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Adult, Infant, and Animal Addiction

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The idea that organisms lacking complex cognitions and social environments—namely, caged animals and human infants—become addicted when exposed to narcotics has been a primary argument for the purely physiological genesis of addiction. The data on fetuses born to mothers using narcotics and other drugs and on laboratory animals that are administered such drugs are complicated and conflicting: primarily they show that the appearance of addiction in these cases depends on a range of psychological and situational variables. These facts tend to disprove a basic irreducible concept of biological addiction. This chapter attempts both to formulate a realistic model of the factors that play a role in addiction for organisms other than adult human beings and to make clear just how profound a phenomenon human addiction really is. There is no exact equivalent among animals or newborn babies to either the addiction, or the resistance to it, that appears in a fully developed human being.

The Effect on the Infant of Mother's Drug Use

Infant Narcotic Withdrawal

The idea of the addiction of the fetus to narcotics and the appearance of postpartum withdrawal is an unquestioned fact for the public and most addiction professionals and researchers. The appearance of infant withdrawal has been regularly observed since the 1970s under a very specific set of research conditions. Only women known to be addicts (and who often label themselves as such), whose drug use and lifestyle are clearly aberrant, and who might themselves be undergoing withdrawal in the hospital alert investigators to the possibility of addicted newborns. By definition, controlled narcotics users would be excluded from this group. Once identified, high-risk subjects (mothers and children) are evaluated carefully for any signs of abnormality. Once observed, to what might these symptoms be attributed? Mothers' drug abuse tends to be global and indiscriminate, involving many licit and illicit substances. Moreover, addicts are less aware of and concerned about health maintenance in general. The women whose children are observed are thus likely to be only those whose overall lifestyle is degraded and marked by multiple drug abuse and a lack of regard for health.

Yet even under such conditions, withdrawal rarely constitutes a distinct pathological entity. The popular portrayal of infant addiction is invariably of a severe and life-threatening condition; Cummings (1979) in his presidential address to the American Psychological Association claimed, without citation, that 92 percent of the children born to heroin-addicted mothers manifested severe withdrawal. In fact, in 75 to 90 percent of cases withdrawal is nonexistent or difficult to detect with such mothers (Kron et al. 1975). Ostrea et al. (1975) did not find a single case of convulsions in 198 cases they studied. What is labeled as infant withdrawal is instead a variable syndrome defined as a "generalized disorder characterized by signs and symptoms of central nervous system excitation" (Desmond and Wilson 1975: 113). Typical indicators are undue crying and ineffective feedings followed cyclically by restless periods of sleep.

There is little or no direct evidence for attributing this distress to narcotic withdrawal. It does not vary in occurrence or severity with the heroin dosage intake reported by the mother (Zelson 1975) or the drug level measured in the infant's or mother's urine or in the cord blood (Ostrea et al. 1975). Rather than comprising a pronounced medical entity, "there are difficulties in diagnosing the narcotic withdrawal syndrome in the absence of prior knowledge of maternal addiction" (Kron et al. 1975: 258). Desmond and Wilson (1975) observed the severity of infant narcotic withdrawal to vary with other metabolic disturbances and particularly with low birth weight. Furthermore, the symptoms they found tended to persist or reappear, indicating more permanent damage rather than withdrawal. These investigators saw the problems of the newborn of heroin addicts to include damage from drug impurities and the cumulative effects of their mothers' lifestyles (many of the mothers

of these infants were prostitutes, for whom infection is a danger along with polydrug use and other unhealthy habits).

Emotional factors have been shown to play a role in severity of neonatal withdrawal. Davis and Shanks (1975) found that—along with protein malnutrition, neglected health, and self-destructive behavior—addicted mothers' guilt and depression contributed to the problematic behavior of their infants. Mothers in this study were especially distressed by nonnutritive sucking, a major symptom of infant withdrawal. Yet ineffective feedings are frequently reported by nonaddicted mothers and the anxiety and personal problems manifested by the addicted women would be especially likely to produce this problem. Infants are also more likely to be separated from addicted mothers in the hospital. Maternal contact has been shown to have a reassuring and beneficial impact for the baby, while absence of maternal contact has been shown to exacerbate behaviors that could be described as withdrawal (Klaus and Kennell 1981). A conventional research design involving blind observation of narcotics- and nonnarcotics-using mothers would thus not only allow most infants of using mothers to pass undetected (as in Kron et al. 1975) but would label as undergoing withdrawal at least some babies of nonnarcotics users (see below).

It is true, for a host of reasons that are difficult to separate, that both narcotics-using mothers and their offspring are likely to experience greater-than-average amounts of postpartum trauma. Coppolillo (1975) suggested an interactive model of what has been labeled withdrawal based on disturbances in addicted mothers' relationships with their newborn. Addicted mothers in this study were unusually likely to be upset by their children and to derive less than ordinary amounts of maternal gratification, creating a cycle of abnormal and nonnurturing behavior. Such a complex model of withdrawn neonate functioning is a far cry from the specific biological addiction syndrome claimed to exist independent of infant (or adult) social and psychological setting. We may even recall that infants were commonly dosed with paregoric and other opium preparations in the nineteenth century in the United States and England (Berridge and Edwards 1981; Courtwright 1982) without parents' being aware of the phenomenon of infant withdrawal. Nonetheless, all public accounts of infant withdrawal depict it in the most monochromatic, lurid light possible, as if to recognize its frequent mildness or its complexity would encourage more pregnant women to take illicit narcotics (see, for a recent account, "Addicted Mothers and Babies" 1984).

Fetal Alcohol Syndrome

Desmond and Wilson's (1975) analysis of neonate withdrawal as a misidentification of more basic damage to the fetus from a variety of causes has proved prescient for later developments in the field. In the mid 1970s and increasingly into the 1980s there was a shift in concern from neonatal narcotic withdrawal to the effects of alcohol on the fetus. The term "fetal alcohol syndrome" (FAS) was applied to abnormalities in offspring of alcoholic

women, most of whom had serious alcohol-related health problems (Hanson et al. 1976; Jones and Smith 1973). FAS incorporates a large number of observed deficits in such infants, including increased mortality, birth defects, and smaller size to "failure to thrive, hyperirritability and motor dysfunction" (Cushner 1981: 202). The syndrome has been conceived from the beginning as involving long-term organic damage, even though reported symptoms are often similar to those attributed to heroin withdrawal. Also from the onset of this research, complications have been noted in separating the factors contributing to the appearance of FAS, particularly because heavy drinking and heavy smoking are strongly correlated (Ouellette et al. 1977).

