Chapter 1

Sign-Tracking Model of Loss of Self-Control of Drug-Taking

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Abstract

The transition from voluntary, controlled drug use into poorly controlled drug abuse has long been recognized as fundamental to the drug addiction process; however, the causal mechanisms that mediate the loss of control of drug-taking are not well understood. Here we propose that the loss of control of drug-taking is due to the development of Pavlovian sign-tracking conditioned response (CR) performance. According to the Sign-Tracking Model (STM), each act of voluntary drug-taking provides the user with a pairing of an object with reward, and repeated object-reward pairings induce Pavlovian conditioning of sign-tracking CRs. The sign-tracking CR performance is an involuntary Pavlovian reflexive response, over which the subject has little or no control. Thus, STM provides an account of the transition from well-controlled, intended, or voluntary alcohol drinking into the mysterious realm where drug-taking escapes self-control and symptoms of drug abuse emerge.

From Drug Use To Drug Abuse

Initiation of Drug Use

When drug use is initiated, each individual act of drug-taking is a discrete, decision-based event. In the beginning, the drug is taken only because the user has consciously formed the specific intention to consume the drug. In the beginning, the drug is never taken unless the user explicitly decides to do it. In other words, the user is consciously aware of their option to either take the drug or to not take the drug, and they fully realize that this decision is entirely theirs. And so it is, at least at the beginning, drug-taking is under strict voluntary control.

Repeated Acts of Voluntary Drug-Taking

For many users, voluntary drug use transitions into poorly controlled drug abuse. How does this happen? While there are many factors that may contribute to the loss of control of drug-taking, one thing is certain. The transition from drug use into drug abuse requires repeated acts of drug-taking, over and over again, which leads to dramatic changes in the quality and the character of the drug-taking response. In the beginning, the drug-taking response was strictly a voluntary decision-based action. The drug was taken only when the user actually decided to do it. But, after many repeated acts of voluntary drug-taking, a more reflexive and automatic form of drug-taking begins to emerge. The user will pick up and consume the drug, and do so without any conscious awareness of actually deciding to do it. In other words, the action of taking the drug was performed even though the user did not form the specific intention to do it. The drug-taking response is now, at times, executed on automatic pilot. Due to repeated acts of voluntary drug-taking, a thoughtless, mindless, habitual form of drug-taking has developed. It is this unintended form of drug-taking that provides the first indication that drug-taking has begun to slip outside of the realm of the user's self-control. This is indicative of the loss of self-control because the drug is now taken

without a thought and despite the fact that the user did not decide to do it.

Sign-Tracking Model (STM)

While the transition from controlled drug use into poorly controlled drug abuse has long been recognized as fundamental to the drug addiction process, the causal mechanisms that mediate the loss of control of drug-taking are not well understood. In this paper, we propose that the loss of control of drug-taking is due to the development of Pavlovian sign-tracking conditioned response (CR) performance. According to the Sign-Tracking Model (STM), each act of voluntary drug-taking provides the user with a pairing of an object with reward, and repeated object-reward pairings induce Pavlovian conditioning of sign-tracking CRs. For example, consider the case where the object is a cocktail glass and the reward is alcohol's euphoric effect. Repeated acts of drinking alcohol from the cocktail glass will provide the user with pairings of the cocktail glass (object) with alcohol's euphoric effect (reward). These object-reward pairings will induce the development of the Pavlovian sign-tracking CR. Note that the sign-tracking CR is an acquired reflexive response. The sign-tracking CR consists of a complex sequence of directed motor actions: the subject will approach the object, then contact the object, and then consume the object. While the act of consuming the cocktail glass that contains the alcoholic beverage constitutes the action of alcohol drinking, it should be noted that this Pavlovian act of alcohol drinking is not decision-based. The sign-tracking CR performance is an involuntary Pavlovian reflexive response, over which the subject has little or no control. Thus, in this way, repeated acts of voluntary intended alcohol drinking from the cocktail glass will come to empower the cocktail glass to trigger unintended, thoughtless and automatic acts of Pavlovian-based alcohol drinking, and so it is that drug-taking escapes self-control.

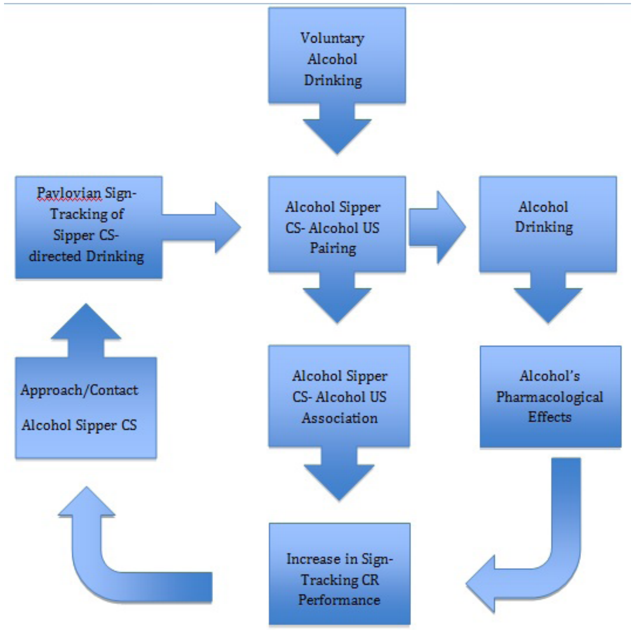

Figure 1: Sign-Tracking model using the example of voluntary alcohol drinking transitioning into poorly controlled alcohol drinking due to the induction of Pavlovian sign-tracking CR performance.

What is Sign-Tracking?

Sign-tracking (also called autoshaping or conditioned approach) is a Pavlovian conditioning procedure that consists of the presentation of a small object conditioned stimulus (CS) followed immediately by the response-independent delivery of a rewarding unconditioned stimulus (US). Repeated pairings of, for example, a lever CS with food US leads some rats to acquire and maintain sign-tracking conditioned response (CR) performance. These sign-tracking rats approach and contact, then direct feeding-appropriate responses at the CS, including sniffing, licking, gnawing, and chewing the lever CS. Crucial to the understanding of sign-tracking, the subject is not required to perform the CR to obtain the US. The rewarding US is delivered regardless of what the subject does. Also important to the understanding of sign-tracking, the CR is an acquired Pavlovian conditioned reflex. The performance of the CR is an involuntary action that is difficult to suppress or control, and the CR is likely to be expressed whenever the subject encounters the CS (for reviews of sign-tracking, see [1-3]).

The key ingredients in sign-tracking procedures are repeated pairings of an object (CS) with a reward (US). It should be noted that drug-taking procedures in humans typically provide these key ingredients. In humans, the act of drug-taking typically involves the use of a small object employed as a conduit to assist in the taking of the drug. During each act of drug-taking, the user necessarily sees that small object just before experiencing the drug's rewarding effects. Thus, drug-taking procedures in humans provide for the essential ingredients of a Pavlovian sign-tracking procedure, that is, repeated object-reward pairings.

