

attenuated by pretreatment with a variety of 5-HT antagonists. Furthermore, administration of other agonists for the 5-HT_{1a} receptor (8-hydroxy-2-(di-n-propylamino) tetralin, ipsapirone) did not attenuate fear-potentiated startle. Finally, buspirone's action was not attenuated by opiate, alpha₂-adrenergic, or benzodiazepine antagonists. Thus, the mechanism by which buspirone attenuates anxiety measured with the fear-potentiated startle paradigm remains to be determined. (Studies presented were carried out in collaboration with Dr. James V. Cassella and Dr. Michael Davis in the Department of Psychiatry.)

THE INTERACTION OF PHARMACOTHERAPY WITH FAMILY THERAPY IN THE TREATMENT OF SCHIZOPHRENIA Michael J. Goldstein, University of California, Los Angeles

Recent developments have indicated that maintenance pharmacotherapy fails to protect from 40–50% of schizophrenic patients from a relapse over the 12 month period after discharge. The search for other risk factors have identified certain attributes of the family environment. Attempts to modify these attributes in the context of regular pharmacotherapy will be reviewed and the results of four successful controlled clinical trials summarized. The interaction of these efforts with new directions in modifying the dosage levels and patterns of antipsychotic drug administration (low dose and targeted dose strategies) will be explored.

INVITED ADDRESS:

STATE OF THE ART ADDRESS

Saturday August 29, 1987 • 2:00 p.m. – 5:50 p.m.
Marriott Marquis Hotel • Boothe/Edison Room
 Chair: *Hugh L. Evans*, Institute of Environmental Medicine, New York University Medical Center, New York

A PRIMATE MODEL OF LEAD-INDUCED BEHAVIORAL IMPAIRMENT IN CHILDHOOD Dr. D. C. Rice, Toxicology Research Div., Health and Welfare Canada, Ottawa, Ontario, Canada

PRESIDENTIAL ADDRESS

Sunday August 30, 1987 • 4:00 p.m. – 4:50 p.m.
Marriott Marquis Hotel • Olmstead Room
 Chair: *Conan Kornetsky*, Division of Psychiatry, Boston University School of Medicine

DRUG-PRODUCED AND SENSORY STIMULI: A COMPARISON OF PROPERTIES Donald A. Overton, Departments of Psychiatry and Psychology, Temple University, Philadelphia, PA 19122

This paper compares the formal properties of contextual and discriminative control by sensory and by drug-induced stimuli. Many important parallels can be drawn based on experiments which test for habituation, overshadowing and blocking with drug stimuli, threshold and maximum-discriminable dosages, intensity-response curves, and just noticeable differences. Other important comparisons are not yet possible because the necessary data have not been collected for the drug-stimulus case. These include data allowing analysis of the number of qualitative dimensions of drug-

induced sensory experience, the degree of independence/overlap of the stimuli induced by pharmacologically dissimilar drugs, the significance of feature-positive/feature-negative effects in discriminative control by drug states, and the role of normal 'no drug' background sensory stimuli.

BUSINESS MEETING

Sunday August 30, 1987 • 5:00 p.m. – 5:50 p.m.
Marriott Marquis Hotel • Olmstead Room
 Chair: *Donald Overton*, Department of Psychology and Psychiatry, Temple University

NEW FELLOWS ADDRESSES

Monday August 31, 1987 • 11:00 a.m. – 11:50 a.m.
Marriott Marquis Hotel • Odets/Wilder Room
 Chair: *Klaus Miczek*, Tufts University

THINKING OF BEHAVIORAL PHARMACOLOGY AS TOXICOLOGY (AND VICE VERSA) Ronald W. Wood, Research Associate Professor of Environmental Medicine, New York University Medical Center, New York, NY 10016

Since Paracelsus observed that dose makes something *not* poisonous, the task of pharmacology has been to trade off useful effects of chemicals against their toxicity or as my colleagues in the pharmaceutical industry call it, "side effects." These friends must approach the problem of finding the useful effects of chemicals quickly, and consequently they push the dose to characterize the compound, the contributions made by the discipline are obvious in the ability to identify and characterize useful products with this approach. However, in most cases, the doses used are so high that the effects they produce would have to be characterized as behaviorally toxic effects. Behavioral toxicology has certainly profited from the substantial contributions made by behavioral pharmacology to our understanding of the acute effects of psychoactive chemicals (examples are many, and a few will be offered emphasizing not only the direct actions of chemicals, but also their stimulus properties). But the task of behavioral toxicology is not just the characterization of prominent effects, and the determination of the location of maximal and rate-decreasing effects. The behavioral toxicologist frequently must identify effects at very low doses (in the therapeutic range), where effects are likely to be small and could even be characterized as beneficial if exposure was deliberately undertaken. Simply adopting the pharmacologist's strategy of one or two replications at many doses, would result in missing minimal effects, and of recommending exposure levels that are imprudently high. The techniques of behavioral pharmacology are more than sensitive enough for this purpose, the experimental designs just need more attention to the "power" of the experiment. Applying these approaches to the study of psychoactive and abused drugs would surprise many, as it would undoubtedly show effects of our favorite prototypical drugs of abuse at very low levels, and to have longer durations of effects than currently anticipated. In addition, it is likely to erase the "species"-ist (arrogant) supposition that the rat (or the non-human primate) is routinely much less sensitive than man. Behavioral pharmacologists should consider some of their frequently used preparations as acute toxicity evaluations, and their prolonged tolerance and self-administration experiments as chronic toxicity evaluations, behavioral toxicologists should continue to study "pharmacologic"

reference substances, and to be prepared for the discovery of new drugs and behavioral phenomena in seemingly unlikely contexts I remain convinced that these sister disciplines should pay attention to each other, because there are many insights to be gained by both behavioral pharmacology and toxicology