Research on FAS has advanced to include a more general, multivariate framework where other factors—such as time during the woman's pregnancy when drinking occurred—are taken into account. In addition, earlier dramatic reports about FAS have been replaced by more modulated accounts of the nature of the syndrome. Chernick et al. (1983) called the current definition of FAS inadequate because among heavy-drinking mothers (who were typically also heavy smokers), the extreme morphology that had been reported for FAS was infrequent. Wright et al. (1983) found *no* cases of FAS among 903 women even though some were very heavy drinkers, causing the chief investigator to remark that FAS "is a rare disease . . . associated with pathologically heavy drinking" ("Drink/Smoke Combo . . ." 1983). The only difference due to drinking found by these investigators was in birth weight, with moderate drinking (50 to 100 grams of alcohol weekly) being associated with a slightly higher risk of delivering a lightweight baby (Chernick et al. 1983 did not note moderate drinking to be a risk). Greater drinking and smoking increased this likelihood, with mothers who were heavy drinkers and smokers being about four times as likely as moderate drinkers to produce lightweight offspring.

Perhaps the most comprehensive study of fetal alcohol syndrome to date was conducted at Boston City Hospital, employing 1,690 mothers and their infants. Hingson et al. (1982) approached the question by reviewing a range of studies that both have reported the appearance of FAS and have failed to find it. Their own data revealed "neither level of drinking prior to pregnancy nor during pregnancy was significantly related to infant growth measures, congenital abnormality, or features compatible with the fetal alcohol syndrome" (p. 544), although the number of seriously alcoholic mothers in the study was limited. What did predict infant size at birth and other features representing FAS were lower maternal weight gain, maternal illnesses, cigarette smoking, and marijuana use. "The results underline the difficulty in isolating and proclaiming single factors as the cause of abnormal fetal development. . . . In this study the quantitative impact of each behavior was relatively minor, whereas the impact of a lifestyle that combines smoking, drinking, marijuana use, etc., is more marked" (p. 545).

At this point, a fair summary might be that introducing any of a (large) variety of foreign substances during pregnancy is potentially risky, the more so when this reflects an overall lack of concern for health, heavy alcohol or

licit or illicit drug use, and other problematic maternal behavior. To connect serious and clear-cut abnormalities, either short-lived or more enduring, to use of specific substances by mothers has not been possible. Once again, in the case of fetal alcohol syndrome as with infant narcotic withdrawal, the focus and magnitude of attention directed at a cause of fetal distress or defect has been determined more by external social forces than by the evidence at hand. In the early 1970s, when infant withdrawal was discovered, concern was focused on narcotics epidemics (see chapter 6), while in the late 1970s and the 1980s, coinciding with FAS publicity, we have had a concerted campaign against drinking (see chapter 2). Predictably, in the current climate toward alcohol use, early discoveries of dangers from drinking by pregnant women were built into the recommendation from the U.S. Surgeon General that prospective mothers abstain entirely, a claim from which investigators whose study prompted the recommendation have dissented (Kolata 1981).

The Addicted Animal

The fact that laboratory animals, under the right conditions, will persistently ingest opiates and other drugs has been generalized by many drug commentators to a belief that human beings, along with other mammals, find such drugs inherently rewarding and their use self-perpetuating. This generalization has led to the proposal of metabolic and conditioning theories that support the concept of an inexorable, pharmacological addiction process (see chapter 3). As with other data on drug use and addiction, experimentation with animals yields far more complex results than has been recognized. In particular, research indicates that animals consume opiates only under very limited circumstances. Moreover, research that takes the *setting* of the animal's drug use into account strongly suggests that many of the same environmental and even psychological mechanisms that play a role in human drug use in fact also do so for animals.

Opiates have generally been at the forefront of the attention of animal researchers in the United States. Studies of animal narcotic self-administration were pioneered by Seevers (1936), who showed that morphine-habituated monkeys willingly submitted to continued injections. Subsequently, Nichols et al. (1956) demonstrated that rats could be made to drink morphine solutions in preference to water. In the 1960s, investigators at the University of Michigan developed a technique whereby restrained animals were able to inject themselves with drug infusions through a permanently implanted catheter (see Weeks and Collins 1968, 1979; Woods and Schuster 1971). This led to a profusion of studies of the self-administration of such substances as cocaine, amphetamines, and other CNS stimulants; heroin, morphine, methadone, and other narcotics; and alcohol, tobacco, and hallucinogenic drugs. Overall, the quantity and regularity of self-dosing were highest for the stimulants but were also high for the narcotics. Tobacco, alcohol, and hallucinogenics were taken

less consistently, although this may result from difficulties in administering these substances (Kumar and Stolerman 1977).

Aided by the self-administration apparatus, researchers investigated such pharmacological areas as the effects of physiological states on self-administration rates and different schedules of drug reinforcement. However, the most prominent result from this work has been the idea that drugs (particularly narcotics) are powerfully reinforcing—even irresistible—to the organism with free access to them. This conclusion has regularly been put forward (see Bejerot 1980; Dole 1972; Goldstein 1972, 1976a; Jaffe 1980; McAuliffe and Gordon 1980; Wikler and Pescor 1967), one version of which is as follows (Goldstein 1972: 291–92):

> *Extensive studies on self-injection of opiates by monkeys show that any animal, having discovered that pressing a lever injects a narcotic intravenously, will inject itself repeatedly, raise the frequency to maintain drug effects . . . and develop full-blown addiction. It seems, therefore, that becoming addicted requires nothing more than availability of the drug, opportunity for its use, and (in man) willingness to use it.*

Such conclusions have provided the major scientific support for popular conceptions about heroin addiction in the United States, including the belief that there is a biological and neurological underpinning for addictive behavior (Peele 1977). The nature of this putative mechanism in addiction—whether a metabolic process, cellular adjustment, or chemical change in the brain—has never been established, as Seevers (1963) made clear. Currently, the endorphins and opiate receptors in the brain are being investigated to find the key to addiction. Pharmacologists express caution and appropriate scientific modesty about this search (Goldstein 1976b), a restraint not apparent in writing by popularizers of work in the neurosciences (Restak 1979).

Biological and neurological theory have had notable difficulty in explaining basic data from animal psychopharmacology studies: for example, the large range of dissimilar chemicals that animals have been found to self-administer chronically. No single physiological mechanism seems likely to be triggered by such a diverse array of substances, each with its individual molecular structure. Moreover, animal researchers and pharmacologists have been forced to create elaborate, abstract conceptions to fit laboratory results. When Wikler and Pescor (1967) found some rats relapsed to morphine use months after having been withdrawn, they hypothesized that withdrawal symptoms had been conditioned to appear in response to cues associated with the animals' previous drug use (see chapter 3). Keller (1969) described these researchers' hypothesis to be an "arbitrary pronouncement—remembering that they had not demonstrated any biochemical changes in the delayed withdrawal symptoms of their post-addicted rats, but only a behavioral syndrome." Keller suggested "that these investigators are addicted to the physicalist-pharmacological explanation of anything that involves drugs" (p. 13).

