The present study investigates the interactive effects of smoked marijuana administration and task performance on cardiovascular responsivity. Nine healthy male marijuana users (ages 23–31) smoked either a placebo or active marijuana cigarette during 5 daily testing sessions. Ten minutes after drug administration, 5 subjects (Group I) performed a 10 minute modified repeated acquisition task and 4 subjects (Group II) rested quietly. Mean arterial blood pressure (MAP) was sampled at 2 minute intervals and heart rate was recorded continuously. Although both marijuana and task performance administered independently produced elevated MAP, the combination of drug and task produced MAP increases of consistently greater magnitude while sustaining marijuana induced heart rate elevations.

CONTRAST ADDICTION THEORY: RIDING THE ESCALATOR TO PARADISE LOST. John M. Berecz. Andrews University.

Contrast Addiction Theory (CAT) is an experiential-perceptual theory in which *contrast* is a primary construct. Users seek to enhance contrast between existing body concentrations of a drug and self-dispensed concentrations. The users attempt to maintain the potency of the original high is constantly eroded by the organism's adaptational processes, necessitating ever higher levels of drug ingestion in order to experience a "buzz." Like a dog chasing it's tail, this turns out to be futile, since increasing dispensed concentrations simultaneously increases tissue drug concentrations—reducing instead of enhancing contrast. A "marriage" is proposed between CAT and TSD (Theory of Signal Detection). The well-developed mathematical technology of TSD and the integrative constructs of CAT provide the basis for innovative research in addictive disorders.

COMPLIANCE FOR PHARMACOTHERAPY AND PSYCHOTHERAPY IN ADD CHILDREN. Ronald T. Brown. Dept. of Psychiatry, Emory University School of Medicine; Kathi A. Borden. Roosevelt University; and Phillip Jenkins. University of Houston.

Patient adherence to treatment protocols has only recently been recognized as an important consideration in pediatric psychopharmacology research. The present study examined demographic, child, and family characteristics of patients who fully adhered, partially adhered, or prematurely discontinued treatment in one such project studying the effects of methylphenidate and adjunct treatment on Attention Deficit Disordered (ADD) children. Approximately one-fourth of the participants adhered to the treatment protocol. The preponderance of nonadherence is discussed as a possible explanation for the rather dismal findings of long-term treatment studies with ADD children. Several characteristics of adherents and nonadherents were reported.

EFFECTS OF PIMOZIDE, CLOZAPINE AND AMPHETAMINE ON MULTIPLE RANDOM INTERVAL PERFORMANCE. Joseph H. Porter and Heidi B. Freese. Virginia Commonwealth University.

Fifteen rats at 80% body weight were tested on a four component MULTIPLE RANDOM INTERVAL food reinforcement schedule with mean intervals of 10, 40, 80 and 160-sec. Both pimozide and clozapine produced a significant dose-dependent decrease in barpressing, while amphetamine had no effect. Motor capacity (as measured by response duration, Matching Equation parameter k, and an independent measure of photocell activity) was decreased by pimozide and clozapine. Amphetamine produced an increase in photocell activity. Reward performance (as measured by the parameter, R_e) was not significantly changed by any of these drugs. Possible motor and reward effects of neuroleptic drugs on operant performance are discussed.

Paper Session: Maxine L. Stitzer, chair
Tuesday, August 26, 1:00–1:50 p.m.
Monroe East, Washington Hilton

SMOKING SATISFACTION: SENSORY AND PHARMACOLOGIC COMPONENTS. Jed E. Rose and Carol Hickman. University of California, Los Angeles.

The sensory and pharmacologic actions of cigarette smoke were dissociated in order to compare their relative importance in mediating smoking satisfaction. Two conditions of smoke inhalation were compared: (1) deep inhalations of large volumes of extremely dilute smoke (33 cc puff of smoke in 2 liters of air). These puffs delivered a pharmacologically effective dose of nicotine, but were intended to have little sensory impact; (2) shallow inhalations of concentrated smoke (60 cc of air followed each 35 cc puff of smoke). These puffs delivered little nicotine, as only a small fraction of smoke particles are absorbed in the upper airways. The dilute smoke inhalations produced significant physiological effects (increased heart rate and expired air carbon monoxide concentrations); however, puffs were rated weak and did not reduce craving for cigarettes. In contrast, shallow inhalations of smoke were rated strong and satisfied craving for cigarettes, despite the absence of nicotine effects. Under conditions of mild cigarette deprivation (30 min), the sensory reinforcing effects of cigarette smoke overshadowed the pharmacologic reinforcing effects of nicotine.

EFFECTS OF MECAMYLAMINE ON SUBSEQUENT SMOKING AND PLASMA NICOTINE LEVELS. Cynthia S. Pomerleau, Ovide F. Pomerleau and Mark J. Majchrzak. Dept. of Psychiatry, University of Michigan School of Medicine; Jean-Jacques Hajjar, M.D. and William R. Shanahan, M.D. Dept. of Internal Medicine, University of Connecticut.

