

deprivation. Effects on alertness and cognitive performance were assessed for 12 hours following drug administration. Results from the Multiple Sleep Latency tests show that caffeine reversed sleep deprivation-induced decreases in alertness for 6 hours. Caffeine did not increase sleep latencies to presleep deprivation levels, however. Cognitive performance degraded by sleep deprivation was improved following drug. The highest dose tested improved accuracy on a sustained attention task and on a logical reasoning task, and speed on a choice reaction time task to presleep deprivation levels for 12 hours.

EFFECTS OF TRIAZOLAM AND LORAZEPAM ON HUMAN LEARNING AND PERFORMANCE. Craig R. Rush, Stephen T. Higgins, Warren K. Bickel and John R. Hughes. University of Vermont, Burlington, VT.

The present experiment assessed whether triazolam (0–0.75 mg) and lorazepam (0–6 mg) differentially affect human discriminated-operand behavior. Eight healthy male volunteers were tested during an 8-hour session using a counterbalanced, crossover design. Experimental tasks included the repeated acquisition and performance of behavioral sequences, Digit-Symbol-Substitution Test (DSST), Visual-Analog Rating Scales (VAS), and Addiction Research Center Inventory (ARCI). Both drugs disrupted responding under the repeated acquisition and DSST procedures in a dose- and time-dependent fashion. Similar dose- and time-dependent effects were evident with subject ratings of drug effects. The two compounds differed in terms of onset, duration of effect, and potency (7:1; TZ > LZ), but did not differ in magnitude of effect. These results suggest that the liability associated with the use and abuse of triazolam and lorazepam are comparable, as measured via discriminated-operand procedures and subject ratings of drug effects.

CONTINGENT TOLERANCE TO CHLORDIAZEPOXIDE (CDP) IN RATS: DIFFERENTIAL EFFECTS OF BENZODIAZEPINE (BZ) AND NON-BZ DRUGS. C. A. Sannerud, A. J. G. Alastra and P. L. Harger. The Johns Hopkins University Medical School, Baltimore, MD.

Environmental variables can influence the development of tolerance to the effects of BZ. The interaction between drug administration and the ability to perform the task can result in differential tolerance that is a function of chronic daily dose and duration of treatment. The present study evaluated the role of environmental variables in the development of tolerance to the sedative effects of CDP and the effect of chronic CDP on the sensitivity to acute administration of other BZ and non-BZ drugs. Sprague-Dawley rats were trained to respond under a multiple time-out 10 min, fixed ratio 30 schedule of food pellet delivery. Cumulative dose response curves for CDP, midazolam (MDZ), flumazenil (RO), pentobarbital (PB), caffeine, and *d*-amphetamine were determined prior to and during chronic CDP. Rats received 18 mg/kg CDP either before (PRE, $n=4$) or after (POST, $n=5$) exposure to the daily experimental session for 7 weeks. Tolerance testing was accomplished by generating dose-response curves for CDP at weekly intervals. Large group differences were seen in the rate and degree of tolerance development to CDP. Group PRE showed 2- to 5-fold shifts to the right in the weekly CDP dose-response curves, 3- to 10-fold tolerance to MDZ and increased sensitivity to RO. Group POST showed no tolerance to CDP or MDZ, and only a slight change in sensitivity to RO. Only Group PRE showed cross-tolerance to PB. Neither group showed a change in sensitivity to caffeine or

d-amphetamine. (Supported by NIDA grant DA 01147.)

CONTEXTUAL MODULATION OF HUMAN STIMULANT SELF-ADMINISTRATION. Kenneth Silverman, Kimberly C. Kirby and Roland R. Griffiths. The Johns Hopkins University School of Medicine, Baltimore, MD.

This study assessed the influence of environmental context on *d*-amphetamine self-administration in seven recreational stimulant users. Initially, subjects were given color-coded capsules containing either placebo or *d*-amphetamine in random order across days. Environmental contexts were manipulated by scheduling one of two activities each day immediately following drug ingestion: A relaxation activity or a computer vigilance activity. In a subsequent choice phase, six of seven subjects reliably chose (≥ 9 of 10 choices per subject) to take *d*-amphetamine when the vigilance task was scheduled and placebo when the relaxation task was scheduled. The study provides evidence for the contextual modulation of drug self-administration.