A potentially more important issue for evaluating theories about drug use derived from the observation of laboratory animals is that the animals that are studied are deprived of normal social life, environmental richness, and mobility. The investigation of drug self-injection by animals has taken place for the most part with animals who are encaged and harnessed to an implanted catheter, conditions that may well be painful and that certainly prohibit the normal activity of a healthy animal. Animal researchers like Yanagita (1970) have declared strong reservations about generalizing from behavior under these conditions—in which social inhibitions are absent, drugs are constantly available and require next to no effort to obtain, and the organism is deprived of stimulation and is under constant stress—to the behavior of human beings.

Furthermore, the behavior of these laboratory animals may not generalize *to animals in natural environments.* Animals, even in laboratory environments, do not readily self-administer hallucinogenic drugs (Griffiths et al. 1979). The study of hallucinogen behavior has been extended to animals in the field, where similarly most herbivores do not self-administer the drugs, except episodically (R. Siegel 1979). Yet when placed in sensory isolation chambers for several days, rhesus monkeys were found continually to self-administer the hallucinogen DMT (Siegel and Jarvik 1980). This study indicates that the restrictiveness of the animal's environment is a crucial determinant of its drug-taking behavior. To what extent is this also true of the use of narcotics by animals in the laboratory, a phenomenon on which pharmacologists have built the notion of the inherent addictiveness of narcotics?

Animal Narcotics Use in Rat Park

An ongoing body of research at the Simon Fraser University Drug Addiction Research Laboratory (conducted by Patricia Hadaway, Robert Coambs, Barry Beyerstein, and Bruce Alexander) has addressed the question of how physical and social environment affects opiate use among rats. Rats—along with mice, monkeys, and apes—are the usual subjects in drug experiments. The Simon Fraser experiments utilized Wistar strain albino rats, which are easy to obtain and are extremely gregarious, curious, and active. Their progenitors, wild Norway rats, are intensely social animals (Lore and Flannelly 1977) whose social responses remain largely intact even after hundreds of generations of laboratory breeding (Grant 1963). The opiate used in the experiments was morphine hydrochloride (MHCI) a salt of morphine manufactured by ICN Canada and used in morphine tonics for oral consumption. Both popular and clinical experience indicate that morphine and heroin are readily interchangeable (Zentner 1979), and Lasagna (1981) has made a clear case that there are no important differences in the relative analgesic efficacy of the two drugs for humans.

The purpose of the Simon Fraser studies was to determine whether and how laboratory housing conditions influenced the animals' consumption of the morphine solution. The hypothesis was that animals in isolated,

constrained housing—that typical for the University of Michigan and other laboratories in which animal research has been conducted—would ingest more morphine than animals in more nearly natural surroundings. To test this initial, basic idea, a housing environment was constructed that differed radically from the typical cage and that mimicked the rats' natural environment as much as possible. This laboratory environment was dubbed Rat Park. It was more spacious than a standard cage (about 200 times as large in square footage), was more stimulating (with painted walls and objects rats seem to enjoy such as tin cans strewn about), and contained a rat colony (groups of sixteen to twenty rats of both sexes).

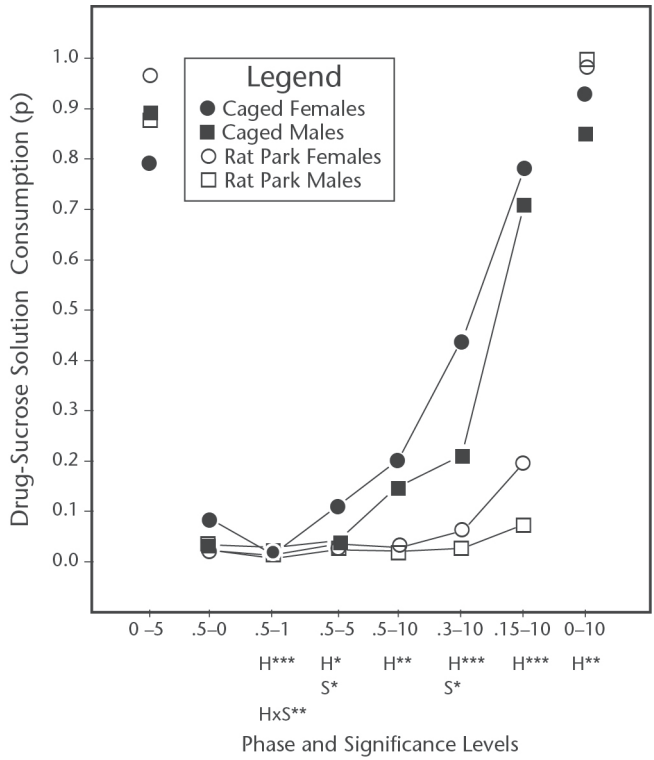
Measuring each rat's consumption of morphine solution is a straightforward matter in a cage. In these experiments, a drinking bottle of the solution was fastened next to the animal's regular water bottle on the side of the cage. Weighing both bottles daily provided a measure of drug solution and of water (or other inert substance) that was consumed. The rats in Rat Park required a more elaborate mechanism to measure individual consumption. Accordingly, a short tunnel was built which allowed one rat at a time access to two drop dispensers. One dispenser contained the drug solution and the other the inert control substance; a device automatically recorded how many times each rat activated each drop dispenser, while a photoelectrically activated camera recorded an identifying dye mark on the back of the animal (see Coambs et al. 1980 for a full description). Raw consumption data were converted into three measures of each rat's daily morphine consumption: grams of morphine solution, mg morphine/kg body weight, and proportion of morphine solution to total fluid consumption.

Morphine solutions are unpleasantly bitter to human taste and also, apparently, to rats, since they reject it with the same signs of distaste as they show towards extremely bitter nonnarcotic solutions. Offered a simple choice between water and morphine solution, rats take only a drop or two of the drug solution and ignore it thereafter. Khavari et al. (1975) found concentrations of morphine and sucrose that were sweet enough that rats would drink them in preference to water in quantities great enough to produce signs of withdrawal when the solution was removed.

An early Rat Park experiment was designed to measure differences in the consumption of sweetened morphine solution between eighteen individually caged rats (nine of each sex) and eighteen rats (also nine of each sex) living in a Rat Park colony (see Hadaway et al. 1979). In order to discover any differences that the two housing environments produced in attraction to the taste of sugar, an initial phase in the experiment offered the rats a choice between tap water and sugar solution without morphine. The second phase offered rats a choice between water and morphine (no sugar) solution. In five subsequent phases of the experiment, the solution contained both sugar and morphine. The morphine was made increasingly palatable to the rats in each successive phase by either raising the concentration of sugar or lowering the

concentration of morphine compound. In a final phase, sugar solution alone was again presented.

