

assessed 1, 2, 3, 4, 6, 8, 12 and 23 hours after drug administration. Tolerance to the error producing effects of diazepam developed to a greater extent in the performance than the acquisition performance. Recovery (return to placebo levels) was also quicker in the performance component. Response rate in the acquisition component showed greater tolerance and quicker recovery to the rate decreasing effects of diazepam than the performance component. Overall, the effects of chronic effects of diazepam in humans are consistent with the effects obtained in non-human studies examining the effects of chronic dosing on the repeated acquisition of behavioral chains.

#### DIURNAL RHYTHM OF HOMECAGE ACTIVITY IN THE MACAQUE MONKEY AFTER TRIMETHYLTYN

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Trimethyltin's (TMT) effects on activity have been reported for nocturnal species such as the rodent, but its effects in diurnal species have not been reported. Homecage diurnal activity of individually housed adult female cynomolgus monkeys was continuously monitored following an acute dose (1 mg/kg, PO) of TMT. A 12 hr light dark cycle was automatically maintained. At 2-3 days post-TMT hyperactivity was observed during the light portion of the diurnal cycle, little activity change was seen during the dark phase. Activity was below baseline 7-8 days post-TMT during both light and dark. TMT also altered the diurnal pattern of activity. These results indicate that (1) acute TMT alters the amount and pattern of homecage activity in a time-dependent manner, and (2) while these changes occur homecage behavior remains under control of the environmental lighting schedule.

#### ADAPTIVE MECHANISMS PRODUCE HYPERPHAGIA FOLLOWING AMPHETAMINE-INDUCED ANOREXIA

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Evidence is accumulating, that suggests that the time course of psychoactive drugs on behavior is biphasic—initially reflecting the drug's primary effect but later reflecting the presence of adaptive responses. The effect of three doses of amphetamine on eating during the first, third, fifth, and seventh postinjection hours was examined for twelve consecutive treatment days. The results clearly show that the time course of the drug's effect is biphasic, i.e., anorexia followed by hyperphagia, and demonstrate that increases in the adaptive response over repeated drug exposure account for the pharmacodynamic tolerance observed.

#### NICOTINE, BODY WEIGHT, FOOD CONSUMPTION, AND BODY COMPOSITION IN RATS

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The present study examined the effects of nicotine administration and cessation on body weight, food consumption and body composition in rats. Administration of nicotine was associated with attenuated body weight gains and cessation was associated with increased body weight gains. Changes in body weight were paralleled by changes in percentages of total body fat and protein. There were no consistent differ-

ences in percentages of total body water between groups or across time. Changes in food consumption paralleled changes in body weight in the high nicotine group only. These results suggest that nicotine administration may adversely effect body composition.

#### NEUROBEHAVIORAL CONSEQUENCES OF FLUOXETINE ADMINISTRATION TO NEONATAL PUPS

Maria S McLean Thomas Moore College

Fluoxetine is an experimental serotonin re-uptake inhibitor currently undergoing clinical trials as an antidepressant agent. This experiment determined the behavioral effects on neonatal rat pups of several doses of Fluoxetine (0.025 mg/10 g, 0.05 mg/10 g, 0.10 mg/10 g) administered alone and in conjunction with PCPA from PN-3 to PN-21. A battery of behavioral tests were administered during this period to assess physical growth and maturation, reflex ontogeny, neuromuscular development, and sensorimotor functioning. Levels of amino acids in blood and in brain and levels of neurotransmitters in brain were also measured. In most instances, animals receiving Fluoxetine alone did not differ behaviorally from Saline controls. Most animals receiving Fluoxetine injections, however, exhibited dose related weight loss. It was recommended that behavioral teratological studies be conducted with the drug, since it may soon become available as a clinical antidepressant. The combined weight loss effects of Fluoxetine plus PCPA appeared to be greater than that of either drug alone. It was suggested that with chronic administration of Fluoxetine a negative feedback mechanism may operate which further diminishes the level of 5-HT.

#### THE B-VITAMIN, PANTOTHENIC ACID CAN REVERSE THE MOTOR EFFECTS OF ETHANOL IN SQUIRREL MONKEYS

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Pantothenic acid, a B vitamin, is the precursor to Coenzyme A, which, in turn, is a precursor to acetylcholine. Recent work in our laboratory suggests that the motor impairment induced by ethanol can be blocked by pre-administration of pantothenic acid. These effects are critically dependent upon the route of administration and timing. For example, pantothenic acid administered orally is ineffective at all doses tested but when administered IV it reverses the acute effects of ethanol. Interactions of these two substances were studied in a preparation that allows monitoring of both operant behavior and tremor in squirrel monkeys. The subjects were trained to maintain a lever in a specified position for 8 sec for fruit juice reward. A transducer coupled to the lever provided a precise measure of displacement. Ethanol altered the tremor spectrum by decreasing high frequencies at low doses and all frequencies at higher doses. When pantothenic acid was administered IV before ethanol dosing, response rate and many features of tremor returned to control levels. (Supported by AA05188 and ES01247)

#### INFLUENCES OF ALCOHOL CONSUMPTION ON CIGARETTE SMOKING TOPOGRAPHY

Robert M Keenan, Dorothy K Hatsukami and Roy W Pickens University of Minnesota, Minneapolis and The National Institute of Drug Abuse

This study examined several durational and frequency

components of cigarette smoking topography (number of cigarettes, number of puffs, puff duration, pause duration, cigarette duration) as a function of a smoker's history of alcohol consumption. Smokers were grouped as a function of their self-reported and observer-verified current drinking status over the three months prior to the study, as well as a history of alcohol abuse as assessed by DSM-III criteria. Data analysis showed significant differences between groups for nicotine content of the cigarettes smoked ( $p < 0.0001$ ), number of cigarettes smoked ( $p < 0.0001$ ), cigarette duration ( $p < 0.002$ ). The data indicate a history of alcohol use is associated with increased daily smoke exposure.