DRUGS, ENVIRONMENTAL EVENTS AND HUMAN AGGRESSIVE AND ESCAPE RESPONDING Don R Cherek Department of Psychiatry, Louisiana State University Medical Center

An overview of a number of different experiments will be

presented which have investigated the relationship between aggressive and escape responding by human subjects and the presentation of aversive stimuli in a controlled laboratory setting, and how these relationships may be affected by drug action The following factors will be discussed (1) effects of instructions and number of sessions on responding, (2) effects of contingencies maintaining responding on drug action, (3) effects of instructions relating to the context of aversive stimulus presentation on drug action, (4) drug effects on temporal relationships between aversive stimuli and aggressive responses, and (5) effects of frequency of aversive stimulus presentation and contingencies on choices between aggressive and escape responding

SYMPOSIUM

Pharmacological Adjuncts in Drug Abuse Treatment

Saturday August 29, 1987 • 11 00 a m -12 50 p m

Marriott Marquis Hotel • Jolson/Cantor Room

Chair *John Grabowski*, Department of Psychiatry, Center for the Study of Drug Development, Tufts University

COCAINE ABUSE NEW AND EMERGING PHARMACOTHERAPEUTIC INTERVENTIONS Frank H Gawin, M D Yale University School of Medicine, Stimulant Abuse Treatment Program, Department of Psychiatry, Yale University School of Medicine, 34 Park Street, New Haven, CT 06511

Recent research has produced encouraging preliminary data on general pharmacological treatments for cocaine abuse as well as on pharmacotherapies whose efficacy is specific to cocaine abusers with Axis I psychiatric disorders This presentation will describe pharmacotherapy trials in chronic cocaine abusers as well as recent clinical, diagnostic, and pre-clinical studies Cocaine dependence has long been thought of as a "psychological" addiction without a "physiological" withdrawal syndrome Recent basic research demonstrates that chronic cocaine can cause multiple neurophysiological adaptations in brain reward pathways, and recent clinical research suggests that cocaine abstinence symptoms (1) follow a predictable three phase pattern, (2) include anhedonia consistent with the preclinical studies indicating decreased reward and (3) can be distinguished from co-existent Axis I Psychiatric disorders Severe cocaine abuse may thus produce a physiological addiction whose clinical expression is psychological There is no standard pharmacotherapy for cocaine abuse Systematic investigations were begun only two to three years ago New open and double-blind trials indicate that specific pharmacotherapies produce distinct benefits applicable to components of cocaine craving in each withdrawal phase Neurotransmitter precursors may ameliorate acute post-binge symptoms Antidepressant treatment may ameliorate protracted post-cocaine anhedonia and facilitate abstinence in abusers who do not exhibit other depressive symptoms More preliminary work indicates that classically conditioned craving may be ameliorated pharmacologically by dopaminergic and anti-epileptic treatments It is thus likely that pharmacotherapy will be increasingly employed in future stimulant abuse treatment

OPIATE ABUSE TREATMENT DRUG AND PATIENT POPULATION CONSIDERATIONS Maxine L Stitzer, Ph D The Johns Hopkins University School of Medicine, Behavioral Pharmacology Research Unit, Psychiatry Department D-5-West, Francis Scott Key Medical Center, 4940 Eastern Avenue, Baltimore, MD 21224

This paper will review the pharmacological properties of three drugs in relation to their use as treatments for opiate abuse/dependence The major advantages and disadvantages of each agent will be discussed and related to utility of different types of treatment patients Methadone, which is the standard and best currently available treatment for chronic opiate abuse, has several advantages as a treatment agent Its reinforcing effects help to maintain high rates and long durations of treatment participation especially among poorer prognosis patients (i e , lower socioeconomic and social stability) These same reinforcing properties allow for implementation of drug-dispensing contingencies that improve behavioral control Methadone's partial blockade of opiate agonist effects suppresses illicit opiate use during treatment Disadvantages include the physical dependence that is induced and its classification as a narcotic drug which dictates the need for limited treatment availability under rigidly controlled and monitored dispensing procedures Buprenorphine is a promising new mixed agonist-antagonist that is not currently available for drug abuse treatment but that has a profile of effects that should make it a desirable treatment agent for general opiate abusing populations Buprenorphine retains the reinforcing effects of an opiate agonist but produces less physical dependence and stronger pharmacological blockade of opiate effects than direct agonists such as methadone More evaluation is needed before it can be marketed with a drug abuse treatment application Naltrexone is a pure opiate antagonist that has recently been marketed in the US The opiate agonist blockade produced guards against resumption of illicit drug use and may promote extinction of drug-related environmental