For humans performing the actions involved in voluntarily taking the drug, object-reward pairings are experienced each time the user engages in an act of drug-taking. For example, with respect to alcohol drinking, the cocktail glass or the beer bottle is an object that is paired with alcohol's rewarding effects. For the marijuana user, the joint or the bong is an object that is paired with the marijuana high, and for the cocaine user, the pipe or the tooter is an object that is experienced just before getting high on cocaine. STM provides a novel theoretical account of the etiology of drug abuse in humans. As applied to alcohol abuse, repeated pairings of, for example, a distinct or particular or favorite alcohol glassware (CS), such as a cocktail glass, with alcohol's rewarding effects (US) may lead to the acquisition of Sign-Tracking CRs, as indicated by the development of poorly controlled alcohol drinking. The subject will be reflexively triggered to approach, contact, and consume the alcohol glass, resulting in an unintended and involuntary act of alcohol drinking. Thus, STM provides an account of the transition from well-controlled, intended, or voluntary alcohol drinking into the mysterious realm of the slippery slope, where al-

cohol drinking escapes the bounds of strict intention and becomes increasingly difficult to control.

Sign-Tracking and the Loss of Self-Control

With respect to obtaining the rewarding US, the performance of the sign-tracking CR is completely unnecessary. It serves no purpose and is a complete waste of time and energy. This is because the subject receives the rewarding US regardless of whether or not the sign-tracking CR is performed. For this reason, therefore, the performance of the sign-tracking CR is a bit odd or bizarre, and may be construed as somewhat maladaptive. The performance of the sign-tracking CR makes little sense because moving toward the lever CS typically serves to move the subject away from the location of the trough where the food US will soon be delivered. Thus, performing the sign-tracking CR serves to delay the opportunity to eat the food reward US. It seems reasonable to expect that if the subject were able to control the performance of the sign-tracking CR, then we would expect that the subject would simply stop doing it. But that is not the case. Subject after subject, in experiment after experiment, perform the sign-tracking CR during trial after trial, even though the performance serves no purpose, indicating that the sign-tracking CR is not easily brought under voluntary control.

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Sign-Tracking Despite Reward Omission

Suppose that the sign-tracking procedure is altered so that the object CS is paired with the food reward US, but the subject is prohibited from performing the sign-tracking CR. That is, the subject receives the food reward US provided that the subject does not contact the object CS on this trial. This is the omission training procedure, and the penalty for touching the object CS is that the delivery of the food reward US is canceled or omitted. Sign-tracking studies employing omission training procedures reveal that the sign-tracking CR is acquired and maintained even in the face of an explicit omission training contingency designed to eliminate it. This provides compelling evidence that the sign-tracking CR is difficult to control or suppress. Obviously, performing the response that cancels the reward is maladaptive and counterproductive, and we would expect that subjects would refrain from doing it. Remarkably, they do not refrain. Sign-tracking CR performance is so persistent during omission training procedures that most subjects lose the majority of the rewards available to them [4]. The data indicate that sign-tracking CR performance is reflexively elicited by the object CS that has been paired with the reward US, and there is no indication that the subjects can prevent themselves from performing the sign-tracking response despite extensive training with losing the rewarding US for doing so [5-8].

In other words, during omission training procedures the subject receives the rewarding food US regardless of what it does, as long as the subject does not perform the single prohibited response, touching the CS that signals the delivery of the food US. Persistent performance of sign-tracking CRs despite extensive training with reward omission procedures has been reported in numerous studies employing a wide range of species [8].

The performance of sign-tracking CRs induced during reward omission training procedures appears to be arguably compulsive [3]. The omission training contingency simply requires that the subject refrain from contacting the object CS in order to obtain the reward; yet, despite this strict prohibition, subjects contact the object CS, and this behavior persists despite extended experience with its maladaptive consequences. The sign-tracking CR, therefore, appears to be extremely difficult for the subject to control, suppress or restrain. This serves as the first of many demonstrations showing that the sign-tracking CR is largely refractory to a wide range of negative consequences that have been placed upon it.

Long Box Studies

Further evidence that the sign-tracking CR is poorly controlled is provided by long box studies. These interesting data were originally described by Hearst and Jenkins [9], who paired brief illumination of a keylight CS in a long box with the subsequent raising of a food (US) tray at a distance from the keylight CS. Although no response was required to receive the food reward US, the pigeons began to approach and peck the keylight CS, performing the sign-tracking CR, even though this removed them from the vicinity of the food US, which was available for a limited amount of time. Sign-tracking of pecking the keylight CS was maladaptive because the amount of time it took to travel from the keylight CS to the food US reduced the amount of time available to eat. Nevertheless, subjects continued to run to peck the keylight CS, losing much of their access to the food US, and they persisted in doing so for trial after trial after trial.

Moving the keylight CS even further away from the food trough, increased travel time between the keylight CS and the food US tray, which reduced further the time available to eat; nevertheless, the pigeons continued to run to peck the keylight CS and persisted in doing so as long as they could obtain even a single grain of food US on each trial. Finally, the keylight CS was moved so far away from the location of the food tray that the keypecking pigeon could not run to the food tray quickly enough to obtain even a single grain of food. On these trials, they ran and pecked the keylight CS, but they received no food US, self-imposing a CS-No US extinction trial. Eventually, the effect of receiving several consecutive CS-No US extinction trials was to extinguish sign-tracking CR performance. That is, when the keylight CS was illuminated, the pigeon did not run and peck it, and, as a consequence, the pigeon was able to eat the food US from the tray on that trial. This

pairing of the illumination of the keylight CS with food US was sufficient to convince the pigeon to reinstate running to peck the keylight CS on subsequent trials.

The long box studies reveal that the pigeons were unable to resist the impulse to approach, contact, and consume the keylight CS that signaled the food US. Apparently, the keylight CS was so irresistible, so overwhelmingly attractive, that they persisted in pecking it, even when doing so reduced their access to the real food US reward. The subjects appeared unable to control the keypecking that was so detrimental to eating the food US, and this was the case despite their experience with eating the food US on trials where they did not engage in keypecking.

Sign-Tracking Despite Contingent Shock Punishment

Brief presentation of a visual cue that signals cocaine infusion induces Sign-Tracking of cue-directed approach responses [10]. It has recently been reported that the cocaine cue is so irresistibly attractive that rats will cross an electrified grid floor to approach the location of a light cue that had previously been established as a signal for the operation of an infusion pump that delivered intravenous injections of cocaine [11]. This effect was observed even though during drug self-administration training the sign-tracking response had no effect on cocaine delivery and, during the shock punishment test, the light cue was presented without infusions of cocaine. Thus, the illumina-

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tion of the cue light that had previously signaled cocaine infusion "goaded" the rats into crossing the shock grid even though there was no reason for the subject to run across the electrified grid floor, other than to approach the cocaine cue light. In other words, sign-tracking CR performance was directed at a drug cue despite the aversive consequence of the contingent shock punishment, and this effect was observed even though there was no drug reward for executing the response. The effect is consistent with the hypothesis that the sign-tracking CR is not under the control of the subject.