COGNITIVE MOTIVATIONS, SENSATION SEEKING, AND DRINKING PROBLEMS: A LONGITUDINAL STUDY. Alan W. Stacy, M. D. Newcomb and P. M. Bentler. University of California, Los Angeles, CA.

We evaluated the longitudinal effects of adolescent cognitive motivation for alcohol use and sensation seeking on adult drinking problems and driving while intoxicated (DWI). Results indicated that the cognitive motivation factor was a significant, independent, nine-year predictor of a factor of drinking problems. Over this same period, certain cognitive motivation and sensation seeking indicators independently predicted DWI, and the sensation seeking factor independently predicted cognitive motivation and alcohol use factors. The independent effects on problem drinking demonstrated that psychosocial vulnerability appeared across a range of consumption levels, consistent with previous notions that drinking problems are not fully mediated by consumption patterns alone.

PERSONALITY CHARACTERISTICS IN SUBSTANCE ABUSE AND RELATIONSHIP TO PHYSIOLOGICAL PARAMETERS IN HUMANS. J. M. Stapleton, B. C. K. Yung, M. L. Spurgeon, M. J. Morgan, R. L. Phillips, N. G. Cascella, J. H. Jaffe, D. F. Wong and E. D. London. NIDA Addiction Research Center, Johns Hopkins Medical Institution, Baltimore, MD.

Personality characteristics were measured and related to physiological parameters, including regional cerebral glucose metabolic rate (rCMRglc), derived from placebo sessions of ongoing positron emission tomography (PET) studies. Details of methods may be found in London et al. (Arch. Gen. Psychiatry 47:73–81; 47:567–574; 1990). Substance-abusing subjects scored higher than published norms on several personality measures, including the Assault Subscale of the Buss-Durkee Hostility Inventory (AS-BD), the Psychoticism scale of the Eysenck Personality Questionnaire, and the Novelty Seeking scale of the Tridimensional Personality Questionnaire. The AS-BD score was positively correlated with mean rCMRglc across all frontal regions of the brain [$r(20)=+.613$, $p<.01$]. Scores on the Reward Dependence subscale of the Tridimensional Personality questionnaire were negatively correlated with rCMRglc in superior temporal gyrus [left: $r(12)=-.631$, $p<.02$; right: $r(12)=-.701$,

$p < 0.01$]. These data suggest that substance abuse is associated with personality characteristics that may have specific identifiable neural substrates.

PCP-INDUCED ABNORMAL SOCIAL BEHAVIOR: POSSIBLE RELATION TO SCHIZOPHRENIC PHARMACOLOGY. R. E. Steinpreis, K. J. Mahan, D. J. Reser and J. D. Salamone. The University of Connecticut, Storrs, CT.

Amphetamine has been criticized as a drug model of schizophrenia because of its inability to produce the negative as well as the positive symptoms of schizophrenia. Phencyclidine (PCP) induces a psychosis that includes both the positive and negative symptoms and is virtually indistinguishable from schizophrenia. While the motor effects of these drugs in rats have been well established, the effects on social interaction could provide a more useful tool in the understanding of psychotic behavior. An "intruder" paradigm was used in which a rat was injected with drug (0.5 mg/kg amphetamine, 1.0 mg/kg amphetamine, 4.0 mg/kg PCP or saline), placed in a stable colony of three other rats, and observed for 30 minutes. Both PCP and amphetamine reduced the frequencies of various social behaviors. A second study employed microdialysis methods to measure PCP-induced increases in extracellular dopamine (DA) and its metabolites in the nucleus accumbens. These results indicate that some of the pharmacological and behavioral properties of PCP in rats may be related to the mechanisms involved in schizophrenic symptoms.

