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 1 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 coexistent Axis 1 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 dopamimetic 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

stimuli Naltrexone is a very safe drug since it has virtually no agonist or side-effects Naltrexone generally fails to maintain treatment participation by lower socioeconomic clients but may be used beneficially with paying drug abuse patients such as health care practitioner abusers Its use by psychologists treating opiate abusers in private practice should be promoted

TOBACCO DEPENDENCE BEHAVIORAL PHARMACOLOGICAL BASIS FOR NICOTINE REPLACEMENT Jack Henningfield, Ph D , Chief The Johns Hopkins University School of Medicine, Biology of Dependence and Abuse Potential Assessment, Laboratory, NIDA Addiction Research Center, 4940 Eastern Avenue P O Box 5180, Baltimore, MD 21224

The fundamental premise of replacement therapy is that the physiologically based feelings of discomfort and disruption of functioning which characterize drug withdrawal, can be therapeutically managed by administration of a chemical which produces cross-tolerance and cross-dependence with the one to which the person is already dependent The chemical may be different in structure, or may be identical in structure but administered in another route or vehicle, or it may even be of identical structure and form but is given according to a prearranged therapeutic schedule The putative replacement chemical should substitute for the abused substance on measures relevant to treatment of the drug-seeking behavior The rational basis for the utility of a replacement approach (vs antagonist administration) to treat tobacco dependence is that nicotine administration produces many of the effects of tobacco that are critical in the dependence process These effects of nicotine include, physiologic dependence which results in withdrawal following tobacco abstinence, and also many of the desirable effects of tobacco such as mood regulation, appetite control, and enhancement of concentration and verbal ("cognitive") performance Although no satisfactory nicotine substitutes have yet been developed, nicotine delivered via different routes of administration (e g , inhaled and IV), and with different vehicles (e g , tobacco smoke, snuff and polacrilex) produce similar effects on a variety of behavioral and physiologic measures However, differences related to the vehicle and pharmacokinetics of each preparation confer various advantages and disadvantages on each as a putative therapeutic nicotine replacement form For instance, cross-tolerance and cross-dependence are obtained for both cigarette smoke-delivered nicotine and polacrilex-delivered nicotine, but cigarette smoke better satisfies the desire to smoke than does the polacrilex Therapeutically managed nicotine replacement for tobacco can currently be accomplished by the administration of nicotine polacrilex (gum) Such administration produces dose-related reduction of withdrawal-related performance impairment and of other signs and symptoms of tobacco withdrawal These beneficial effects are dependent on adequate dose levels of nicotine being administered, and achievement of such levels may require dosing regimens to be specified by the clinician Desire to smoke ("craving") is relatively insensitive to nicotine replacement, however, there is evidence that the reinforcing efficacy of cigarettes is nonetheless reduced by administration of the polacrilex It is plausible that other routes of nicotine replacement would better satisfy the tobacco users desire to use his or her preferred form of tobacco Taken together, these findings are consistent with those regarding replacement therapies in general and confirm that nicotine replacement via polacrilex is well-based on scientific principles

ALCOHOL ABUSE BEHAVIORAL FUNCTIONS OF PHARMACOLOGICAL ADJUNCTS George E Bigelow, Ph D The Johns Hopkins University School of Medicine, Behavioral Pharmacology Research Unit, D-5-West, Psychiatry Department, Johns Hopkins/Key Medical Center 4940 Eastern Avenue, Baltimore, MD 21224

It is in the alcoholism field that the most diverse rationales for pharmacological treatment of substance abuse problems have been articulated and acted upon These rationales have ranged from medical safety (prevention of withdrawal seizures), to subjective palliation (reduction of subjective distress during detoxification), to treatment of presumed underlying disorders thought to cause excessive drinking (prescription of antianxiety or antidepressant medications), to direct efforts to alter the effects of alcohol so as to make drinking less reinforcing (treatment with disulfiram) The last of these approaches—treatment with disulfiram—is the only pharmacological approach currently receiving extensive application in treating the behavioral aspects of alcohol dependence This presentation will review the various approaches and rationales for pharmacological treatment of alcohol abuse but will focus primarily upon disulfiram treatment and upon the use of behavioral procedures to enhance the efficacy of this pharmacological modality Disulfiram is a pharmacologically efficacious agent which has had limited clinical efficacy due to widespread behavioral nonadherence to medication use The action of disulfiram is to cause an aversive reaction if alcohol is consumed thus, its behavioral function is that of a punisher, and its limited self-administration by patients is not surprising Data will be presented illustrating the effective use of behavioral procedures to promote disulfiram use and to enhance clinical outcomes In addition, the presentation will discuss the possibility of utilizing the reinforcing effects of other medications to promote retention and participation in nonpharmacologically-based treatments for alcohol abuse Relevance of these approaches to other aspects of drug self-administration and medication compliance will be discussed

SYMPOSIUM

Conditioned Drug Tolerance Empirical and Theoretical Developments

Friday August 28, 1987 • 10 00 a m –11 50 a m
Marriott Marquis Hotel • Julliard/Imperial Room
Chair *Stephen Tiffany,* Purdue University

ENVIRONMENTAL CUES FOR DRUG ADMINISTRATION ROLE IN TOLERANCE AND RELAPSE Riley E Hinson Department of Psychology, University of Western Ontario, London, Canada

It is well established that environmental stimuli affect the display of tolerance and the occurrence of relapse An account of the role of environmental stimuli originally elaborated by Siegel suggests that environmental cues of drug administration elicit conditional responses (CRs) that tend to cancel the drug effect producing tolerance Most of the research on the conditioning model of tolerance has empha-