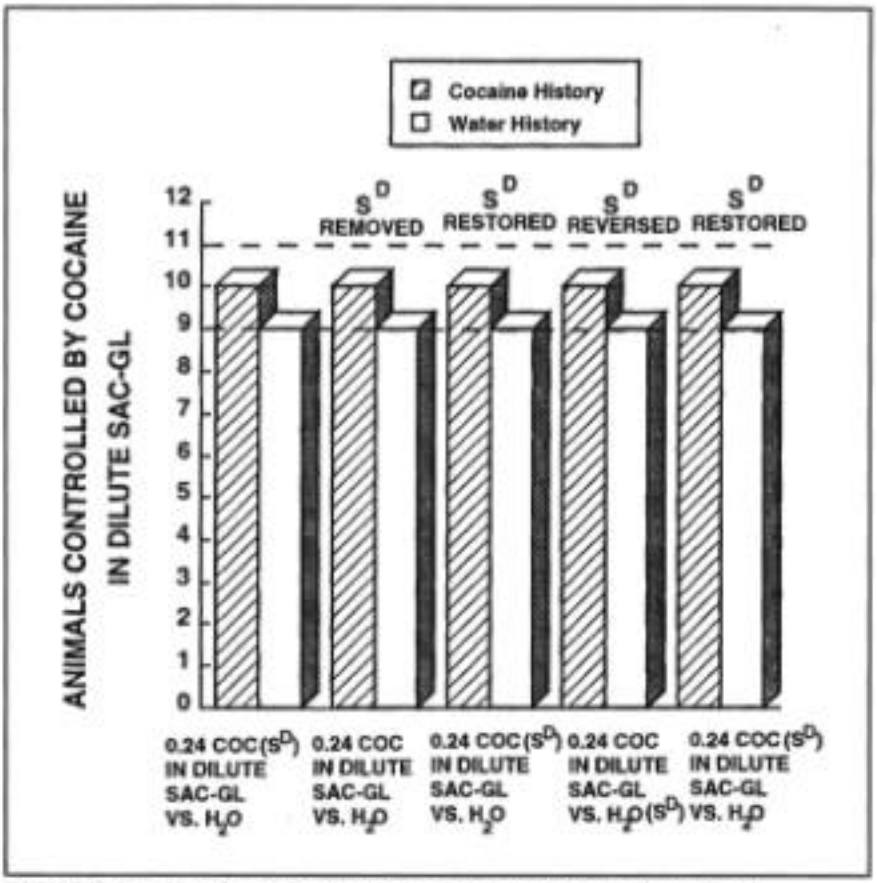

FIGURE 6. *Number of animals in the two groups whose fluid polydipsia preferential choices were controlled by cocaine (0.24 mg/mL) in dilute sac-gl solution as S^D was manipulated.*

PROVISIONAL PRINCIPLES DERIVED FROM THESE AND RELATED STUDIES

A number of provisional principles may be derived from these and previous studies, which begin to clarify the role of environmental and individual history variables in the institution and maintenance of drug abuse.

1. By the simple expedient of making an important commodity such as food available intermittently, excessive adjunctive behavior can be