The Misbehavior of Organisms

The "misbehavior of organisms" was first reported by professional animal trainers, Keller and Marian Breland, who successfully applied instrumental reward contingencies in the training of animals in a variety of tasks [12-14]. They did, however, experience some rather perplexing instances where things did not go according to plan. Their failures were carefully noted in a log, and before long an interesting pattern was discernible.

In a typical example, a raccoon was initially trained to simply pick up a wooden coin for a food reward. This was quickly learned. Then, the raccoon was rewarded with food for picking up the wooden coin and then carrying the wooden coin to the location of a small metal box. Then, still an additional requirement was added to the response chain. The raccoon had to pick up the coin,

carry it to the box, then deposit the coin through a slot in the box. For doing so, the raccoon was promptly rewarded with a morsel of food. While initially things went well, with further training, the raccoon began to experience problems. The raccoon seemed unable to let go of the coin, spending several minutes handling two of them with their forepaws and "rubbing them together in a most miserly fashion" [12]. The raccoon often dipped the coin into the slot only to pull them out again. In the end of the coins were chewed, licked, scratched, clawed, rubbed, and washed, but rarely deposited. Remarkably, the actions of the raccoons made it appear as though they were trying to clean a morsel of food.

Procedures conducive to misbehavior require the subject to contact then relinquish a small object in order to obtain food reward. Misbehavior develops after a period of successful performance of the required response, when formerly well-behaved subjects begin to persist in maintaining contact with the object and appear reluctant to let it go, even though they are required to do so to obtain the reward. Thus, a prohibited response, maintaining contact with the small object, occurs and persists despite contingent loss of the food reward. The deterioration of performance occurred after a period of successful training with food reward. Moreover, once the raccoon began to perform these feeding-appropriate responses, in lieu of relinquishing the coin, these responses became more of a problem with each passing day. In the end, the raccoon was receiving a very small percentage of the available food rewards. In an attempt to increase the raccoon's motivation for the food rewards, the trainers increased the raccoon's hunger drive by imposing a longer period of food deprivation prior to the training session. Increasing the raccoon's motivation to eat the food rewards only made matter worse. Ultimately, the trainers were forced to give up with this raccoon and start over with a new raccoon subject, only to learn that the same thing happened in raccoon after raccoon. Other abandoned projects attempted similar training with pigs, rats, squirrel monkeys, chickens, turkeys, otters, porpoises, and whales [12-13].

The misbehavior effect reveals the loss of self-control induced by sign-tracking CR performance. Note that the raccoon experienced sign-tracking procedures, repeated pairings of the small coin object CS with food reward US. After repeated coin CS-food US pairings, the raccoon began to exhibit sign-tracking CRs, approaching, contacting, and consuming the coin CS. Note that performing the sign-tracking CR is maladaptive, delaying, sometimes endlessly, the time of the delivery of the real food rewards.

Sign-tracking is important because it provides us with a way of understanding how behavior can become irrational and defy free will. Consider the intention of the raccoon. The raccoon is very hungry and very much interested in eating the morsels of food offered as the reward, but eventually, after many pairings of the coin and food, his intention to devour those tasty morsels is seldom ob-

served. Instead, his actions are those of sign-tracking. The disconnect between the raccoon's intentions and the raccoon's actions are not unlike those of the drug abuser, who intends to restrain drug-taking, but, instead, finds himself or herself unable to control the impulse to have yet another. In both cases, the subject is unable to control the action of consuming the object that predicts reward.

Sign-tracking induces loss of control of action directed at the object that signals reward. This pretty much summarizes the essence of the problem of the drug addict. The drug addict is unable to control their drug-taking. They take the drug even when they are trying not do, and like sign-tracking, their drug-taking consists of action directed at the object that signals the reward. For example, addicts exhibit the symptoms of sign-tracking after they experience the object (cocktail glass) as a signal for reward (alcohol). In the presence of the cocktail glass they are drawn toward the glass, and cannot resist reaching out and drinking from the glass. This suggests that the overlooked basis for the loss of control of drug-taking, the inability to terminate an ongoing drug use episode, is sign-tracking of drug-taking.

Features Common to Sign-Tracking and Drug Abuse

The hypothesis is that the development of sign-tracking CR performance mediates the transition from voluntary, controlled drug use into poorly controlled drug abuse. This hypothesis predicts that the characteristics of sign-tracking CRs will closely resemble the symptoms of drug abuse. The following are features common to sign-tracking and drug abuse:

Acquired: Both responses are acquired as a function of experience with pairings of stimulus object (CS) with a reward (US).

Reflexive: Both responses exhibit properties of an acquired reflex, performed automatically without the formation of a specific intention.

Triggered: Both responses are triggered or elicited by a stimulus object (CS) that has been repeatedly paired with the reward US.

Involuntary: Both responses are difficult to restrain, control or suppress.

Compulsive: Both responses are performed even in the face of a specific intention not to do it.

Durable: Once responding has developed, there is little evidence that it can be eradicated. Relapse-like effects include spontaneous recovery, reacquisition savings, and long-term retention.

Sign-Tracking of Drug-Taking

Sign-tracking procedures have been extensively employed to induce lever-pressing of drug self-administration in rats. For example, Carroll and her associates have reported that pairings of the insertion of a lever CS with intravenous administration of drug reward US induced the automatic shaping of lever-pressing for drug self-administration in rats. Procedures of this sort have been employed to induce reliable lever-pressing for the self-administration of the ocaine

US [15-25] see also [26-29] or the self-administration of the amphetamine US [16] or the self-administration of the heroin US [20,24-25]. In all of these studies, rats developed increasingly frequent lever-pressing as a function of experience with repeated pairings of lever CS with rewarding drug US. The role of sign-tracking, however, remains unclear, because when lever-pressing occurred, the drug reward US was administered more quickly than when lever-pressing was not observed. Thus, the drug reward US was not presented independently of responding, as is the case during “pure” sign-tracking procedures. An additional problem is that none of these studies included controls for pseudo-conditioning, leaving open the possibility that the development of lever-pressing was due to mere experience with repeated presentations of the lever CS per se or to repeated presentations of the drug reward US per se.

