Pharmacology Biochemistry & Behavior, Vol. 27, pp. 365–366. © Pergamon Journals Ltd., 1987. Printed in the U.S.A. 0091-3057/87 $3.00 + .00

INTRODUCTION

The Experimental Analysis of Drug Self-Administration

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THE nature of drug dependence is complex and differs between drugs. However, it is possible to divide this phenomenon into distinct categories, including drug-seeking behavior. Studies in this area grew out of work on drug reinforced behavior originally established in the 1960s (Deneau *et al.* [1]; Thompson and Schuster [3]; Weeks [4]). Many drugs have been shown to serve as positive reinforcers in several species, and in general, animals self-administer those drugs that humans abuse, and they do not self-administer drugs that humans do not abuse (Griffiths *et al.* [2]). In most self-administration studies the intravenous route has been used; however, drugs can also function as reinforcers when other routes are used.

The following series of papers are based upon presentations given during a symposium on the experimental analysis of drug self-administration. This symposium was held during the 1986 meeting of the American Society for Pharmacology and Experimental Therapeutics. The objectives of the symposium were to provide updated reviews of research dealing with factors controlling drug self-administration, and to introduce new methods and findings relevant to this field of study. The methodology and principles of operant conditioning are a focal point for these papers, but important considerations are also presented with regards to other relevant variables, including genetics, pharmacokinetic factors, and environmental variables such as food deprivation.

In the first paper, Richard Meisch provides a concise overview of factors controlling drug reinforced behavior, with an emphasis on psychoactive stimulants. In addition, an outline of control procedures and methods important in the development of animal models of drug taking behavior is provided.

In the next paper, Gerald Young and Naim Khazan discuss findings obtained in their laboratory concerning the pharmacodynamics and pharmacokinetics of opioid drugs. An important and unique aspect of this work is the development of methods whereby brain EEG-EMG and related power spectra measurements can be obtained from animals which are self-administering drugs. This allows for the qualitative and quantitative assessment of changes in brain activity following drug taking behavior. This technique has been successfully used to demonstrate that behaviorally active amounts of drugs are self-administered by animals, that changes in EEG patterns consistent with the development of tolerance occur following repeated self-administration of opioids, and that different EEG patterns and spectra are found when various opioids are administered to animals, providing a marker for drug interactions with different opioid receptor populations.

The third paper, by Frank George, presents findings which demonstrate large genetic differences in the establishment and maintenance of the most widely abused drug, ethyl alcohol, as a positive reinforcer under operant conditions. The results from these studies show that the relative degree of operant self-administration of alcohol across the rat and mouse stocks studied correlates highly with the predisposition of these same genotypes towards high or low alcohol preference under home cage choice conditions. The results of these experiments illustrate the importance of genetic control in drug studies, and suggest that genotype may be a critical factor in determining the reinforcing efficacy of drugs.

Phencyclidine (PCP) is still a prominent drug of abuse, and work on this drug is reviewed by Karen Marquis and Edward Moreton in the fourth paper. Self-administration of PCP in animal models of drug abuse has been reported since the early seventies in rhesus monkees, baboons, dogs, and rats. Early reports of rodent self-administration tested only a few doses and did not assess reinforcing efficacy. Data presented in this symposium expands reports of PCP and PCP analog self-administration in rats and indicates the relative reinforcing efficacy of phencyclinoids using the progressive ratio test. While some differences are noted between species in response to PCP, rodent intravenous self-administration provides a model from which to expand the investigation of the neuropharmacological and behavioral basis of PCP abuse.

The final paper in this series is by Nancy Ator and Roland

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Griffiths. This work is a review of the literature on self-administration of barbiturates and benzodiazpines, and includes work done using intravenous, intragastric and oral routes of administration. Also included in this paper are summary tables which concisely outline the current literature on self-administration of these drugs. These tables incorporate results from unpublished studies on the self-administration of barbiturates and benzodiazepines in humans and laboratory animals. This paper also presents additional findings on oral self-administration of triazolam and diazepam which suggest that these compounds do not function as reinforcers to the same degree as other drugs such as methohexital.

This series of papers should be of interest to a diverse group of researchers, including those working in the areas of operant behavior, psychopharmacology, and behavioral genetics. Hopefully, these papers will serve not only as a useful source of reference materials but will also serve to stimulate further interest in operant models of substance abuse and the behavioral and biochemical determinants of drug-seeking behavior.

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