Mecamylamine, a centrally active nicotinic antagonist, has been shown to block in a dose-related fashion certain behavioral and physiological responses to nicotine. Acute administration, however, has also been shown to increase amount of smoking, a phenomenon interpreted as compensatory behavior designed to overcome mecamylamine's blocking effects. We now report significantly greater increases in plasma nicotine following smoking of high-nicotine (2.87 mg) research cigarettes in subjects when pretreated with mecamylamine than when pretreated with placebo, even in the absence of significant differences in puff

volume or puff number. These findings confirm the inference that smokers, at least when they are smoking cigarettes capable of delivering large amounts of nicotine, may be able to overcome the effects of mecamylamine through self-regulation of nicotine intake.

PITUITARY HORMONE RESPONSE TO NICOTINE IN CIGARETTE SMOKERS. Ovide F. Pomerleau, Cynthia S. Pomerleau and Mark J. Majchrzak. Dept. of Psychiatry, University of Michigan School of Medicine.

Integrating data from two experiments in our laboratory, we report the following pattern of pituitary hormone response to different levels of nicotine intake: At high plasma nicotine levels (mean peak nicotine in excess of 60 ng/ml) nausea occurred, and plasma levels of prolactin, adrenocorticotropic hormone, beta-endorphin/beta-lipotropin, growth hormone, arginine vasopressin, and neurophysin I, increased significantly over pre-cigarette baselines without changes in thyroid stimulating hormone, luteinizing hormone, or follicle stimulating hormone. At intermediate plasma nicotine levels (mean peak nicotine between 30 and 40 ng/ml), no nausea occurred and a more selective pattern was observed, with significant elevations limited to beta-endorphin/beta-lipotropin, arginine vasopressin, and neurophysin I. At low plasma nicotine levels (mean peak nicotine less than 10 ng/ml), there were no significant hormonal elevations over baseline.

New Fellows Address: Conan Kornetsky, chair
Saturday, August 23, 11:00–11:50 a.m.
Map Room, Washington Hilton

NEURAL MECHANISMS OF FEAR CONDITIONING MEASURED WITH THE ACOUSTIC STARTLE REFLEX. Michael Davis. Dept. of Psychiatry, Yale University School of Medicine.

The acoustic startle reflex is an excellent model system to analyze how drugs alter both unconditioned and conditioned behavior. Startle is mediated by a simple neural circuit consisting of four central synapses. Startle is increased when elicited in the presence of cues previously paired with shocks. This effect is decreased by drugs such as diazepam, morphine, alcohol, clonidine, or buspirone. Small lesions of the central nucleus of the amygdala block fear-enhanced startle. Currently we are evaluating anatomical connections between the amygdala and the startle pathway and sites of action of drugs that are known to affect fear-enhanced startle.

New Fellows Address: Donald A. Overton, chair
Saturday, August 23, 1:00–1:50 p.m.
Caucus Room, Washington Hilton

BEHAVIORAL PHARMACOLOGY OF NICOTINE DEPENDENCE. Jack E. Henningfield, NIDA Addiction Research Center, Baltimore, MD.

An overview of tobacco and nicotine research that was conducted at The Johns Hopkins University School of Medicine and the National Institute on Drug Abuse, Addiction Research Center was presented. The primary focus of the Hopkins studies was to assess tobacco self-administration as any other form of drug self-administration would be studied, manipulating independent variables such as dose and reinforcement schedule value, while measuring dependent variables such as response rate and amount of substance obtained. The primary focus of the Addiction Research Center studies was to apply the methods used to assess the abuse liability and dependence potential of opioid like compounds in humans to evaluate nicotine. The main conclusion from the results of these studies was that tobacco dependence is an orderly, behavioral pharmacologic process, in which nicotine is critical.

New Fellows Address: Nancy A. Ator, chair
Monday, August 25, 3:00–3:50 p.m.
Map Room, Washington Hilton

BEHAVIORAL PHARMACOLOGY OF OPIOID TOLERANCE. Alice M. Young. Wayne State University.

My Fellows address will review psychological and pharmacological variables that modify the development and expression of tolerance to the behavioral actions of morphine and related opioids. Ongoing work from our laboratory will be used to illustrate how learning processes can modify tolerance development. Behavioral end-points discussed will include ongoing rates and patterns of schedule-controlled behavior, discriminative stimulus profiles, and analgesic effects. The implications of the impact of learning factors on tolerance development for our understanding of tolerance processes and the factors underlying opiate abuse will be considered.

BEHAVIORAL TOLERANCE TO ALCOHOL: EXPECTANCIES AND INCENTIVES. Muriel D. Vogel-Sprott. University of Waterloo.

Tolerance to alcohol refers to the observation that the intensity of response to a given dose diminishes after it is repeatedly administered. Such tolerance cannot be solely a function of drug exposures, for studies holding exposures constant indicate that environmental variables are also influential. This paper reviews one such research program which examines behavioral tolerance to a moderate dose of alcohol in social drinkers. These studies employ an instrumental learning paradigm to demonstrate that the outcomes of behavior under drug affect the acquisition, extinction and transfer of behavioral tolerance to alcohol. An interpretation in terms of contemporary cognitive learning theory is proposed, and practical implications for understanding and predicting behavioral tolerance or impairment in social drinkers is discussed.