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Pairing a visual CS with alcohol US induces sign-tracking CR performance in rats. For example, after providing rats with pairings of a light CS with alcohol US, [30] observed that they approached the location of the light CS, resulting in increases or decreases in operant lever-pressing for alcohol reinforcement, when the light CS was located either near or far away from the operant lever, respectively. Sign-tracking using alcohol US has also been reported by [31] who reported that only three pairings of a star CS with alcohol US were required to induce reliable Pavlovian conditioned approach to the star CS as revealed by place conditioning procedures in mice. Tomie and his associates have employed sign-tracking procedures consisting of alcohol sipper CS paired with food US to induce alcohol sipper CS-directed consummatory responding, resulting in alcohol drinking [32] Exps 1 and 2, [33-34] Exps 1 and 2, [35-37]. Similar procedures have been employed with chlordiazepoxide in the sipper CS to induce sign-tracking of sipper CS-directed chlordiazepoxide drinking in rats [38]. Most significantly, there is evidence that the drinking of alcohol from the sipper CS, an action that provides the rat with pairings of sipper CS with alcohol US, induces a pattern of alcohol drinking that is indicative of sign-tracking of sipper CS-directed alcohol drinking in rats [33-36]. Thus, the hypothesis that sign-tracking CR performance develops as a function of repeated pairings of an object CS with drug reward US is well supported. Our view is that repeated pairings of an object CS with drug reward US are experienced by humans during the drug-taking sequence, and this leads to the development of sign-tracking CR performance of reflexive and poorly controlled drug-taking.

Sipper CS - Alcohol US Pairings

STM proposes that repeated pairings of the alcohol sipper CS with alcohol US will give rise to sign-tracking CR performance of sipper CS-directed alcohol drinking. Specifically, alcohol drinking should vary as a function of the positive contingency between the sipper CS and alcohol US. Note that this positive contingency is no more elevated in a group receiving the alcohol sipper paired with the food US as compared to a group receiving the alcohol sipper randomly related to the presentation of the food US. For both groups, the schedule of presentations of the sipper CS is the same, and for both groups the alcohol US is available only when the sipper CS is inserted into the chamber. That is, for both groups the absence of the sipper CS perfectly predicts the absence of the alcohol US. The similarity of their experiences with the sipper CS and alcohol US may account for the elevated alcohol drinking observed in groups receiving the alcohol sipper paired or randomly related to the food US [37-39].

Robust levels of alcohol drinking have been reported in groups receiving alcohol sipper CS randomly with respect to either food US [37-39]. This alcohol drinking may be due to pairings of sipper CS with alcohol US. To evaluate the possibility that the food US may have contributed to the initiation (but not the maintenance) of sipper CS-directed alcohol drinking, groups of rats received 25 daily alcohol sipper CS trials but no food US presentations were provided at any time during the entire duration of the study [40]. Alcohol intake for this group (see Intermittent Sipper group in Fig. 2) did not differ from that of a group that received similar training except that the alcohol sipper CS was paired with the presentation of the food US (see Intermittent Sipper group in Fig. 2). Thus, robust sipper CS-directed alcohol drinking is initiated [40] and maintained [39] in Random controls by mere experience with intermittent presentations of the alcohol sipper CS per se, even when there are no presentations of the food US.

The Intermittent Sipper group consumed far more alcohol than did the Continuous Sipper group, even though the duration of access to the alcohol sipper during each session was far less for the former group relative to the latter group. On the other hand, the contingency between the alcohol sipper CS and alcohol US was far greater for the Intermittent Sipper group than for the Continuous Sipper group. This is because the alcohol sipper CS and the alcohol US were both absent for the majority of the daily drinking session. Sign-tracking CR performance is sensitive to the CS-US contingency; therefore, the elevated CS-US contingency in the Intermittent Sipper group should lead to sign-tracking of alcohol sipper CS-directed responding, resulting in more sign-tracking of alcohol drinking. Thus, there is solid evidence that sign-tracking of sipper CS-directed alcohol drinking is sensitive to the

positive contingency between the alcohol sipper CS and the alcohol US.

Sign-Tracking and Alcohol Drinking Styles

STM predicts that poorly controlled alcohol drinking will more likely develop when a particular or specific of glassware (conditioned stimulus, CS) is repeatedly employed to consume an alcoholic beverage (unconditioned stimulus, US). This is because sign-tracking CR performance of glassware CS-directed alcohol drinking will be induced to the degree that the glassware CS and alcohol's rewarding US effects are experienced in a positively correlated fashion, and this positive correlation or contingency between the glassware and alcohol will be particularly elevated when alcohol always follows the glassware, and in addition, when the glassware is employed exclusively for the purpose of consuming an alcoholic beverage. Under these conditions, therefore, poorly controlled alcohol drinking is especially likely to be triggered by and directed at the glassware CS, and thus the alcohol abuser will be more likely to lose control and consume the alcoholic beverage even when he/she intended not to do so. On the other hand, repeated experiences with alcohol's effects in the absence of the glassware will reduce the positive correlation between the glassware CS and alcohol US, resulting in reduced sign-tracking CR performance of glassware CS-directed alcohol drinking. An additional arrangement that serves to reduce the positive correlation between the glassware and alcohol is when the glassware is employed for purposes other than drinking alcoholic beverages.

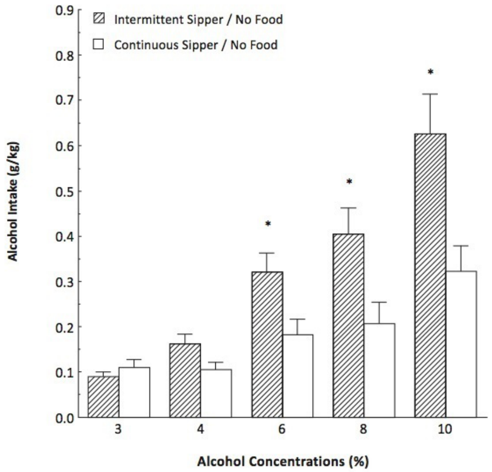

Figure 2: Mean grams of alcohol consumed per kilogram of body weight (g/kg) during the last three sessions of training with signtracking procedures at each of the five concentrations of alcohol [3%, 4%, 6%, 8%, and 10% (vol./vol.)]. Rats in the Intermittent Sipper group received 25 trials during which the alcohol sipper was inserted into the drinking chamber for 10 seconds. For the rats in the Continuous Sipper group, the alcohol sipper was inserted into the drinking chamber during the entire duration of the experimental session (approximately 30 minutes). The single asterisk (*) indicates that mean g/kg alcohol intake was significantly higher for the Intermittent Sipper group than for the Continuous Sipper group ($P < .05$) when the sipper contained the 6%, 8% and 10% alcohol concentrations (Fisher's LSD). From Tomie A, Miller WC, Dranoff E, Pohorecky LA. Intermittent presentations of ethanol sipper tube induce ethanol drinking in rats. Alcohol and Alcoholism. 2006; 41: 225-230.

