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ABSTRACTS

PRESIDENTIAL ADDRESS

Chair: *Robert L. Balster,* Medical College of Virginia, Virginia Commonwealth University, Richmond, VA.

AGGRESSION AND VIOLENCE: PHARMACOTHERAPEUTIC OPTIONS. Klaus A. Miczek. Tufts University, Medford, MA.

Aggressive behavior and its underlying neurobiology have evolved with adaptive purposes at every level of our phylogenetic history, to compete with rivals, to secure resources, to raise young, to defend against predators. Yet, aggressive behavior in excess, against inappropriate targets, under unusual circumstances needs to be controlled. Alcohol and other pharmacological states may engender excessive aggressive and violent behavior. Preclinical research has identified the most conducive conditions for alcohol and drugs of abuse to promote aggressive behavior. Pharmacotherapeutic options for the management of violent behavior rely on incomplete knowledge of the neurobiological mechanisms mediating the initiation, execution and termination of aggressive acts as well as their burst-like patterning. Substances acting on specific subtypes of GABA-A, 5-HT_1 and opioid receptors selectively modulate endocrinological, cardiovascular and motoric components of aggressive, defensive and submissive behavior.

INVITED ADDRESS

Chair: *Roy Pickens,* NIDA Addiction Research Center, Baltimore, MD.

ANXIOLYTIC DRUGS: NOVEL DEVELOPMENTS. James E. Barrett. Lilly Research Laboratories, Indianapolis, IN.

Several drugs that produce effects through distinct neuropharmacological mechanisms are effective in preclinical animal models of anxiety. These include compounds that act through the BZ/GABA receptor system and those that function through the 5-HT_{1A} receptor. In addition, drugs active at other 5-HT receptors have been suggested to be effective anxiolytics. These include the 5-HT_2 and 5-HT_3 antagonists, as well as compounds that act simultaneously at two 5-HT receptors as 5-HT_{1A} agonists and 5-HT_2 antagonists. Recent research suggests that cholecystokinin receptor antagonists may also be anxiolytic. This paper will review evidence for anxiolytic activity for each of these drug classes, concentrating on animal behavior models that involve punished or conflict behavior. The range of compounds effective in the treatment of anxiety attests to the neurobiological complexity of this disorder and to the multiple avenues for intervention, treatment and eventual understanding.

INVITED ADDRESS

Chair: *John G. Grabowski,* University of Texas Health Science Center, Houston, TX.

MEDICATION DEVELOPMENT FOR DRUG ABUSE TREATMENT: CLINICAL RESEARCH APPROACHES. George E. Bigelow. The Johns Hopkins University School of Medicine, Baltimore, MD.

The federal government has mounted an extensive research and development program to identify, evaluate, and bring to clinical availability new medications for the treatment of drug abuse. This presentation will discuss clinical research methods and progress in this drug abuse medications development area. Drug abuse pharmacotherapies might act through any of a number of different pharmacological mechanisms and behavioral mechanisms; these will be outlined, and examples described. The two primary methods for clinical evaluation of potential pharmacotherapies are clinical treatment trials and human laboratory assessments; these methods will be described, and examples provided. Examples will be given of the integration of the two methods within single studies. Data presented will illustrate steps in the development and assessment of buprenorphine as a treatment for opioid abuse, as well as efforts to find pharmacotherapies for treatment of cocaine abuse.

INVITED ADDDRESS

Chair: *Sharon Hall,* VA Medical Center, San Francisco, CA.

SMOKING CESSATION IN CANCER PATIENTS: BIOLOGICAL, CLINICAL AND BEHAVIORAL CONSIDERATIONS. Ellen R. Gritz. Department of Surgery and Jonsson Comprehensive Cancer Center, University of California, Los Angeles, Los Angeles, CA.

The benefits of smoking cessation in individuals already diagnosed with malignant disease have received scant attention. Biological risks of continued smoking, treatment-related morbidities and psychological factors suggest that cessation is an important priority. Studies of cancer patient smoking behavior reveal a high prevalence of addicted heavy smokers. However, the opportunity to capitalize on the "teachable moment" of diagnosis/treatment may lead to enhanced motivation and cessation. Prospective data will be provided from lung, and head and neck cancer patient populations. The role of the physician will be exemplified by a model currently being tested in a randomized controlled trial.

INVITED ADDRESS

Chair: *Klaus A. Miczek,* Tufts University, Medford, MA.

THE NEUROBIOLOGY OF DRUG DEPENDENCE: EVIDENCE FOR AN OPPONENT PROCESS. George F. Koob. Department of Neuropharmacology, Research Institute of the Scripps Clinic, La Jolla, CA.