The results show clearly that the caged rats ingested more morphine than the animals in Rat Park (see Figure 4–1). There was no housing effect on preference for the plain sugar water in the initial phase, and the Rat Park animals actually drank more of the sugar solution in the last phase. In the first couple of phases in which morphine-sugar solution was used, few of the rats in either environment drank any morphine solution. As the flavor improved, caged rats increased their consumption of morphine dramatically, while those in Rat Park increased theirs by only a small amount. The differences in morphine consumption were large and highly significant in the last three morphine-sugar solution phases. Alexander et al. (1981) replicated this experiment with a second pretest in addition to the one offering rats a choice between water and a sugar solution. This additional phase presented rats with water and a bittersweet quinine-sugar solution that was, to the human palate, almost indistinguishable from one of the morphine-sugar solutions. The purpose of this pretest was to rule out the possibility that the differences in morphine consumption were due to an aversion to the bitterness of the morphine solution. There were no significant housing effects on either pretest in the replication, and the differences in the subsequent morphine phases were about as large as those in the first Rat Park experiment.



Morphine-sucrose solution consumption as proportion of total fluid consumed. Numbers identifying phases are mg MHCl per ml followed by percentage of sucrose in solution. Significance levels from analyses of variance for each phase use the following symbols: H = housing effect, S = sex effect, H x S = housing by sex interaction; * = $p < .05$, ** = $p < .01$, *** = $p < .001$.

Figure 4–1. First Rat Park Experiment

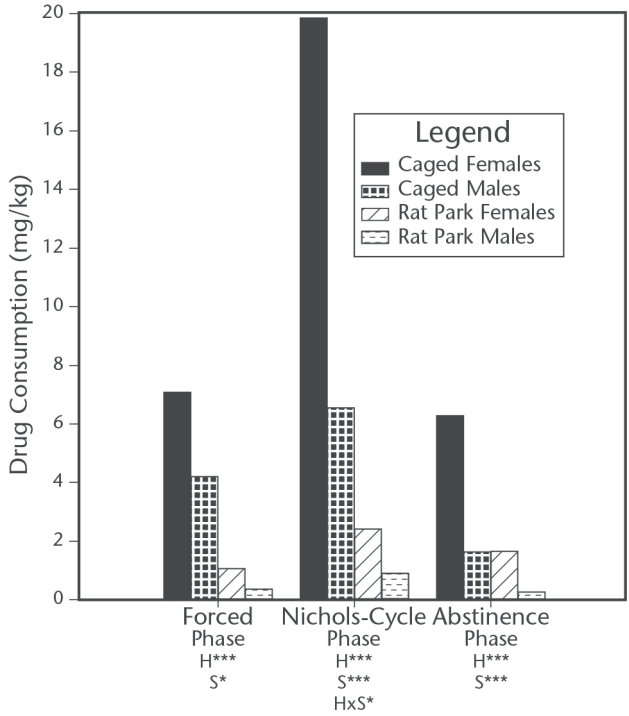
Habituating the Animals in Rat Park

Rats in Rat Park were less likely to be lured into drinking a sweetened morphine solution than were caged rats. Would this same difference in susceptibility to narcotic effects also hold for animals that had first been habituated to the drug? In other words, would Rat Park animals ingest less narcotic than caged animals when both groups were being withdrawn from narcotics use?

To test the housing effect under these conditions, Alexander et al. (1978) habituated caged and Rat Park rats to narcotics by making morphine solution (0.5 mg morphine hydrochloride/ml water) their only source of fluid for fifty-three days. A number of prior experiments indicated that the amount of narcotic these animals ingested was more than enough to cause withdrawal symptoms (e.g., Fuentes et al. 1978). Interspersed in this forced consumption phase were four choice days during which the rats in both environments

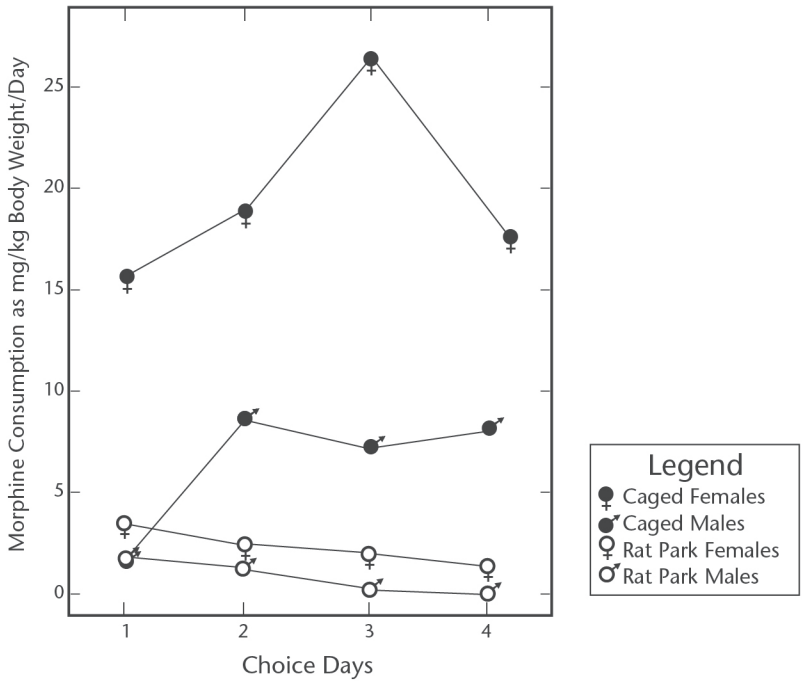
were given access both to water and to morphine solution. At the end of this fifty-seven-day period, in the second phase of the experiment, the rats were put on a training regimen developed by Nichols et al. (1956) to teach rats that drinking morphine solution would relieve their withdrawal symptoms. The Nichols phase of the experiment consisted of repeated three-day cycles comprising one day of no fluids, one of only morphine solution, and one of only water. This cycle was repeated eight times interspersed with four morphine-water choice days. In the final, abstinence phase of the experiment, all morphine was withdrawn except for two morphine-water choice days, one each at two weeks and five weeks after the Nichols cycle phase.

Again results were highly significant. In all these phases of the experiment, caged rats consumed more morphine; during the Nichols phase, caged rats consumed about eight times as much morphine solution during the four choice days as did Rat Park rats (see figure 4–2). Figure 4–3 examines the changes in morphine consumption that took place during the Nichols cycle. The training regimen apparently achieved the purpose of teaching the caged rats to take the drug in response to withdrawal, and they increased their morphine consumption over the four choice days. The Rat Park animals, on the other hand, decreased their consumption slightly over the same period, as if learning about the drug's effects *reduced* their willingness to ingest it. The results of this second Rat Park experiment call into question conventional notions of withdrawal as the impetus to opiate consumption. Just as with human beings, an animal's response to being withdrawn from a narcotic is influenced by situational factors. Withdrawal from even a regularly administered narcotic is not so overwhelming as to eliminate the creature's concern with other drives and attractions. When given reasonable alternatives, animals in this experiment did *not* act as though the motivation to avoid withdrawal discomfort were an all-purpose reinforcer with which ordinary motivations could not compete.



