work from which specific hypotheses can be generated regarding the mechanism of drug action. Receptor theory provides one theoretical framework which has proven to be valuable at more molecular levels of drug analysis; however, it is only relatively recently that the principles of receptor theory have been evaluated for their applicability in analyzing and predicting the effects of drugs on behavior. In general, two pharmacological constants describe the effects of drugs that act at receptors: affinity and efficacy. All drugs that interact at receptors have affinity (i.e., the attraction between a drug and a receptor), whereas only agonists have efficacy (i.e., the ability to initiate biological responses by occupation of receptors). Behavioral studies have been used to quantify affinity and efficacy, to estimate fractional occupancy of agonists, to characterize the nature of drug interactions at receptors (e.g., reversible or irreversible), and to ascertain the receptor type(s) through which drugs produce specific behavioral effects. The biochemical and behavioral complexity inherent to drug studies *in vivo* can restrict the conditions under which the assumptions of receptor theory can be satisfied and, therefore, the range of conditions under which this approach can be applied. Nevertheless, it is becoming increasingly clear that the theoretical framework provided by receptor theory can be especially helpful for: interpreting behavioral data; generating specific hypotheses for empirical evaluation of mechanism of action *in vivo;* and directing the development of drugs as well as procedures towards specific pharmacological and behavioral endpoints. This approach to behavioral analyses of drug effects might be particularly useful in the development of pharmacotherapies for drug abuse.

**INVITED ADDRESS**
Chair: *Jonathan L. Katz*, Addiction Research Center, Baltimore, MD.

BENZODIAZEPINES AND BEYOND: REINFORCEMENT, DISCRIMINATION AND DEPENDENCE. Nancy A. Ator, Johns Hopkins University School of Medicine, Baltimore, MD.

Drugs that enhance the major inhibitory neurotransmitter GABA generally have anxiolytic, anticonvulsant, muscle relaxant, and sedative/hypnotic effects to varying degrees. Initially barbiturates (e.g., Seconal) and then benzodiazepines (e.g., Valium) provided most of the clinically useful drugs of this type. However, chronic barbiturate use rapidly produces physical dependence with a severe and often life-threatening withdrawal syndrome. Furthermore, among those who abuse drugs, a subset have favored barbiturates. Under prolonged dosing conditions, benzodiazepines, too, can produce physical dependence, albeit with a less severe withdrawal syndrome; and they also have been subject to misuse and abuse.

Greater understanding of the structure and functions of the GABA receptor complex has facilitated the development of novel compounds that may show more selective pharmacological profiles (e.g., nonsedating anxiolytics). To the extent that such compounds might have less abuse liability or produce little or no withdrawal syndrome, they could be of great therapeutic advantage.

Laboratory study of abuse liability typically involves study of a drug's ability to serve as a reinforcer under intravenous and oral drug self-administration procedures. Some information on other effects, such as the way a test drug is "classified" under a drug discrimination procedure, also has been interpreted in abuse liability assessment. The extent to which chronic drug administration can produce physical dependence has been assessed separate from reinforcing efficacy. Comparison of barbiturates, benzodiazepine agonists and partial agonists, and of novel nonbenzodiazepine anxiolytics/hypnotics across a range of procedures in the same species is useful not only for assessing abuse liability and dependence potential of novel compounds but also for investigating predictions about variables that contribute to a drug's efficacy as a reinforcer and about the relationship between reinforcing efficacy and dependence. Profiles of recently introduced compounds will be compared with those for established standards from research with nonhuman primates.

**INVITED ADDRESS**
Chair: *Charles R. Schuster*, Addiction Research Center, Baltimore, MD.

NEW PHARMACOTHERAPIES FOR HEROIN ADDICTION. James H. Woods, University of Michigan, Ann Arbor, MI.

Methadone has been established as a standard of reference for the treatment of heroin addiction since its introduction to medicine in the late 1960s. Naltrexone, a competitive $\mu$ receptor antagonist, is also available, but its usefulness appears restricted only to a certain set of addicts. Recently, a long acting $\mu$-agonist, 1-$\alpha$-acetyl-methadol, was approved for this indication. Buprenorphine, a long-acting, $\mu$-partial agonist, is undergoing extensive trial for treatment of heroin addiction as well. The speaker will describe still another class of compounds, chemically and pharmacologically different in their mechanisms from those above, that may also have potential for the treatment of heroin addiction. These compounds are codeinones that appear to interact irreversibly with the $\mu$ receptor; they are converted metabolically to irreversible antagonists. The theory and the behavioral pharmacology of the use of these pharmacotherapies will be discussed.

**NEW FELLOWS ADDRESS**
Chair: *Warren K. Bickel*, University of Vermont, Burlington, VT.

PRIMING EFFECTS WITH DRUGS AND OTHER REINFORCERS. Harriet de Wit, University of Chicago, Chicago, IL.

Many positive incentive stimuli, including drugs of abuse, produce transient increases in the likelihood or vigor of responding to obtain those stimuli shortly after they are presented. For example, noncontingent presentations of rewarding stimuli such as food, water, rewarding electrical brain stimulation or drugs temporarily increase operant rates of responding to obtain these stimuli. This "priming" effect has been studied in laboratory animals, and, more recently, also in human volunteers. In the context of drug abuse, the priming effect has relevance for our understanding of the determinants of reinitiation and maintenance of drug use, and relapse to drug abuse. Sampling of a small amount of a preferred drug may increase an individual's desire for more of the drug and, relatedly, increase the likelihood that the individual will

consume more drug if it is made available. Several recent studies have examined this phenomenon in human volunteers, including cigarette smokers, alcoholics and normal social drinkers. Chornock et al. (1993) examined the likelihood of relapse to cigarette smoking after a forced exposure to smoking in abstinent smokers. Smokers exposed to the brief forced smoking condition were more likely to resume regular smoking than subjects who remained abstinent. Our laboratory has studied the priming effect of alcohol in social drinkers, using measures self-reported desire for alcohol and likelihood of consuming alcohol. Small preloads of alcohol increased both self-reported desire for alcohol and the reinforcing value of alcohol (i.e., the likelihood that more alcohol would be consumed). The priming effect with drugs may be an example of a more general priming effect observed with all positive incentive stimuli.