Employing the glassware to drink water or other non-alcoholic beverages will reduce the positive correlation between the glassware and alcohol which, in turn, will lower the likelihood that sign-tracking CR performance of glassware-directed alcohol drinking will be elicited by the presence of the glassware, and, therefore, in the presence of the glassware, excessive and poorly controlled alcohol drinking will less likely be observed.

The Broad Drinking Repertoire

The broad drinking repertoire is an alcohol drinking style where the user consumes alcoholic beverages from a wide range of containers, including bottles, cups, cans, etc. As noted above, the positive correlation between a particular glassware and alcohol is reduced each time alcohol is experienced even though the particular glassware has not been presented. There is evidence in the Pavlovian conditioning literature on sign-tracking that degrading the positive correlation between the CS and US by presenting the US without presenting the CS reduces the expression of sign-tracking CR performance [40-47]. Thus, drinking alcohol from a broad range of receptacles will reduce the tendency to develop poorly controlled problem drinking that is due to sign-tracking. This is because drinking alcohol from the cocktail glass CS will strengthen the cocktail glass-alcohol association, but, at the same time, reduce the association between alcohol and all other alcohol drinking receptacles (i.e., beer mugs, wine goblets, etc.). Thus, the broader the range of the drinking repertoire, the more likely any single receptacle will not be employed when drinking alcohol, and consequently the more frequently the contingency between that absent receptacle and alcohol will be degraded. It follows, therefore, that an analysis of loss of control of alcohol drinking based on sign-tracking predicts that there will be a relationship between drinking style and problem drinking. Specifically, STM predicts that the loss of control of alcohol drinking due to sign-tracking CR performance will be mitigated by the broad drinking repertoire. That is the drinking style that includes consuming, for example, beer from a variety of objects (such as a beer can, a beer bottle, a red Dixie cup, and a metal beer mug) will less likely induce sign-tracking CR performance of alcohol drinking. It is most significant that sign-tracking does not attribute the loss of control of alcohol drinking to the amount of alcohol consumed per se, but rather to the range of the drinking repertoire through which alcoholic beverages are consumed. In this respect, STM is unique among models of alcohol abuse in that this model attributes the loss of control of alcohol drinking to the positive correlation between alcohol's rewarding effects and the glassware or object used to consume the alcohol.

STM predicts that heavy drinking per se does not necessarily presage loss of control of alcohol drinking, and there is evidence to indicate this effect. For example, results derived from prospective or longitudinal studies reveal that during the lifespan peak alcohol consumption is noted in 18- 25 year olds [48-50], but most of these individuals mature out and do not subsequently develop a pattern of problem drinking in adulthood [51-58]. The lack of a stronger connection between high levels of alcohol drinking and the subsequent development of problem drinking may be due to the broad range of the drinking repertoire typically reported by youthful individuals experimenting with the initiation of alcohol use [59, 60]. Investigators have reported that alcohol drinking amongst college students typically includes a broad range of alcoholic beverage types [59-63]. Thus, there is evidence suggesting that in humans elevated alcohol drinking in combination with the broad drinking repertoire does not presage the initiation or induction of subsequent problem drinking, and these effects are consistent with predictions derived from STM.

The Narrow Drinking Repertoire

While STM predicts that the broad drinking repertoire will not be conducive to the induction of poorly controlled drinking, STM also predicts that the narrowing of the drinking repertoire will presage elevated levels of problem drinking. With the broad drinking repertoire, alcohol is frequently experienced in the absence of the glassware, whereas, with the narrow drinking repertoire the opposite is true. That is, alcohol is almost never experienced in the absence of the glassware, or, in other words, alcohol is experienced only when the glassware is present. As noted above, the positive correlation between glassware and alcohol is elevated when alcohol's effects are experienced under the conditions of the narrow drinking repertoire. Therefore, STM predicts that the narrow drinking repertoire will be conducive to the expression of poorly controlled alcohol drinking. For example, consider the user who drinks all alcoholic beverages, including his/her most favorite drink (i.e., dry martinis, extra dry with a twist and an olive) only when served in a stemware crystal cocktail glass. The narrow drinking repertoire of this individual will result in a high positive correlation between the glassware and alcohol. Thus, STM predicts that this narrow pattern of alcohol drinking will likely induce sign-tracking CR performance of poorly controlled binge-like episodes of glassware CS- directed alcohol drinking. There is data suggesting that the development of problem drinking is not merely a function of the absolute level of alcohol intake, but rather is also determined by the tendency to exhibit beverage exclusivity [62] or to drink alcohol only in a particular way [63-64].

STM predicts that the recovering alcohol abuser would more likely end a period of abstinence and succumb to the desire to have a drink when temptation includes the specific glassware, such as a cocktail glass, formerly employed to consume a favorite alcoholic beverage. The recommended therapeutic remedy, therefore, would require that the recovering alcohol abuser avoid situations in which alcohol drinking may occur and most especially when the specific favorite glassware is likely to be encountered. STM predicts that the lapse back into alcohol drinking is far more likely to be initiated by the presence of the cocktail glass CS that elicits reflexive and poorly controlled sign-tracking CR performance of cocktail-glass CS-directed alcohol drinking.

Drinking only from a particular beer bottle may be the drinking style that provides for the narrowest of drinking repertoires. This is because the favorite beer bottle CS is virtually identical each time that alcohol is consumed, while cocktail glasses likely differ slightly from one another. Studies of stimulus generalization of sign-tracking CR performance [66-69] indicate that decremental generalized responding is elicited by stimuli that resemble the training CS. The beer bottle, on the other hand, would not be subject to decremental generalization, and, therefore, drinking only directly from the favorite bottle may be a particularly dangerous drinking style.

Altering the Range of the Drinking Repertoire

Evidence from longitudinal studies suggests a positive relationship between the range of the drinking repertoire and the prevalence of poorly controlled alcohol drinking. Specifically, the evidence indicates that the nosological progression of an individual subject from a broad to a narrower drinking repertoire is often accompanied by elevated risk of problem drinking. Thus, the narrowing of the drinking repertoire has been broadly recognized as a risk factor for the development of alcohol abuse [64, 70-74]. That is, alcohol abuse researchers have reported data

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indicating that uncontrollable alcohol drinking is often preceded or accompanied by the narrowing of the drinking repertoire [64, 70, 72-73]. Nosologists have reported that the progression into alcohol abuse is often marked by the narrowing of the repertoire as alcohol drinking is repeated in a ritualistic and habitual fashion [75-76] resembling an automatic action schemata [77]. As alcohol drinking becomes habitual, a highly preferred way of automatic drinking develops. Thus, a favorite type of alcohol beverage will be consumed repeatedly and habitually from the same type of glassware. According to STM, the narrowing of the drinking repertoire often observed in the transition to alcohol abuse, will serve to increase the positive predictive relationship between that glassware CS and alcohol US, resulting in the induction of sign-tracking CR performance, revealed by poor control of alcohol intake when the user is in the presence of that favorite glassware.