Morphine consumption on choice days in three phases as mg MHCl/kg body weight. Significance levels indicated as in Figure 4–1.

Figure 4–2. Second Rat Park (Forced Consumption) Experiment



Morphine consumption as mg MHCl/kg body weight/day on choice days during Nichols-cycle phase.

Figure 4–3. Nichols-Cycle Phase of Second Rat Park Experiment

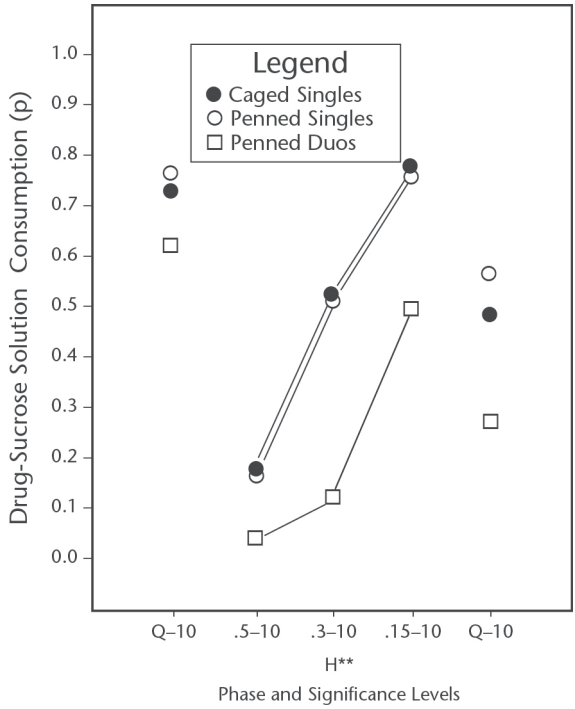
What Factor(s) Cause the Rat Park Housing Effect?

The Rat Park data that have been reviewed so far had an essentially negative purpose: to disprove an ill-founded generalization from previous research on caged animals. The data clearly show that the readiness to consume opiates displayed by caged animals does not hold for rats living in an environment that resembles the animals' natural setting, even after the rats have been habituated to drug use. While these data show that differences in housing conditions can produce a considerable difference in the amount of morphine rats consume, the many distinctions between Rat Park and a standard cage make it impossible to pinpoint the specific factors that affect the animals' morphine intake. This section reports studies that explored these factors in an attempt to cast light on the reasons for continued morphine consumption in animals and in human drug addiction.

Social interaction, which is known to be a powerful factor in animal and human behavior, was the first environmental feature tested for its effect on morphine consumption. A group-size experiment was devised that placed one, two, and four rats in single cages about two-and-a-half times the size of a standard cage. Some of the duos and quads were all female, some all

male, and some mixed. The animals were then exposed to the same sequence of solutions used in the first Rat Park experiment and their consumption of morphine measured by weighing the bottles in their cages. The results of this experiment clearly supported the null hypothesis—that group size per se did not affect morphine consumption. Groups of four rats (whatever the sexual composition) ingested about four times as much morphine as one rat and twice as much as two.

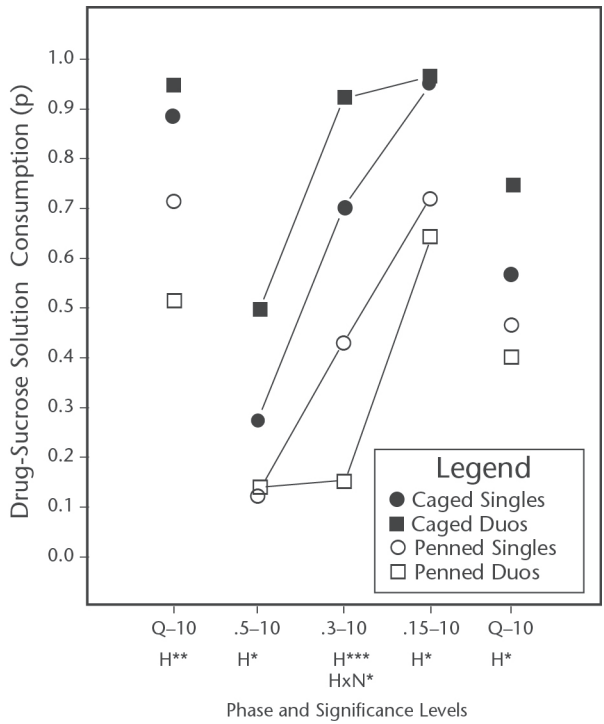
Space was taken as the next most obvious environmental feature to be explored. Twelve pens, each five-feet square (making them one-third the size of Rat Park but still more than sixty-five times as large as standard cages), were constructed. Four of the pens contained single males, four single females, and four male-female pairs. A comparison group of twelve rats (six male and six female) were housed in individual cages. Both a quinine solution pretest and posttest were employed along with the presentation of three increasingly sweet morphine solutions. No significant differences were found between the caged and the penned singles in the pretest or posttest or in any of the morphine-intake phases. However, as figure 4–4 shows, the *penned pairs* drank *less* morphine than both the penned and the caged singles. The housing difference for the .3–10 phase was significant for the proportion data.



Morphine consumption as proportion of total fluid consumed. All abbreviations same as for figure 4–1, with the addition of Q–10 to represent 0.06 mg quinine sulfate/ml water + 10 percent sucrose.

Figure 4–4. Morphine Consumption by Individual Rats in Cages and Individual and Paired Rats in Pens

The last result suggested that it is neither space nor the presence of other rats taken alone but rather the *combination* of space and companionship that brings about the housing effect noted in Rat Park. To test this possibility directly, rats in an experiment with four housing conditions—caged singles (six male and six female caged single rats), caged duos (six caged male-female pairs), penned singles (five male and five female penned single rats), and penned duos (five penned male-female pairs)—were exposed to morphine according to the standard design. The results of this study corroborated the important finding in the earlier study: rats that have both space and a companion ingested significantly less morphine in the .3–10 phase than those lacking either or both of these assets (see figure 4–5). In this experiment space alone did seem to make a difference, with both penned singles and duos consuming less morphine than rats in either of the two caged conditions. No such effect was found for the social condition alone. In fact, the caged duos ingested more morphine than the penned *or* caged singles.



Morphine consumption as proportion of total fluid consumed. H represents housing factor (cage vs. pen) and H x N is interaction between housing and number of rats (one or two).