## NEW FELLOWS ADDRESS

Chair: *Jalie A. Tucker*, Auburn University, Auburn, AL.

NATIONAL RECOVERY: A MAJOR PATHWAY TO RECOVERY FROM ALCOHOL PROBLEMS. Linda C. Sobell, Addiction Research Foundation and University of Toronto, Toronto, Ontario, Canada.

Most research on recovery from alcohol problems emanates from studies of alcohol abusers in treatment, and, therefore, is only safely generalizable to individuals who seek treatment. Such individuals are in a minority; the ratio of treated to untreated alcohol abusers has been estimated to range from 1 : 3 to 1 : 13. Little research has investigated why most alcohol abusers do not seek treatment, and how alcohol abusers recover without treatment. The few existing studies have serious methodological flaws that preclude drawing firm conclusions.

This address will present the results from two studies that examined natural recoveries (i.e., self-change) from alcohol problems. The first study conducted in depth interviews with alcohol abusers who had recovered without either treatment or self-help groups. The second study reports general population survey prevalence data on adults who recovered without treatment. Both studies report abstinent and nonabstinent recoveries.

The first study was a longitudinal investigation of alcohol abusers who had recovered on their own. Interviews were conducted with 120 naturally recovered alcohol abusers. Results of these interviews were contrasted with those from 62 alcohol abusers who when interviewed had active, similarly severe alcohol problems and who had never received treatment (i.e., control group). Subjects were recruited through advertisements and a collateral had to corroborate the problem history and resolution for each subject. The average length of recovery at the first interview was about 7 years. The objective of the first phase of the study was to identify factors, particularly life events, which promote and maintain natural recoveries from alcohol problems.

Since the initial data analyses did not find any specific pattern or constellation of life events associated with the majority of the subjects' resolutions or differences between recovered and nonrecovered subjects, a preliminary content analyses of subjects' taped interview responses about the reasons for their resolutions was conducted. Subjects' reasons were categorized into 1 of 3 categories: cognitive evaluation/appraisal, immediate (no associated thought process reported), and other. The category that accounted for the majority (57%) of all subjects' reasons for their recoveries was "cognitive evaluation or appraisal of drinking." If a cognitive appraisal process is instrumental in facilitating problem resolution, then treatment outcomes might be improved by including a technique specifically designed to encourage cognitive appraisal. It is also important to note, however, that a substantial proportion of subjects did not report cognitive evaluations as preceding their recovery.

The second phase of this study involved reinterviewing all subjects and their collaterals five years after their first interview. The most important objective was to evaluate the stability of natural recoveries from alcohol problems. The relapse rate was found to be 14%. In relation to treated subjects, this rate is quite low. Three factors appear to be associated with relapse in naturally recovered subjects: (1) length of resolution—subjects with shorter recoveries were more likely to relapse; (2) subjects who were smoking at the first interview were significantly more likely to relapse than those who were not smoking; and (3) at the end of the first interview, all resolved subjects were asked about what situations, if any, they thought might contribute to a future relapse—subjects who answered "definitely nothing" were less likely to relapse than those who mentioned some specific situation. In summary, this study found that the risk of relapse decreases dramatically with a longer recovery period.

The second study used data from a Canadian National Alcohol and Other Drugs Survey to investigate the prevalence of natural recoveries or self-change from alcohol problems in a general population sample. The survey, conducted by Statistics Canada in March 1989, interviewed almost 12,000 respondents about their alcohol and drug use. Because this survey included a broader range of questions on alcohol use than previous surveys, issues about the nature of recoveries (i.e., self-change vs. treatment; abstinence vs. nonabstinence) could be explored. The sample from which potential respondents could be drawn consisted of 10,796 people 20 years of age or older. The three key findings in this study were that of all recovered respondents ($n$ = 575): (1) almost 80% resolved without treatment or self-help groups; (2) 40% of recoveries were nonabstinent drinking recoveries—i.e., moderate drinking; and (3) almost all (94%) nonabstinent recoveries occurred in the absence of treatment.

Compared to respondents who chose an abstinent recovery, respondents who chose a moderate (nonabstinent) drinking recovery were more likely to be female, to be younger, to have higher incomes, to have some post secondary education, and to have white collar jobs. Respondents who reported nonabstinent recoveries without treatment also reported significantly fewer alcohol-related consequences prior to their resolution.

The drinking of Resolved Nonabstinent No Treatment and Social Drinker survey respondents did not differ significantly on 5 of 6 drinking variables, and drinking reported by both of these groups for these 5 variables was significantly less than that reported by current Problem Drinkers Basically, the Resolved Nonabstinent respondents' drinking greatly resembled that of social drinkers in the population who had never reported having an alcohol problem. This study yielded three important findings: (1) there are multiple pathways to recovery from alcohol problems; (2) the predominant pathway to recovery in this survey was self-change—this finding parallels that for cigarette smokers where the vast majority stop on