NEGLECT IN RATS FOLLOWING UNILATERAL LESIONS OF CAUDAL PCm. Von R. King and James V. Corwin. University of New Orleans, New Orleans, LA.

Hemispatial neglect in the rat is seen following unilateral ablation of medial precentral cortex (PCm). Anatomical and physiological studies indicate rostral and caudal PCm (cPCm) may be discrete areas. This division is supported by the findings of the current study which showed that cPCm lesions resulted in greater polymodal neglect than did lesions of rostral PCm or the "entire" PCm. In addition, as with PCm operates, the dopamine agonist apomorphine attenuates neglect in cPCm operates in a dose-dependent fashion. The above study indicates that cPCm may be the focal point for the production of neglect in the rat.

INFORMAL DISCUSSION—HOSPITALITY SUITE

Drug Development and Behavioral Pharmacology

SUNDAY A.M.

SYMPOSIUM

Contingent Versus Noncontingent Drug Delivery: Behavioral and Neurobiological Consequences

Chair: *Steven I. Dworkin,* Wake Forest University, Bowman Gray School of Medicine, Winston-Salem, NC

Discussant: *Nancy Ator,* Johns Hopkins University School of Medicine, Baltimore, MD

INTRODUCTION. Steven I. Dworkin. Wake Forest University, Bowman Gray School of Medicine, Winston-Salem, NC.

Numerous studies indicate that the behavioral effects of most environmental stimuli can be altered by the arrangement of contingent relationships between behavior and the delivery of the stimulus. The concepts of "the law of effect" and schedules of reinforcement are a direct confirmation of the essential of contingent relationships for reinforcement. Although this principle is well accepted for most environmental events (i.e., food and water), there is a tendency to view psychoactive drugs as reinforcing in the absence of any contingent relationship. This symposium will present data from diverse paradigms that clearly demonstrate contingent drug delivery results in different behavioral and neurobiological effects than noncontingent drug administration. The implications of these findings for drug abuse research in both research and clinical settings will also be discussed. Dr. Linda Porrino will present a review of her work related to the neurobiological consequences of contingent and noncontingent stimulation of discrete brain sites. Dr. Porrino has detected major differences in both glucose utilization and neurotransmitter turnover rates related to the contingent versus noncontingent brain stimulation. The implications of these findings for drug abuse research will be discussed. Dr. Conan Kornetsky will review his work using the electrical brain stimulation procedure to provide a model of drug-induced euphoria and his recent work with ethanol which demonstrate the importance of contingent drug administration for the manifestation of the reinforcing effects of the drug. Dr. Steven Dworkin will present his findings related to the contingent versus noncontingent delivery of cocaine using the self-administration procedure. His data indicate that the noncontingent delivery of cocaine produces greater behavioral disruption and toxicity compared to contingent infusions. Dr. James Smith will review his research which provided the initial impetus for investigations of the differences between contingent and noncontingent drug delivery. His work has provided a model for which to investigate the neurobiological mechanisms of drug reinforcement. He will also review findings related to opiate self-administration in a clinical setting (patient controlled analgesia) and will provide an evaluation of the behavioral and neurobiological mechanisms related to enhanced therapeutic effect of this procedure.

EFFECTS OF EXPERIMENTER VERSUS SUBJECT ADMINISTERED ETHANOL ON REWARDING BRAIN STIMULATION. Conan Kornetsky. Boston University Medical Center School of Medicine, Boston, MA.