Figure 4–5. Morphine Consumption by Individual and Paired Rats in Cages and Pens

Unfortunately, in this case alone among the experiments reported here, there was a significant quinine phase pretest difference in the same direction as the difference in morphine consumption. It is thus possible that differences in morphine consumption among the groups could have resulted from an aversion to bittersweet solutions somehow produced by the different housing conditions. Still, the differences in the .3–10 phase were larger than the quinine pretest differences, even though the bittersweet taste of the quinine– and morphine–sucrose solutions were matched for these phases. An analysis of covariance yielded a significant housing effect for this phase when the initial taste preference was partialed out. Because it is not possible to test all the assumptions about these data required for analysis of covariance (see Ferguson 1981: 370–73), these results can only indicate trends in the data rather than establishing a firm level of significance.

Complications in Rat Park

Separating out the influences of type of narcotic, measurement system, and type of rat from that of environment in producing the Rat Park housing effect may be a long process or even an impossible one. At the same time, housing differences in narcotic consumption were also found at the Drug Addiction Research Laboratory for rats housed in pens and cages. The Rat Park and related studies have demonstrated, under specific conditions, that environmental factors will affect narcotic consumption, as Siegel and Jarvik (1980) have found to occur with hallucinogens. Environmental effects in Rat Park and related studies, all with their limitations, must be analyzed with reference to corroborating data from both the Drug Addiction Research Laboratory and other investigators. More important than the specific housing effect in these data may be some overriding results concerning the likelihood of rats consuming narcotics under all conditions.

What Causes Animals to Accept Narcosis?

Not only the rats in Rat Park but the comparison animals in cages failed to consume opiates with the avidity that Goldstein (1972) described or that seems typical for animals studied at the University of Michigan and elsewhere. In the current studies, rats only took a drug when it was presented in a highly sweetened solution and then only irregularly—with high day-to-day variation in consumption. These results suggest a need to reevaluate the extant hypotheses for why caged animals seek narcotic effects.

Relief of stress and pain. The Rat Park and similar data on the impact of isolation and being caged could be explained by the stress that constrained housing causes the animals and that narcotics relieve. Working against this interpretation is the surprising absence of independent evidence that stress or pain induces opiate consumption in rats. In several experiments, Chipkin (1976) found that intermittent electric shocks spread over periods as long as fourteen days failed to increase methadone consumption in caged rats. In the

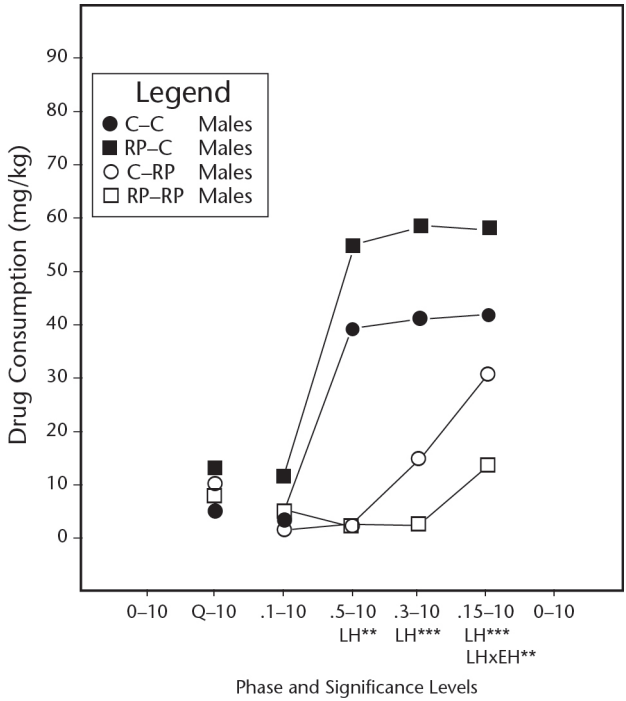
Drug Addiction Research Laboratory at Simon Fraser, Brunke et al. (1980) found no increase in the oral self-administration of morphine for caged rats that underwent surgical implantation of venous catheters.

Constitutional differences. Panksepp (1980) has presented evidence that brief isolation makes young rats more sensitive to pain. Such sensitivity could be caused by an inability to maintain normal endorphin levels or by other physiological deficits that enhance the utility of the pain relief provided by narcotics. Some support for this idea comes from reports that long-term isolation can increase the effectiveness of morphine for relieving pain (DeFeudis et al. 1976; Kostowski et al. 1977). However, some of the same studies have also shown that long-term isolation does make animals more sensitive to pain (Adler et al. 1975; DeFeudis et al. 1976) and that isolation makes animals sensitive to the analgesic effects of morphine (Katz and Steinberg 1970; Kostowski et al. 1977). The latter data suggest an alternative physiological hypothesis that partially contradicts the first. If morphine has less of an analgesic effect on rats in isolation, then it could be that isolated rats need to consume more morphine than those living with other rats to achieve the same level of pain relief.

Both of these arguments bear an obvious affinity to those that trace human addiction to inherited or acquired endorphin deficiencies (cf. Goldstein 1976b). Both also fit with animal research showing that quality of the early post-weaning environment for rats has major effects on the anatomy and physiology of the developing nervous system (cf. Greenough 1975; Horn et al. 1979; Rosensweig 1971), some of which have been related to later drug use (Prescott 1980). To the extent that isolation has its effect through permanent or long-term changes in the animal's nervous system, isolation early in life should be more influential than later isolation in the consumption of morphine. This possibility was explored at the Simon Fraser Laboratory. Thirty-two rats (sixteen of each sex) were divided between individual cages and Rat Park at weaning (age 21 days). At age 65 days, half the rats in each setting were moved to the other, creating four housing conditions: C-C, or caging both early and late; C-RP, or caging early and Rat Park late; RP-C, Rat Park early and caging late; and RP-RP, Rat Park both early and late. At age 80 days the rats began a sequence of choice tests, starting with a sucrose and a quinine-sucrose pretest, proceeding through the usual sequence of morphine-sucrose solutions, and ending with a sucrose posttest.

Figure 4–6 depicts results of this experiment for male rats (data on female rats indicate the same effects, although not with the same degree of statistical significance; see Alexander et al. 1981). No significant pretest or posttest difference appeared. Significant results were found for late housing, with rats housed in cages consuming much more morphine than did rats living in Rat Park. Early experience had no consistent effect on the rats in this experiment, although there was a slight tendency for the C-RP rats to consume more morphine than RP-RP rats over all the measures reported in Alexander et al. (1981). These data showed clearly that the Rat Park housing

effect is more the result of the environment of the animal at the time it is tested than of its early post-weaning experiences and is less attributable to constitutional differences than to situational factors.