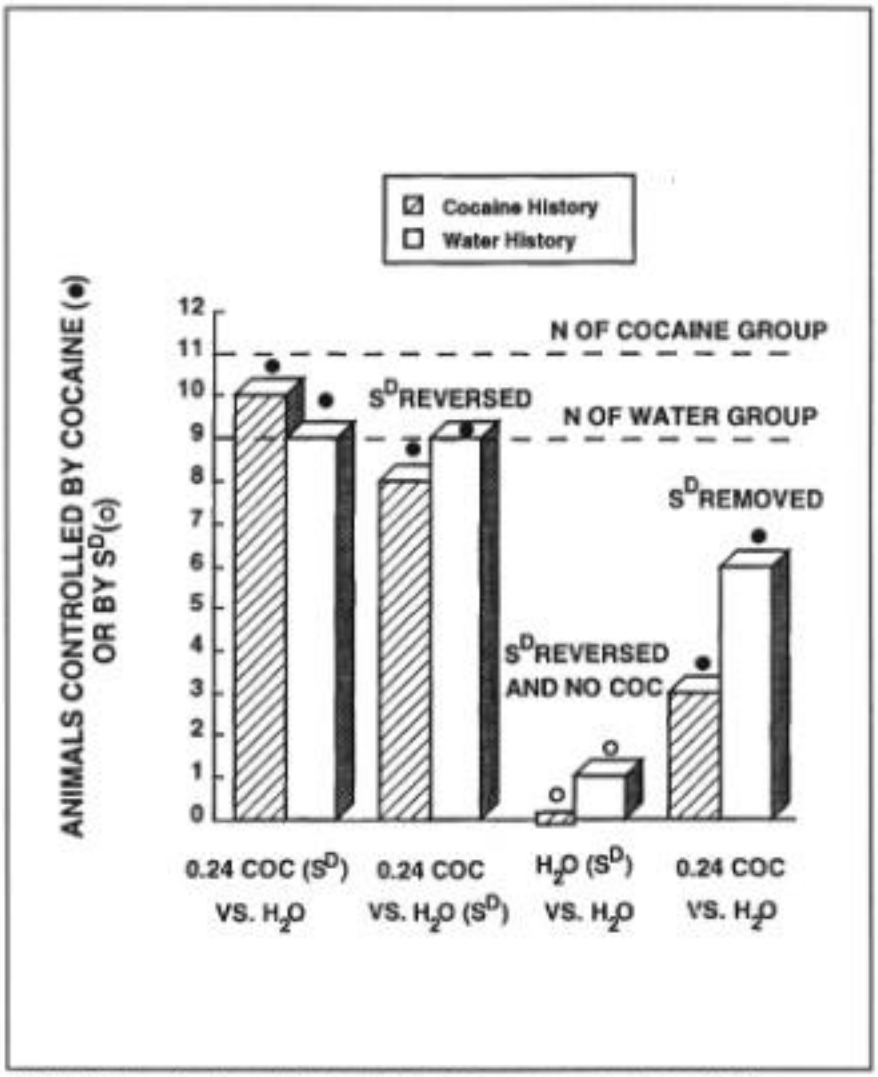

FIGURE 7. *Number of animals in the two groups whose fluid polydipsia preferential choices were controlled by cocaine (0.24 mg/mL, filled circle above bars) or by S^D (open circle over bars) as S^D was manipulated.*

generated, which includes oral vehicle and drug taking, as well as the potentiation of low rates of IV saline and drug self-injection.

2. If adjunctive behavior comes under S^D control, this control can function to transfer excessive behavior preferentially to an S^D-indicated commodity in the presence of behavioral alternatives. The commodity with respect to which the adjunctive behavior is transferred can be a drug possessing potential reinforcing properties of its own, or a substance that is not pharmacologically active. The first two principles combine to suggest that drug abuse and its preferential engagement of behavior can be viewed and manipulated profitably as a special case of excessive behavior

generation. The schedule of availability of important commodities can result in the generation of adjunctive behavior, the discriminative control of which is a function of an individual s behavioral history (Falk 1994).

3. Transfer of S^D control to another S^D (e.g., from an S^D light to a drug gustatory stimulus), or to another commodity (e.g., from S^D-indicated ethanol to cocaine or lidocaine, or from S^D-indicated cocaine to water) occurs with much higher probability when the transfer is done gradually, rather than abruptly.

4. The efficacy of an S^D in controlling preferential choice of a commodity (e.g., cocaine) can be enhanced by having interposed a history of pairing the drug plus the S^D with a drug vehicle of higher oral acceptability. In general, a drug may acquire an increased and enduring reinforcing efficacy for having once been imbedded in a context with enhanced reinforcing features.

5. By effecting a series of S^D removals, reversals, and restorations, the efficacy of the light S^D for controlling preference can be weakened so that preferential control may be transferred to the gustatory S^D properties of a drug.

6. At present, although strong and enduring oral preferential choices for both pharmacologically active and inactive fluids can be instituted by schedule induction and S^D control, the specific, additional contri-bution that an intrinsic reinforcing property of a drug might contribute to this preference has not yet been isolated.

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