Many abused substances, including ethanol, have been reported to increase the sensitivity of animals to rewarding self administered electrical stimulation to the brain, a model of drug-induced euphoria. The effects of ethanol, however, are often variable or not present while those of drugs like cocaine or heroin, at proper doses, are compelling and relatively invariable. Since ethanol is usually administered by intraperitoneal injection or gavage, it is possible that the aversiveness of the method of administration precludes reinforcing effects and/or that contingent administration of ethanol is needed for it to cause a reinforcing effect. Since we have not been able to demonstrate an effect of ethanol on brain-stimulation reward using intraperitoneal administration, we determined the effects of oral self-administered ethanol. On experimental days animals trained to drink ethanol were allowed 30 minutes of free drinking of an ethanol/sucrose solution immediately prior to brain-stimulation reward testing. In two separate experiments, doses of ethanol between 0.8 and 1.6 g/kg caused an increase in rate of responding of increased sensitivity (lowers the threshold), respectively, for rewarding intracranial electrical stimulation. Yoked animals who were prepared with an indwelling gastric cannula and receive ethanol at the same dose and same rate as a paired ethanol-drinking animal, showed no increased sensitivity to the rewarding stimulation. Since the yoked animals were not subjected to the stress of IP or gavage ethanol administration the observed results demonstrate the importance of contingent drug administration for the manifestation of the reinforcing effects of ethanol. [Supported in part by NIAAA grant AA055950 and Research Scientist Award (C.K.) DA00099.]

DIFFERENTIAL NEUROCHEMICAL EFFECTS OF CONTINGENT AND NONCONTINGENT ELECTRICAL BRAIN STIMULATION. Linda J. Porrino. Clinical Neuroscience Branch, National Institute on Neurological Diseases and Stroke, Bethesda, MD.

Animals will work in order to receive brief trains of electrical stimulation directly to discrete brain sites (self-stimulation). The essence of this behavior is the contingent association between the response (in this case lever-pressing) and its consequences (brain stimulation). In contrast, animals will work to turn *off* electrical stimulation for which they had previously worked if it is presented in a noncontingent or response-independent manner (Steiner *et al.*, 1968). Using the 2-[^{14}C]deoxyglucose method (Sokoloff *et al.*, 1977) to map changes in functional activity that accompany brain stimulation, comparisons were made between animals self-stimulating to the ventral tegmental area and animals receiving experimenter-administered electrical stimulation to the same site at rates and parameters for which they had previously worked. Self-stimulating rats showed a pattern of changes in local metabolic activity distinctly different from and more extensive than the pattern of changes seen in rats stimulated noncontingently. Glucose utilization in the prefrontal cortex, nucleus accumbens, lateral septum, and mediodorsal thalamic nucleus was increased bilaterally in self-stimulating animals, but not in animals receiving

noncontingent stimulation. Simultaneous determination of dopamine, norepinephrine and serotonin turnover rates in the same groups of animals also showed that, despite the identical electrical stimulation, dopamine and serotonin turnover in the nucleus accumbens and ventral tegmental area was different in animals receiving stimulation contingency vs. those receiving it noncontingently. These differences in glucose utilization and neurotransmitter turnover rates serve to emphasize the significance of the behavioral context of stimulus presentation in determining the neurochemical effects of a stimulus.

TOXIC CONSEQUENCES OF CONTINGENT AND NONCONTINGENT COCAINE ADMINISTRATION. Steven I. Dworkin. Wake Forest University, Bowman Gray School of Medicine, Winston-Salem, NC.
(Abstract not available)

PATIENT CONTROLLED DRUG DELIVERY: IMPLICATIONS FOR SUBSTANCE ABUSE ISSUES. James E. Smith. Wake Forest University, Bowman Gray School of Medicine, Winston-Salem, NC.

One of the defining features of substance abuse is the compulsion to repeatedly self-administer a drug to the detriment of both social and occupational functioning. Significant advances in understanding the etiology of drug abuse resulted from laboratory studies using the self-administration paradigm to investigate this component of drug abuse. Research in this area has elucidated behavioral, pharmacological and neurobiological factors related to engendering and maintaining compulsive drug taking. Nonetheless, several apparent anomalies have been observed in nonlaboratory settings. For example, iatrogenic drug use rarely leads to a substance abuse problem. In the past, several important procedural differences between the laboratory and clinical situation may have contributed to this differential effect. However, the advent of patient controlled analgesia (PCA) has provided the opportunity to more fully understand conditions resulting in drug abuse. Research on the use of PCA has indicated that patients use less drug over the course of treatment and discontinue drug use sooner when given control over dosing, as compared to traditional procedures. Thus, the contingent self-administration appears to result in a more evocative analgesic action and/or an attenuated reinforcing effect of these drugs. Evaluations of the behavioral and neurobiological mechanisms related to this enhanced therapeutic effect may increase our understanding of factors related to both drug abuse and more effective analgesic treatment.