Morphine consumption as mg morphine/kg body weight/day. Additional abbreviations for housing conditions are C for caged and RP for Rat Park and for analysis of variance significance levels are EH for early housing and LH for late housing.

Figure 4–6. Morphine Consumption for Rats Housed Early/Late in Cages and Rat Park

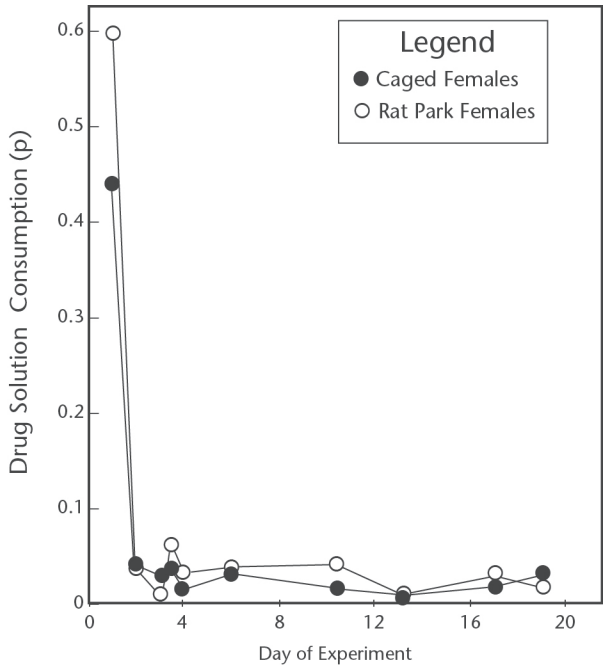
Interference with normal activity. The importance of contemporaneous environment for morphine consumption supports the results of the study of penned and caged rats. Both indicate that it is the inhibition of current opportunities for activity that favors the animals' consumption of morphine. The comparison of caged and penned rats alone and together showed that neither space nor companionship taken separately suppressed rats' morphine consumption as much as both together did. Perhaps this is because rats housed in a spacious environment with others of their species perform many complex social activities that are inherently rewarding and with which the drug's effects interfere. Rat sexual behavior, for example, occurs on the run with the female starting and stopping over several square meters while the male keeps up as best he can. Perhaps the caged duos consumed more morphine than caged singles because putting two rats in a cage restricted their individual

activities while not providing enough space for interactive ones. For rats—a colonial species and not a pair-bonding one (Lore and Flannelly 1977}—larger, more populated housing conditions would most closely resemble their natural habitats and might be most effective for inhibiting drug use.

There are other indications that rats learn to avoid morphine because it interferes with complex rodent activity. Even small doses of narcotics significantly reduce sexual behavior (Mumford and Kumar 1979; McIntosh et al. 1980) and social cohesion among rats (Panksepp et al. 1979). Alexander et al. (1978) noted a marked reduction in activity of all sorts among animals forced to drink morphine solution. The case that species-typical behavior is in and of itself reinforcing has been forcefully argued by Glickman and Schiff (1967). Garcia et al. (1974) have meanwhile shown that rats learn to avoid foods or solutions that produce sickness even hours after consumption. Taken together, this information suggests that rats could learn to avoid narcosis when it prevents them from experiencing the rewards brought on by normal activity.

What comes through most strongly in the Rat Park and related studies is how much experimental pressure is required—including heavy sweetening of morphine solutions and forced habituation in addition to deprivational housing—to cause rats regularly to self-administer a narcotic. The fact that rats reject morphine when offered a choice between unsweetened drug solution and water is usually attributed to the bitter taste of the opiate solution. This notion has not born up under testing, however. Huidobro (1964) reported that caged rats whose sense of taste was destroyed (through sectioning their lingual and glossopharyngeal nerves) rejected morphine solutions. Wikler and Pescor (1967) found that naive rats rejected the opiate drug etonitazine even though it was essentially tasteless in the concentration used.

The alternate possibility—that the effects of narcotics themselves are what prevent animals from drinking a morphine solution—was tested in two studies at the Drug Addiction Research Laboratory. In the first of these experiments, rats in cages and in Rat Park were given twenty-four-hour-a-day access to two bittersweet solutions. The bitter taste in one solution came from quinine sulfate and in the other from morphine hydrochloride. The two tasted almost identical to human taste. In this arrangement, rats did not have to sacrifice palatability in order to obtain a drug effect. The results in figure 4–7 for female rats confirm that the solutions were equally tasty to the animals, with both caged and Rat Park animals drinking about half their total fluid intake as morphine for the first eight hours of the experiment. Then both sets of rats drank very little morphine for the remaining nineteen days (Coambs 1977). Caged males did drink significantly more morphine than Rat Park males for the last ten days of the experiment. In the absence of such a difference between Rat Park and caged females, however, the best overall summary of these results is that rats under both housing conditions will not ingest appreciable amounts of morphine when there is an equally palatable and inert alternative.



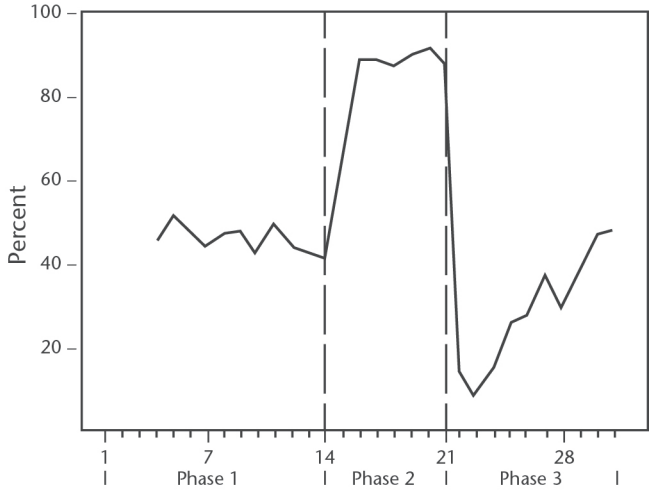
Morphine consumption as proportion of total fluid consumed. Choice was between morphine-sucrose (.5–5) solution and quinine-sulfate solution (.1–5) that were equally bitter to taste. The decline in morphine consumption after the first eight-hour test period was significant at $p < .001$, while differences between housing groups were not significant.

Figure 4–7. Morphine Consumption by Females in Rat Park and in Cages Given Choice of Quinine and Morphine Solutions

In a follow-up experiment, Coambs (1980) gave a choice between sweetened quinine and morphine solutions to caged rats. The quinine concentration was increased with the intention of forcing the animal to drink morphine. The initial effect of what appeared to be an unpleasant choice for the animals was that they did not drink at all for the first few days. In a result that did not occur with any other experimental procedure, the rats eventually split into two distinct groups: Roughly half the rats drank mostly the morphine solution, while the other half drank mostly the quinine. On day 15, naltrexone was introduced into both solutions with the effect of neutralizing the action of the morphine solution. Figure 4–8 shows that there was a dramatic jump in morphine consumption at this point. While the rats that had initially preferred the morphine continued to do so, the rats that had preferred the more bitter quinine solution quickly shifted to the morphine *once its psychoactivity had been removed.* The results of this study unambiguously indicated that even caged rats find the psychotropic effects of morphine to be aversive.

