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 )