It is appropriate to acknowledge that the nosological evidence of the progression into alcohol abuse is correlational and therefore it remains unclear if the relationship between the narrowing of the drinking repertoire and the loss of control of alcohol drinking is actually causal, as suggested by STM. That is, perhaps the loss of control of alcohol drinking causes the subsequent narrowing of the drinking repertoire. According to this view, as loss of control of alcohol drinking develops, each episode of uncontrollable alcohol drinking provides the scene for the next. So the cocktail glass used in the previous drinking bout will most likely be present and readily available to trigger or encourage the next one, leading to the narrowing of the drinking repertoire due to the high frequency of rapidly sequenced episodes of poorly controlled drinking. Thus, the habit of drinking more and more exclusively from the cocktail glass may actually be caused by the loss of control of alcohol drinking, rather than the other way around. Teasing apart the basis of the positive correlation between repertoire narrowing and loss of control of alcohol drinking will require data from longitudinal and prospective studies that include highly detailed information regarding the alcohol- taking implements employed during the transition from alcohol use into alcohol abuse.

Using Common Glassware to Consume Alcoholic Beverages

The contingency between glassware and alcohol is reduced whenever the glassware is experienced but the alcohol is not. Therefore, STM predicts that the development of poorly controlled problem drinking will be less likely to the extent that the glassware has been employed for purposes other than consuming alcohol. For example, suppose that for many years an individual consumes non-alcoholic beverages from common table glasses, then in later years those same glasses are then used for consuming alcoholic beverages. STM predicts that uncontrollable drinking will be less likely, because the correlation between the common table glasses and alcohol's effects will be low, owing to the long history of employing this glassware to consume non-alcoholic beverages.

Evidence of this effect (called “latent inhibition”) in the Pavlovian conditioning literature on sign-tracking is provided by reports of retarded acquisition of sign-tracking CR performance following pretraining consisting of repeated presentations of CS but without any presentations of the US [78-82]. The retarding effects of CS-only pretraining are directly related to the number of times that the CS was presented prior to pairing with the US [42, 45-47]. Thus, STM predicts that many years of consuming non-alcoholic beverages from common table glasses will substantially retard the development of poorly controlled drinking of alcoholic beverages from those glasses.

Using Specialized Glassware to Consume Alcoholic Beverages

If alcoholic beverages are consumed only from distinctive specialized glassware reserved exclusively and employed only for consuming alcoholic beverages, then the specialized glassware would never be experienced without alcohol. Under these conditions, the correlation between the distinctive specialized glassware and alcohol would be elevated, and STM predicts that poorly controlled problem drinking will more likely develop, as problem drinking will be revealed by difficulty in restraining drinking in the presence of the distinctive specialized glassware.

Common vs Specialized Glassware and Problem Drinking

Cross-cultural anthropologists have reported evidence that alcohol glassware may play a role in problem drinking. For example, although Italy has a higher level of per capita consumption of alcohol, the incidence of poorly controlled problem drinking is lower, as compared to Ireland, which has a lower level of per capita alcohol consumption but higher rates of problem drinking and alcohol abuse [82-83]. Levin [84] attributed this difference to the manner in which alcohol is consumed in each country. In Italy, alcohol is typically consumed using the same glasses that are used for drinking non-alcoholic beverages, but in Ireland alcohol is typically consumed exclusively from specialized glassware. Using specialized glassware to consume alcoholic beverages is more typical of northern Europe than southern Europe [82-84], and the prevalence of binge drinking across Europe varies in this way, with more binge drinking reported in northern and central Europe than southern Europe [85]. While there are numerous cultural factors, other than the use of glassware, that may contribute to geographical differences in the incidence of problem drinking, there is, nevertheless evidence that the use of specialized glassware to consume alcoholic beverages varies geographically in the same way as the incidence of poorly controlled alcohol drinking, and this relationship between specialized glassware and poorly controlled alcohol drinking is predicted by STM. This model suggests that the practice of specializing glassware exclusively for the consumption of alcoholic beverages will enhance the positive correlation between the specialized alcohol-use implement and alcohol's effects, which in turn, will increase the incidence of problem drinking.

As noted above, it should be acknowledged that there are numerous additional cultural factors that may have contributed to these geographical differences in the prevalence of problem drinking, including geographical differences in the age of initial exposures to alcohol [86], the types of alcoholic beverages preferred [60], and the distribution of alcohol consumption during the day in relation to main meals [87]. More definitive evidence of a cross-cultural based relationship between the use of common versus specialized glassware and the incidence of problem drinking is not currently available due to the absence of data detailing the specific implements employed to consume alcohol beverages in cross-cultural studies. For example, several studies compared patterns of alcohol consumption cross-culturally in terms of the total amount of alcohol ingested, type of alcoholic beverages, frequency of alcohol intake, or alcohol-related positive or adverse consequences [60,86-89], but regional differences in the use of alcohol drinking implements were not included. There are reasons to consider in greater detail the role of the glassware because STM predicts that removing specialized glassware will have a greater effect on reducing problem drinking than will removing common glassware.

Sign-Tracking of Drug-Taking is Invisible

There is certainly something mysterious about the drug addiction process. This is because the drug addiction process is stealthy. Drug-taking that was well-controlled and well-managed somehow sneaks, gradually, quietly and unnoticed, until it is outside of the tidy realm of our comfortable decision-based activities. Gradually and without sounding an alarm, drug-taking evolves into something seemingly with a mind of its own, as it escapes the arena of our self-control. In the words of the drug addict, the complaints are telling. "I was blind-sided." "It snuck up on me from behind, while I was unawares." "I never saw it coming." "I can't believe this happened to me." "I do not understand." "Why can't I quit?"

The addicts are saying that even though they were on the lookout, it turns out that the enemy was invisible … that they could not see it happening, even while it was happening. STM provides an explanation for the addict's confusion as to why they were blind to their loss of self-control. Consider, for example, the case where the cocktail glass is the reward cue that precedes the rewarding effects of alcohol. Touching the glass, grasping the glass, and consuming the glass are the behaviors of the subject exhibiting sign-tracking responses. The glass is the reward cue; therefore, the glass will trigger the reflexive performance of these sign-tracking responses, and these sign-tracking responses will be directed at the glass (see Flow Chart presented in Figure 1). Thus, the sign-tracking sequence will result in the ingestion of the rewarding alcoholic beverage located inside the glass cue. Sign-tracking of alcohol drinking will develop when the alcohol reward is placed inside the glass, and the user performs repeated voluntary acts of alcohol drinking. In which way, when the alcohol is voluntarily consumed from the glass, the user will experience Pavlovian pairings of the glass cue with the rewarding effects of alcohol. This will encourage the development of sign-tracking directed at the glass, resulting in the drinking of the alcohol inside the glass.