The evidence from both these studies seemingly contradicts a body of research that shows laboratory animals will inject themselves with opiates

continuously without added inducements. The differential performance of animals in the morphine solution and the self-injection experiments may highlight the abnormality of the latter setting (Peele 1977; Yanagita 1970). For caged animals implanted with catheters, normal gratifications are curtailed at the same time that animals are able to produce—almost effortlessly—an immediate, reliable infusion of a drug. Yet research has shown that modifying these forces even slightly, as by increasing the amount of bar pressing required to produce an injection of drug, will reduce the doses that animals self-administer (Kumar and Stolerman 1977).



Morphine consumption as proportion of total fluid consumed. In Phase 1, rats chose between .5 mg morphine hydrochloride/ml water + 8 percent sucrose and .2 mg quinine sulfate/ml water + 8 percent sucrose (first three days omitted because very low intake made calculation of proportions unreliable). In Phase 2, 0.1 naltrexone hydrochloride added to both solutions. In Phase 3, the choice was the above morphine and naltrexone solution and a solution of 0.1 mg naltrexone/ml water + 8 percent sucrose.

Figure 4–8. Morphine Consumption by Caged Rats Given Choice of Quinine and Sweetened Morphine Solutions and Quinine and Morphine-Naltrexone Solutions

Self-injection research has been built on optimum situations for inducing an organism to ingest narcotics. Rats in experiments employing narcotic solutions, on the other hand, must drink an appreciable volume of fluid to gain a somewhat delayed effect in an environment that permits them a wider range of alternative activities. Under these conditions, which better correspond to those naturally obtaining for the animals, most animals seem to react with the same distaste for narcotics that most humans express in ordinary circumstances (see chapter 3). The same holds for alcohol, which laboratory animals regularly reject in preference to water. Falk (1981) was able to induce rats to consume alcohol and other drugs (such as barbiturates) in large quantities by

creating an intermittent feeding schedule that the animals found highly disturbing. As Falk (1983) summarized over a decade's research: "Schedule-induced drug overindulgence remains strictly a function of current induction conditions. Even with a long history of schedule-induced drinking, with the development of physical dependence, termination of the scheduled aspect of feeding produces an immediate fall in alcohol intake to a control level" (p. 389).

The Implications of Infant and Animal Research for Conceptions of Addiction

The most important conclusion to emerge from an examination of animal and infant addiction is that addictive behavior is not rigidly determined by the properties of drugs. Falk (1983) noted the results of schedule-induced alcohol consumption studies: "Once again we have a picture of a reputedly enticing molecule failing to take over behavior in spite of chronic binging" (p. 389). Infants and animals continue to respond to such environmental factors as nurturance and a stimulating environment in the face of narcotic withdrawal pangs. The richness of the organism's repertoire of responses with regard to narcotics and other drugs may enhance our awareness of the complexity of the determinants of the behavior of all mammals and of human beings of all ages, including cognitive, emotional, and experiential complexity that has often gone unnoticed. In particular, the research on animals and infants is reminiscent of findings about narcotics use by adults (such as the Vietnam War data)—namely, that full-fledged craving for narcotics and abhorrence of withdrawal appear mainly under abnormal conditions. Animals and infants apparently share with the adult human being an urge to experience life normally that outweighs the allure of narcosis.

At the same time, we must be careful to avoid the error of overgeneralization that has bedeviled animal self-injection research. Addiction as we know it is a purely human phenomenon (Peele 1977). This is because addiction entails behavior that gains its meaning only in human social and psychological context (see chapter 1). For example, we decide a person is addicted—as opposed to being a controlled user of a substance—when he or she disregards health, personal well-being, and social propriety in order to continue a behavior. There are no real parallels for this among animals and infants. Another distinction between adult human beings and other organisms is the greater cognitive and situational resources the adult human may counterpoise against addiction: Only an adult would quit an addiction like narcotics or cigarettes or overeating because it violates other values, such as a desire for self-control (see chapter 5). The animal or infant must face withdrawal without the benefit of any such salutary resolve.

On the other hand, adult human experience provides unusual opportunities for addiction to take hold. While Robins et al. (1974) found that most soldier narcotics users and addicts gave up their habits when returning home,

a small percentage continued to be addicted. These veterans were more likely to have abused drugs before entering the service. What we see in these men is an enduring disposition—one that transcends situation—to seek narcosis or some other addiction. Peele and Brodsky (1975: 63) attempted to analyze this phenomenon in terms of animal and infant research:

> *When we think of the conditions under which animals and infants become addicted, we can better appreciate the situation of the addict. Aside from their relatively simple motivations, monkeys kept in a small cage with an injection apparatus strapped to their backs are deprived of the variety of stimulation their natural environment provides. All they can do is push the lever. Obviously, an infant is also not capable of sampling life's full complexity. Yet these physically or biologically limiting factors are not unlike the psychological constraints the addict lives with.*

While a concept of addictive personality that disregards the individual's opportunities, life stage, and personal desires is a limited analytic tool, the *absence* of a conception of personal disposition is also limiting in the analysis of addiction. Animal research can illuminate such a personality construct only indirectly. Falk's (1983) insightful analysis of animal and human excess discerned that drug abuse "depends upon what behavior opportunities are available in life's situations, and *whether the individual is prepared to exploit these opportunities*" (p. 390, italics added). The reliance on addiction is, in other words, as much an indication of how people experience and react to their environment as it is a result of the particular addicting properties of a substance or of the environment's objective qualities, barring the most abject environmental impoverishment.

While situations predispose people to addiction, individuals also show greater or lesser susceptibility to it. At one extreme, people who cannot generate productive or rewarding experiences are at a disadvantage in avoiding addiction. Lower achievement values (or greater fear of failure), fewer interests, an inability to structure one's time, less concern for health or other moderating values, and an unfamiliarity with functional coping techniques are elements in the addictive equation. Animal research reminds us that the sources of addiction lie in the ways human beings are denied—or deny themselves—the opportunities for rewarding experiences that characterize life for our species. As Peele and Brodsky (1975) evoked this idea, "The difference between not being addicted and being addicted is the difference between seeing the world as your arena and seeing the world as your prison" (p. 64)—or is it cage? It is striking that animal research in laboratories, even that conducted with a reductionist bent of mind, affirms this complex truth about addiction.