SYMPOSIUM

Drug Use and Job Performance Indicators
Chair: *Steven W. Gust,* Office of Workplace Initiatives, National Institute on Drug Abuse, Rockville, MD
Discussant: *J. Michael Walsh,* Office of Workplace Initiatives, National Institute on Drug Abuse, Rockville, MD

INTRODUCTION. Steven W. Gust. Office of Workplace Initiatives, National Institute on Drug Abuse, Rockville, MD.

Among the consequences of taking a drug are behavioral effects which result in impaired job performance. While there are a variety of physiological, pharmacological, and psychological variables that may affect an individual's response to a drug, generalizations regarding drug effects on performance have been established concerning effects of dose, task complexity, task novelty, and task/duration interactions. Such generalizations, while certainly limiting the specificity with which one can predict whether a particular individual is capable of performing under a particular set of circumstances, nevertheless suggest that group and individual performance may be adversely affected by drug use. This group of papers focuses on recent research relevant to the impact of drug use on job performance. Such data is important because research data provides an empirical base for the development of effective workplace drug abuse policy and programming. These studies represent several perspectives, and use several experimental approaches, but all address an aspect of behavior relevant to worker performance. Data is presented from a field study of job performance indicators and drug use in the U.S. Postal Service, from a longitudinal survey of drug use and its correlates in a sample of young adults followed for 12 years, from a laboratory simulation of the effects of alcohol on management decision making, and from laboratory studies of drug effects on basic psychomotor and cognitive skills with implications for on-site performance assessment. An attempt has been made to bring together research from basic and applied areas bearing on this important issue in order to update the research community on recent research, help identify limitations of such data and additional research needs, and hopefully foster increased interest within the basic and applied research communities to address these important issues.

THE RELATIONSHIP BETWEEN DRUG TEST RESULTS AND JOB PERFORMANCE INDICATORS. Jacques Normand. Office of Selection and Evaluation, United States Postal Service, Washington, DC.

Drug test results were obtained from 5,465 job applicants as part of a blind, longitudinal study of preemployment drug testing. All job applicants who applied for a permanent position with the Postal Service and had their preemployment examinations performed by a Postal Service Medical Officer in one of 21 sites across the country submitted urine samples at the time of their medical examinations. A total of 4,375 job applicants were eventually hired and made up the study sample.This interim report summarizes information regarding the prevalence rate of positive drug test results and data relating to the strength of the relationship between drug test results, turnover, and absenteeism. When these interim analyses were performed, the average tenure of participating employees who had not separated was 8.2 months. Of all the eligible job applicants, 10 percent tested positive for drugs at the time of their medical examinations. The positive rate for new career hires was slightly lower than applicants. The overall positive rate of new hires was 8.8 percent. Thirty-one percent of the eligible job applicants who tested positive for drugs were not hired compared to 22 percent of those who tested negative. This suggests that those eligible applicants who tested positive for drugs were screened out either during the employment suitability process (i.e., the medical and personal check of suitability) or refused career appointments at a higher rate than those who tested negative. An analysis of prevalence rates by race, sex, and age group revealed that the odds of being positive were higher for Blacks, males, and people between the ages of 25 and 35. Those who tested positive were found to have an absence rate 41% greater than those who tested negative. A significant difference in involuntary turnover between the positive and negative groups was detected. The observed difference in involuntary turnover rates reveals that employees who tested positive had a 38.5% higher rate of involuntary separation than those who tested negative. When separate analyses were performed by individual drug types,