But, the actions performed in sign-tracking of drug-taking are perfectly camouflaged to pass for an act of voluntary drug-taking. And the user who is unaware of the existence of sign-tracking will not see this act of drug-taking as an indication of loss of self-control. This automatic and reflexive act of drug-taking will be interpreted as an intended action because this is the only way that the user can make sense of what just happened. So, according to the user, "I changed my mind. I know that I said I was going to stop after two drinks, but I decided to have a few more in order to be sociable." This excuses the behavior, assuages the ego, and allows sign-tracking to remain invisible. Sign-tracking of drug-taking is invisible because it readily passes for decision-based, voluntary drug-taking. The user who is unaware of sign-tracking will be blind to sign-tracking, and is likely to later complain that "I was

blind-sided. I never saw it coming."

Sign-tracking induces the disconnect between the user's action and the user's intention. When the user repeats acts of voluntary alcohol-taking by drinking alcohol from the glass, then sign-tracking of alcohol drinking will develop, and the user will experience diminished control of drug-taking. The user will continue to take the drug, even though their intention is to practice restraint. This story is played out all too often in the bar or tavern, when the user intends to have one or two drinks, but, when in the presence of the glass, the action is to perform repeated acts of drug-taking, and to continue drinking way beyond what was intended. In this way, sign-tracking contributes to the lack of self-control that leads to drug-taking episodes where the amount of the drug that is consumed is in excess of that which was intended.

Experimental laboratory studies conducted by behavioral scientists have reported that frequency counts of voluntary (i.e., operant or instrumental) responding to obtain reward may actually include sign-tracking responses induced by cue-reward pairings. To the naked eye the sign-tracking action sequence is indistinguishable from voluntary responding; however, by using experimental manipulations of the cue-reward arrangement, laboratory investigators have provided compelling evidence that cue-reward pairings induce sign-tracking responding that looks like and is additive with voluntary operant responding (for reviews, [90]; and [91]). It is interesting to note that the convergence of streams of sign-tracking responses with streams of voluntary operant responding results in elevated levels of responding that, prior to the discovery of sign-tracking, were mistaken for voluntary acts of reward-directed actions that were performed to excess [1]. Thus, sign-tracking may be camouflaged so as to be mistaken for voluntary responding, and the conditions that produce this masking effect are precisely those that are employed in drug-taking procedures [8,14].

The implication is clear. Sign-tracking of drug-taking is invisible because, to the naked eye, it passes for voluntary drug-taking. Therein lies the conundrum for the drug abuser, who cannot understand, "Why can't I quit?" The drug abuser can't quit because the action of sign-tracking of drug-taking is disconnected from the intention to quit, and their lack of awareness of sign-tracking keeps them in the dark. Thus, the drug abuser who is blind to the influence of sign-tracking cannot understand why he or she cannot control his or her drug-taking.

Sign-Tracking Confers Vulnerability to Drug Abuse

There are substantial differences between individuals in the tendency to exhibit Sign-Tracking behavior. Addiction scientists exploring the relationship between sign-tracking and drug addiction have found that the tendency of an individual to develop sign-tracking CR performance predicts the vulnerability of that individual to

drug addiction [3,92-93]. In the addiction science laboratory of Professor Terry Robinson and his associates at the University of Michigan Medical School, a large group of rats were assessed for their tendency to develop sign-tracking behaviors in response to the insertion of a lever paired with the delivery of food. Rats that more readily approached and contacted the lever were designated Sign Trackers (ST), while rats that react to the insertion of the lever by approaching the location of food delivery were designated Goal Trackers (GT). All rats are then tested for their tendency to self-administer an abused drug. Each rat was given the opportunity to perform a response that was required in order to receive an injection of an abused drug, such as cocaine, amphetamine, or morphine. ST rats, relative to GT rats, more rapidly acquire the drug-taking response [103], and ST rats, relative to GT rats, take the abused drugs more frequently [104-105]. Moreover, ST rats, relative to GT rats, are more vulnerable to relapse to drug-taking following periods of drug abstinence ([95-96]; for review [97]). Thus, vulnerability to sign-tracking confers vulnerability to drug addiction.

Scientists are now asking the question, Why are ST rats more addiction-prone than GT rats?" One possible answer lies in the specifics of the experience encountered during the act of drug-taking. To obtain the rewarding effects of the drug, the subject is required to perform a voluntary or operant response, typically called the drug-taking response (sometimes called the drug-seeking response). The drug-taking response is almost invariably an action that is directed at a feature of the environment. Most typically the subject is required to make contact with an object. In doing so, the subject will experience the pairing of that object with the rewarding effects of the drug. As a result of extended training with the drug self-administration procedures, the ST rat, relative to the GT rat, will more likely develop Sign-Tracking directed at the object, resulting in contact with the object. And, contacting the object is programmed to produce an injection of the abused drug. In other words, the specific actions of the drug-taking sequence in the drug self-administration laboratory provide experience that is conducive to the development of sign-tracking [14]. It should be noted that drug-taking procedures employed by humans are also conducive to the development of sign-tracking [8]. As noted earlier, humans typically employ an object as a conduit to aid in consuming the drug. Humans drink alcoholic beverages from a cocktail glass, snort cocaine through a coke tooter, and use a bong to smoke marijuana. Thus, drug-taking procedures employed by humans are also likely to lead those prone to sign-track into developing sign-tracking of drug-taking and consequently, prominent symptoms of drug addiction.

Those rats prone to develop sign-tracking also exhibit a constellation of other addiction-like behaviors. For example, ST rats tend to be more impulsive than GT rats,

taking action quickly and without due consideration of the long term consequences [98-99]. ST rats, like human drug addicts, tend to be risk-takers, prone to sensation-seeking and thrill-seeking. In addition, ST rats also tend to respond to novelty with arousal and excitement, rather than with caution [94], and this trait is also observed in humans prone to drug abuse. ST rats also exhibit physiological traits associated with vulnerability to drug abuse [100-101; for review see 93], as well as neurobiological markers differentially associated with drug addiction [102]. Therefore, addiction scientists have concluded that the tendency to perform sign-tracking behaviors may be the overt behavioral expression of a personality trait that confers vulnerability to drug addiction [3].

It seems ironic that GT rats are reward-centric but less prone to addiction, while ST rats, even though they are more focused on the signal than on the reward, are more vulnerable to becoming addicted (for review, see [97]). Clearly, the attractiveness of the reward cue plays a major role in the drug addiction process [2,3,93,103-104].

Sign-Tracking and the Neurobiology of Addiction

How does sign-tracking relate to the neurobiological substrates of addiction? While there is a rapidly developing neuroscience literature relating the two, the scope of our discussion here is to address the congruence of the major features of sign-tracking and dopamine activation.

