subjects In one series of studies, monkeys acquired a different four-response chain each session in one component of a multiple schedule. In the other component (performance), the response chain was the same each session In general, acquisition was more sensitive to the dose-related disruptive effects of drugs (e g , *d*-amphetamine and cocaine) than was performance More recent research has shown that phencyclidine (PCP) disrupts the retention of an acquired response chain, as measured by percent "savings" in errors to criterion, at retention intervals up to several hours

ANALYSIS OF BEHAVIORAL EFFECTS OF DRUGS Jeffrey M Witkin Addiction Research Center, National Institute on Drug Abuse

Behavioral pharmacology has the potential for playing a major role at the forefront of neurobiology Its alliance with the experimental analysis of behavior endows behavioral pharmacology with the ability to address the neurobiological underpinnings of behavior and to provide a comprehensive understanding of the manner in which drugs affect behavior The foundation for this endeavor is a coherent evaluation of behavioral mechanisms of drugs' action, a goal attainable only by insightful experimentation and appreciation of behavior as an appropriate level of analysis Convergent information on the specificity of behavioral effects of drugs from a host of experimental approaches will eventuate in a refined understanding of drug action and its behavioral substrate

COCAINE TOLERANCE UNDER VARIABLE SCHEDULES OF REINFORCEMENT Marc N Branch University of Florida

Pigeons were trained to peck a key under three-component multiple schedules of food presentation in which components consisted of either random-interval schedules or random-ratio schedules The random-interval schedule parameters were 10 sec, 30 sec, and 125 sec, the random-ratio schedule parameters were 5, 25, and 125 Following determination of acute effects of cocaine hydrochloride (1 0–13.0 mg/kg), a dose that reduced pecking rates was administered before each daily session Tolerance developed to the rate-reducing effects, and the degree to which tolerance developed tended to depend on the schedule parameter under the ratio schedules whereas it tended to be independent of schedule parameter under the interval schedules

ACQUISITION AND PERFORMANCE OF RESPONSE CHAINS MODULATION BY ENVIRONMENTAL AND PHARMACOLOGICAL FACTORS Warren K Bickel and Stephen T Higgins University of Vermont

The study of response chains has generated a great deal of data which has contributed substantially to knowledge of the ways behavioral and pharmacological factors influence the acquisition and performance of response chains However, this research has not adequately addressed how response chains should be viewed or how the differential effects of variables on the acquisition vs. performance of response chains fit within our understanding of the ways environmental and pharmacological factors influence behavior Some have suggested that the acquisition and performance of response chains differ in the degree of stimulus control However, a critical analysis of research findings to date suggest that the acquisition and performance of response chains should be viewed as the formation and subsequent maintenance of response units. This reanalysis of the data were discussed with respect to future research and how it contributes to characterizing the features of response units

REAL ESTATE IN BEHAVIORAL ANALYSIS. REINFORCING "PROPERTIES" OF STIMULI John R Hughes, Stephen T Higgins and Warren Bickel Human Behavioral Pharmacology Laboratory, Departments of Psychiatry and Psychology, University of Vermont

According to our literature search, the term "reinforcing properties" is becoming more common in articles on drugs as reinforcers In this paper, we argue that the term is problematic because it suggests a stimulus has inherent and immutable characteristics that are responsible for its ability to serve as a reinforcer Yet, one of the basic findings of the experimental analysis of behavior is the function of a stimulus depends on history and present context We also discuss possible reasons for the increased use of the term reinforcing properties, e g , the increased popularity of theories that the reinforcing effects of drugs are due to their molecular structure As an alternate noun to the term reinforcing properties, we suggest the terms "reinforcing effects" and "reinforcing function" better describe the dynamic function of stimuli

DRUG AND TOXICANT EFFECTS ON DURATION DISCRIMINATION PERFORMANCE Stephen A Daniel Department of Psychology, Mercy College

The dose-effects of drugs and toxicants on behavior controlled by conditional stimuli of differing durations will be reviewed The effects of stimulant, sedative-hypnotic and hallucinogenic drugs and drug combinations, as well as neurotoxicants, such as acrylamide and lead on these discrete-trial procedures will be discussed. In addition, non-pharmacologic procedures will be examined, such as varying discrimination difficulty, methods and species comparisons and other manipulations to. (1) measure the effects of these procedures on dose-effect relationships and (2) help elucidate behavioral mechanisms of action. The advantages of using these procedures in behavioral pharmacology and toxicology will be explored

RELATIONSHIP BETWEEN REINFORCER MAGNITUDE AND RELATIVE REINFORCING EFFECTS STUDIES WITH PENTOBARBITAL AND FOOD R. A Meisch and G A Lemaire University of Minnesota

Two paradigms were used with rhesus monkeys to assess the relative reinforcing effects of different quantities of pentobarbital. Different quantities of pentobarbital were tested at each of several interval and fixed-ratio schedules. As the size of the intermittent schedule increased, fewer drug deliveries were obtained However, the percent decrease was greatest at the lowest drug quantity and became progressively less with increases in drug quantity Thus, relative reinforcing effects rose with increases in drug quantity (either drug concentration or drug volume) Similar studies of rats' food reinforced behavior yielded results that were consistent with these drug self-administration studies Relative reinforcing effects were directly related to reinforcer magnitude In a second paradigm different quantities of pentobarbital were made available under identical concurrently

operating schedules The larger drug quantity consistently maintained higher response rates than did the lower quantity Both paradigms demonstrate increases in relative reinforcing effects with increases in drug amount