Previous studies have implicated the region of the nucleus accumbens in mediating the psychostimulant and reinforcing effects of cocaine and amphetamine. The region of the nucleus accumbens has also been established as an important substrate for the acute reinforcing effects of opiates in nondependent rats

with limited access to the drug. Intracerebral injections of methylnaloxonium into the nucleus accumbens were more effective in blocking heroin self-administration than injections into the lateral ventricle or the ventral tegmental area. In addition, behavioral data indicate that spontaneous or precipitated withdrawal after chronic administration of psychostimulants and opiates leads to "anhedonic and dysphoric" states respectively. Following prolonged access to intravenous cocaine self-administration in rats, intracranial self-stimulation thresholds were increased reflecting a decrease in reward ("anhedonia") during withdrawal. In morphine-dependent rats, local intracerebral injections of methylnaloxonium into the nucleus accumbens were much more effective in disrupting responding for food, reflecting a "dysphoric" state, than injections into the lateral ventricle, periaqueductal gray, or medial thalamus. These results suggest that changes in the neural circuitry of the nucleus accumbens may be the neurobiological substrate for motivational changes that form the basis of an opponent process during chronic drug use.

INVITED ADDRESS
Chair: *Alice M. Young*, Wayne State University, Detroit, MI.

HOW TO INCREASE AND DECREASE THE STRENGTH OF MEMORY TRACES: THE ROLE OF OPIOIDS. Joe L. Martinez, Jr. University of California, Berkeley, CA.

In this presentation, how opioids affect memory will be considered. Interestingly, a fundamental observation in this area is that opioids make memories both stronger and weaker. Research suggests that opioids do not influence the memory trace directly, but instead influence modulatory systems that in turn regulate associative strength. Remarkably, the primary site of action of opioids appears to be outside the blood-brain barrier and may be in the periphery. It is possible that such a mechanism is general, and that many peripheral neuropeptides and hormones act to modulate memory in this fashion. It will be argued that memory involves two distinct processes. One process is the generation of the memory trace itself. Most scientists agree that memory traces exist between sets of interconnected neurons and that physical changes occur in individual neurons to maintain memory. The second involves associative strength that may be conveyed by the modulatory input.

INVITED ADDRESS
Chair: *James H. Woods*, University of Michigan Medical School, Ann Arbor, MI.

ORAL ALCOHOL SELF-ADMINISTRATION IN THE RAT: ENVIRONMENTAL-GENETIC INTERACTIONS. Herman H. Samson. Alcohol and Drug Abuse Institute, University of Washington, Seattle, WA.

The interaction between environmental factors and genetic variability are considered as key to the control of alcohol consumption. This paper will present current research in which genetically selected alcohol-perferring (P) and -nonpreferring (NP) rat lines have been studied in both acute and chronic alcohol self-administration paradigms. The effects of a variety of environmental procedures, including method of initiation to alcohol self-administration, concentrations of alcohol available, and response contingencies required for both alcohol and food presentation in the P and NP lines as well as heterogeneous nonselected rats will be discussed.

NEW FELLOWS ADDRESS I
Chair: *Stephen C. Fowler*, University of Mississippi, University, MS.

SUBSTANCE ABUSE PREVENTION: ADOLESCENT AND PARENTAL PROBLEM-SOLVING AND EXPLANATORY STATEMENTS. Brenna H. Bry. Rutgers—The State University.

Substance abuse prevention efforts typically target words to change relevant behavior on the part of adolescents and parents, whether in media campaigns, prevention workshops, or psychotherapy. Little systematic research, however, has examined the impact of verbal behavior in determining risk behavior. Early studies and clinical observations suggest that how adolescents and parents respond to and explain daily problems in their lives plays an important role in the development and treatment of adolescent substance abuse. This paper will discuss a series of recent studies by the author into defining and modifying family problem-solving and explanatory statements to reduce adolescent substance abuse.

CONDITIONED TOLERANCE AND DEPENDENCE TO THE OPERANT EFFECTS OF BENZODIAZEPINES. Mary Jeanne Kallman. University of Mississippi, University, MS.

A review of several investigations which explored the role of conditioned factors in tolerance and withdrawal to the benzodiazepines (BZs) will be presented. These studies have compared the effects of repetitive administration of different BZs, the dose of drug delivered chronically, and various operant schedules as important variables in the display of conditioned tolerance. Since the nontraditional assessment of force and duration of responses was used in conjunction with the traditional assessment of response rate, these experiments address changes in the topography of responding as a function of drug experience. When rats are exposed to BZs before the daily operant session they display greater drug tolerance than rats exposed to the drug after the daily session but these findings are dependent upon the level of behavioral disruption produced by the dose of BZ administered chronically. Under some conditions the severity of withdrawal is also enhanced by previous drug experience in the testing situation. (Supported by NIDA DA-05253.)

NEW FELLOWS ADDRESS II
Chair: *Nancy A. Ator*, The Johns Hopkins University School of Medicine, Baltimore, MD.

ETHANOL CONSUMPTION AS A FUNCTION OF SCHEDULE OF ACCESS. Henry Marcucella. Boston University.

A series of studies conducted within a foraging context examined the influence of access schedules on the amount and pattern of oral ethanol self-administration. Ethanol, a commodity which may be sought, handled and consumed like food and water, was consumed as a function of its own access schedule as well as the access schedules of the other available commodities, food and water. The access schedule of a commodity was manipulated in a closed economy by varying either the time that the commodity was available or the number of responses required to gain access to the commodity (procurement cost).

NEURON RESCUE AND PLASTICITY PROMOTION BY PHARMACOTHERAPY AFTER BRAIN DAMAGE: HELP-