The experience of a reward is accompanied by an emotional state, often described as a feeling of pleasure, satisfaction, well-being, or euphoria. Scientists have determined that the emotional feelings of euphoria or pleasure are related to activity in an area of the brain called the nucleus accumbens (NAC), which is often called the reward or pleasure center of the brain. The level of activity in the NAC is determined by the synaptic concentration of a brain chemical called dopamine. Higher levels of dopamine in the NAC are associated with stronger positive feelings of pleasure. For example, eating food induces the release of dopamine into the NAC, which leads to positive feelings of satisfaction and enjoyment.

Food, water, and sex are natural rewards. Each of these natural rewards produces an increase in DA levels in NAC that produces the positive emotional feelings of pleasure and euphoria. The elevated DA activity in NAC produces other effects as well. For example, any stimuli that happen to be present at the same time or immediately prior to the time that DA NAC activity is elevated by the natural reward are identified and associated with the positive emotional state produced by the natural reward. So, in addition to producing feelings of pleasure, DA activation of NAC also produces connections to stimuli (people, places, things, sounds, etc) that are present at the time of the euphoric episode. The elevated DA activity in NAC also produces an effect on motor responding called psychomotor activation. Thus, natural rewards induce elevated NAC dopamine, which, in turn produces three different types

of effects: the emotional feelings of pleasure, the association of stimuli present during the experience of pleasure, and the motor responses of the psychomotor activation syndrome. It is the interplay among these three functions of the integrated reward system, each of which arises from the activation of the NAC, that form the major features of the rewarding experience.

The functional biological significance of the integrated reward system warrants further discussion. Consider the story of the starving beast. An ancient beast is on the verge of starvation. The famished beast picks up a small oblong beige object, looks at it closely, then chews and swallows it. Fortunately, it's a grain of wheat, a food reward that activates the NAC. The reward system kicks into play, automatically giving rise to feelings of pleasure, accompanied by a pattern of motor activity called psychomotor activation. The beast just ate a piece of food, and psychomotor activation is the physical motor activity pattern that automatically follows, to organize the process of looking for more food. Psychomotor activation begins with a survey of the situation, an investigation of the environment, and a search for more food reward. To better investigate the environment, the beast may stand erect, rearing and sniffing, looking around, visually scanning, all the while evaluating the environment for food. But the food is laying on the ground, scattered among stones, dirt, twigs, and other non-food items. Because the grain of wheat was the item that the beast looked at just before NAC activation, this small oblong beige food object is highly likely to be associated by the NAC with strong feelings of pleasure. The association of the grain of wheat with the emotional state of pleasure will improve the chances that the wheat grain will be selected as the target of the psychomotor activation syndrome. The beast locates on the ground nearby another small brown oblong object. It's another grain of wheat. Psychomotor activation automatically leads the beast to approach the grain of wheat, pick up the grain of wheat, and eat the grain of wheat. After eating the second grain of wheat, the beast feels another jolt of pleasure, which is experienced right after seeing the grain of wheat, resulting in even more of an association between the wheat grain and feelings of pleasure. In this way, each grain of wheat becomes more tightly associated with pleasure, making the beast increasingly likely to approach, contact, and eat the wheat. Note that the beast is saved from starving by the integrated functions of the reward system (pleasure, association, psychomotor activation). Note also that for this beast, the process of directing eating responses at food was largely automatic, conferring on this individual beast more of a chance of surviving in a patchy world of scarce food resources. The beast survives, increasing the chances of reproductive success, and transmitting this trait, the integrated reward system, to successive generations of progeny. Evolution has equipped the brain of modern beasts with the integrated reward system, deployed upon activation of NAC, to aid in survival. When we experience reward, we experience the emotion of pleasure, the association of the pleasure with stimuli present at that time, and

the psychomotor activation pattern of responding.

Drugs of abuse, such as alcohol, cocaine, and opiates, all activate the same NAC reward system that is activated by natural rewards such as food, water, and sex, but the magnitude of the activation of the NAC by abused drugs may be many times greater than the effect produced by natural rewards. In this way, drugs of abuse hijack the reward system, diverting the system away from the subserving of survival, toward the subserving of addictive behavior.

How the integrated reward system subserves addictive behavior warrants further discussion. Consider the story of Johnny having a drink. Johnny is a moderate, social drinker. He enjoys having a few beers with his friends typically on the weekend. Lately, however, he has noticed that his beer intake has been gradually increasing, so that instead of having two beers at the poker game, he drinks four beers, or more. Drinking beer is pleasurable and mood-improving because the alcohol in the beer produces elevated DA activity in the NAC. In addition, activation of the NAC leads Johnny to associate other stimuli present at that time with these positive emotional feelings, so that Johnny feels good around his drinking pals. The NAC associates the people, places, and things, including sounds, like music, present while drinking beer, with the positive feelings of beer-induced euphoria. We should note that the stimulus that is most closely associated with the DA activation of the NAC is the beer bottle. This is because the beer bottle is seen in the moments in time just before the beer is consumed. The association between the beer bottle and the activation of DA in the NAC will cause the beer bottle to become the target of the psychomotor activation syndrome. This means that Johnny will notice the beer bottle. It conspicuously stands out. Johnny will also find that he is drawn toward the beer bottle. He will reach out and take the beer bottle in his hands, hold the beer bottle, and then drink from it. But the beer consumed due to the psychomotor activation syndrome is not the same as the beer that is consumed as a voluntary, controlled response. The psychomotor activation syndrome is a reflex coming out of the activation of the NAC. Psychomotor activation is not an intended action. Johnny did not decide to drink some more beer. Johnny is drinking beer on automatic pilot. In this way, the integrated reward system leads to beer drinking that occurs but was not intended or subject to self-control. Obviously, beer drinking beyond what is intended is outside the realm of free-will and will be difficult, if not impossible, to manage. Due to alcohol's effects on dopamine levels in NAC, alcohol use can occur even though you do not intend to have a drink. And, the more you drink, the more likely the psychomotor activation syndrome will produce unintended alcohol drinking. In summary, the neurobiological basis of reward and addiction, as revealed by the functions of the integrated reward system (pleasure, association, and psychomotor activation) coincide remarkably with the features of Sign-Tracking.

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Conclusion

Clinical studies of cue reactivity have long noted that the stimuli present when drugs are taken can become associated with the drug's effects, as measured by subjective feelings or physiological responses. The focus of STM is on a particular type of drug-associated stimulus, the object used to consume the drug, and on a particular type of response, the directed skeletal-motor actions of drug-taking. STM addresses the issue of why the drug abuser is unable to control their actions when it comes to drug-taking and why the drug abuser is blind to their loss of self-control as it is happening. STM is unique among addiction models in that STM emphasizes the role of the object used to consume the drug, and, as well, the contingency between that object and the drug reward as the root cause of loss of control of drug-taking. The goal of this paper is to increase awareness of sign-tracking and enhance appreciation of the possible role of sign-tracking in the drug addiction process.

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