NORADRENERGIC PROCESSES IN THE BEHAVIORAL ACTIONS OF PSYCHOMOTOR STIMULANTS Richard E Tessel Department of Pharmacology and Toxicology, University of Kansas

Much evidence indicates that the positive reinforcing, discriminative-stimulus and eliciting properties of amphetamine and cocaine result from the ability of these drugs to increase the net release of the catecholamine neurotransmitter dopamine in brain rather than from their ability to produce similar increases in the release of another catecholamine, norepinephrine (NE) However, NE release may be more important than previously believed Evidence obtained by evaluating the neurochemical and behavioral consequences of altering amphetamine structure, and the use of selective inhibitors of NE re-uptake and the centrally-active alpha$_1$ adrenoceptor antagonist prazosin will be presented that support this contention

THE USE OF NEUROTOXIN LESIONS TO INVESTIGATE THE BEHAVIORAL EFFECTS OF DRUGS Steven I Dworkin Departments of Psychiatry and Pharmacology, Louisiana State University School of Medicine

Investigations of the neurobiological mechanisms of drug actions can discern the neurobiological basis of compulsive drug use Drugs of abuse have several behavioral and neurochemical effects in common These drugs are used compulsively by humans for non-medical reasons and are self-administered by non-humans in experimental situations They have discriminative stimulus properties that augment their reinforcing efficacy These drugs also alter activity levels or response rates in a manner that is both dose related and a function of pre-drug levels The behavioral effects of psychoactive drugs are the result of actions on the central nervous system Moreover, the modulation of specific neuronal systems appears to be involved in the neurobiological mechanisms related to drug abuse Drug self-administration procedures have been used to delineate the neurobiological components of drug reinforcement mechanisms Selective neurotoxin lesions of discrete brain regions have been shown to modify drug intake. However, the changes reported in drug intake using the self-administration paradigm do not necessarily indicate a change in the reinforcing efficacy of the drug Neurotoxin lesions can also modify the activity of the subject, the discriminative stimulus properties of the drug, the effect of the drug on subsequent responding maintained by the drug, or additional unconditioned effects of the drug Therefore, several behavioral procedures must be used in order to more fully evaluate the neurobiological components of compulsive drug use This presentation will consider the behavioral and neurochemical effects of specific neurotoxin lesions on the behavioral effects of abused drugs Behavioral procedures that will be discussed include schedule-controlled behavior, drug discrimination and intravenous self-administration This presentation will discuss the involvement of several neuronal systems and brain regions in the neurobiological mechanism related to the behavioral effects of compulsively used drugs. (Supported in part by DA-03628 and DA-03631 from USPHS )

NEUROTRANSMITTER RECEPTORS AND BEHAVIOR. Nick E Goeders Departments of Pharmacology & Therapeutics and Psychiatry, Louisiana State University Medical Center

The compulsive non-medical use of cocaine has rapidly increased during the last decade Cocaine and related stimulants can result in a paranoid psychosis in some individuals that is difficult to distinguish from paranoid schizophrenia when these drugs are taken long enough at high enough doses If the chronic use of cocaine results in alterations in the central nervous system that are analogous to the neuropathology associated with schizophrenia, then a better understanding of these changes may increase knowledge of the etiology of mental illnesses and may therefore lead to the more effective and efficient treatment and management not only of drug dependence, but also of schizophrenia and related disorders The experiments described in this paper involve an examination of the neurobiological consequences of chronic cocaine intoxication using a multidisciplinary approach involving behavioral pharmacology, neurochemistry and neuroanatomy The development of tolerance or sensitization to the effects of repeated cocaine injections on schedule-controlled behavior was investigated by comparing the effects of presession or postsession injections with saline treated controls The involvement of neurotransmitter receptor systems in the development of this tolerance or sensitization was determined by light microscopic quantitative autoradiographic analysis of the binding sites for these neurotransmitters in serial sections through the brain sites for these neurotransmitters in serial sections through the brain of each rat The role of the various receptor systems in the potential development of the behavioral pathology associated with chronic cocaine intoxication are discussed (Supported in part by USPHS grant DA04293 )

THE NEUROBIOLOGICAL CONSEQUENCES OF RESPONSE CONTINGENT DRUG ADMINISTRATION James E Smith Departments of Psychiatry and Pharmacology, Louisiana State University School of Medicine

The repeated use or self-administration of a drug is one of the necessary defining features of substance abuse The recognition of this behavioral component places appropriate emphasis on the importance of an experimental analysis of drug abuse However, the neurobiological effects of a substance and the interactions of the behavioral and neurobiological consequences of drug administration are also intimately involved in engendering and maintaining drug abuse This presentation will compare the neurobiological effects of contingent and noncontingent drug presentations Data collected from studies using neurotransmitter turnover, receptor binding and 2-deoxyglucose labeling procedures indicate that the contingent administration of a drug has a greater neurobiological sequelae than noncontingent presentations The neuroscience of drug abuse cannot proceed in the absence of a complete behavioral analysis and investigation of the neurobiological effects of behavioral manipulations (Supported in part by DA-01999-10, DA-03628-04, DA-03631-04, DA-03832-04, DA-04293-02 and DA-00114-01 from USPHS )