#### THE EFFECTS OF SMOKING ON DISCRIMINATIVE FORCE EMISSION IN HUMANS

Michael Klitzke, Thomas Lonbardo and Stephen Fowler  
University of Mississippi

In comparison to non-smokers, smokers exerted more force during a fine motor task after smoking a cigarette or when abstinent from smoking. Task performance was assessed in terms of measured peak force exerted, duration of response, interresponse time, number of correct responses, and total number of responses. Significant negative correlations were found between the number of years smokers smoked and peak force exerted during the smoking condition. The findings suggest an important role for force measurement technology in human behavioral pharmacology research.

#### THE ROLE OF PAVLOVIAN CONDITIONING IN OPIATE WITHDRAWAL IN RATS

Jean A Paty  
Clinical Psychology Center, University of Pittsburgh, Howard D Cappell  
University of Toronto

Experiments were conducted to examine the hypothesis that conditioned compensatory responses (CR), which are hypothesized to mediate drug tolerance, are expressed as withdrawal when the drug is not present (Siegel, 1983). In Experiment 1, it was confirmed that saccharin aversion is a reliable, sensitive index of withdrawal from morphine. In Experiment 2, animals were first made tolerant to a dose of 60 mg/kg morphine given in a distinctive environment (DR). They were then left for 30 days to recover from the with-

drawal effects associated with the cessation of a chronic high drug dose. These animals were then given a placebo, saline, in the DR. If the CR was expressed as withdrawal then a saccharin aversion should have occurred in the presence of drug related cues. The results did not confirm this prediction. It is concluded that perhaps non-specific measures of withdrawal will not demonstrate a general withdrawal like effect in the presence of drug related stimuli.

#### BEHAVIORAL EFFECTS OF CHRONIC COCAINE ADMINISTRATION

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Osmotic minipumps continuously infused cocaine (0.1 or 0.3 mg/kg/hr) during 14-day periods in three squirrel monkeys (*Saimiri sciureus*) trained under a fixed-interval 180-sec stimulus-shock termination schedule. Cocaine was administered (IM) acutely using cumulative-dosing procedures once per week prior to and during chronic treatment. Control response rates increased during chronic treatment (0.1 mg/kg/hr) but returned to pre-pump levels following termination of chronic treatment. Tolerance developed to the gross behavioral effects observed initially in all subjects during chronic treatment (0.3 mg/kg/hr) and to rate-suppressing effects observed in one subject. However, tolerance did not develop to the acute effects of cocaine.

#### CLONIDINE, NEGATIVE CONTRAST AND NOVELTY-INDUCED STRESS

Charles F Flaherty, Patricia S Grigson and Melissa K Demetrikopoulos  
Rutgers University

Rats were shifted from 32% to 4% sucrose solutions. The resultant negative contrast effect in consummatory behavior was not alleviated by clonidine (0.00312, 0.00625, 0.0125, 0.025, 0.050 mg/kg). The lower doses had no effect on behavior, the higher doses reduced consumption in both shifted and unshifted rats. In Experiment 2 clonidine (0.0625, 0.0125 mg/kg) raised plasma glucose levels in animals exposed to a novel environment. These results are at variance with those obtained with chlordiazepoxide and other anxiolytics and suggest limits on the degree to which clonidine can be considered to function as an anxiolytic.

#### PAPER SESSION

Human Psychopharmacology

Friday August 28, 1987 • 2:00 p.m. - 3:50 p.m.

Marriott Marquis Hotel • Kern/Sullivan Room

Chair: Stephen A. Daniel, Mercy College

#### TOXICOLOGY SCREENING IN ACUTE SPINAL CORD INJURY

Allen Heinemann  
Northwestern University Medical School, Sidney Schnoll  
University of Virginia, Roger and Mary Keen  
Northwestern Medical School

The validity of self-reported intoxication at time of spinal cord injury (SCI) was examined by comparing self-reports with the results of blood serum and urine analysis for 78 cases at admission to an acute SCI center. Serum ethanol was the most frequently found substance followed by lidocaine, cocaine, cannabinoids, opiates, meperidine, morphine, and methadone. While 51% of the sample reported

being under the influence of some substance at the time of SCI, the relationship between these two measures was not statistically significant. These results suggest that routine drug testing at admission to an SCI center will produce false negatives as well as false positives if presence alone is interpreted as evidence of intoxication.

#### DRUG TYPE, PERSONALITY, PSYCHOPATHOLOGY AND EARLY TERMINATION IN SUBSTANCE ABUSE

Michael J Stark  
Lewis & Clark College, Portland, OR, Barbara K Campbell  
CODA