DRUG-FREE OUTPATIENT TREATMENT: CHANGING CLIENT CHARACTERISTICS AND OUTCOME. Dace S. Svikis and Mary E. McCaul. The Johns Hopkins University School of Medicine, Baltimore, MD.

This paper compares demographic and psychosocial characteristics of clients admitted into drug-free outpatient treatment ($N = 173$) as a function of their primary DSM-III drug diagnosis (alcohol, heroin, cocaine). Heroin and cocaine clients were more likely to be black and single. More alcohol clients had experienced stable full-time employment, whereas heroin clients reported more illegal involvement and income. More heroin and cocaine clients received detoxification prior to current treatment, whereas more alcohol clients were treated in a medical or psychiatric unit or incarcerated. More alcohol clients indicated that the current admission was suggested by the judicial system. Finally, alcohol clients were more likely to report recent psychiatric symptomatology and a prior history of psychiatric hospitalization.

CHANGES IN THE STIMULUS EFFECTS OF COCAINE WITH TRAINING DOSE. P. Terry, J. M. Witkin and J. L. Katz. NIDA Addiction Research Center, Baltimore, MD.

Six rats were trained in 2-lever experimental chambers to press one lever following cocaine injection (3.0 mg/kg, IP), and the other lever following saline injection. D1 receptor-subtype agonists substituted for cocaine with greater efficacy than was the case at higher cocaine training doses, whereas D2 agonists were less efficacious. All three D1 agonists tested substituted more completely for cocaine than did any of the three D2 agonists. The results suggest a preferential activity of relatively low doses of cocaine for the D1 dopamine receptor subtype.

BEHAVIORAL REBOUND HYPERSENSITIVITY OF DOPA-

MINERGIC FUNCTION AFTER ACUTE COCAINE. E. Tirelli and J. M. Witkin. NIDA Addiction Research Center, Baltimore, MD.

To investigate functional changes in dopamine systems upon withdrawal from acute injection of cocaine, mice were injected acutely with 30 mg/kg cocaine 1496, 256 or 16 min before being tested for responsiveness to apomorphine (D1/D2 agonist). When tested at a time when cocaine disappeared from the brain (256 min), effects of apomorphine on gnawing while climbing were enhanced. These effects were less marked than the potentiation produced by cocaine injected 16 min before test. Cocaine injected 1496 min before test was ineffective. These changes were absent 24 hours after test. Our data suggest that this behavioral procedure may provide a model of acute cocaine dependence.

THE REINFORCING AND SUBJECTIVE EFFECTS OF BUSPIRONE AND LORAZEPAM. Joseph R. Troisi, II, Thomas Critchfield and Roland R. Griffiths. The Johns Hopkins University School of Medicine, Baltimore, MD.

The reinforcing and subjective effects of oral buspirone (BUS) (60 mg/70 kg) and lorazepam (LZ) (4 mg/70 kg) were evaluated in nine adult male recreational drug abusers. A double-blind choice procedure was used which involved forced exposure to LZ and BUS (on separate sessions) followed by a single choice session. The strengths of LZ and BUS were rated as equal. LZ was rated as being better liked and having more good effects and fewer bad effects than BUS. There was a modest disliking for BUS. On the choice day, 8 or the 9 subjects chose LZ over BUS. These data suggest that LZ has greater reinforcing effects and produces more liking than BUS.

OPIOID SUPPRESSION OF MALE AND FEMALE ULTRASOUNDS DURING SOCIAL DEFEAT. J. A. Vivian, M. Haney and K. A. Miczek. Tufts University, Medford, MA.

Ultrasounds (US) in rats occur in socially significant situations such as agonistic and sexual behavior and may serve to communicate affect. Male and female Long-Evans rats were administered morphine and US were studied during: 1) three brief exposures to attacks and threats by a resident opponent and, 2) three prolonged exposures to the threat of attack by a resident opponent. The attack and threat situation consisted of brief agonistic interactions until the intruder rat displayed submissive postures (crouch, supine) for five s; subsequently, the intruder was exposed for 25 min to threats by the opponent while protected from physical contact by a wire mesh. Male and female intruders received ca. 10 bites in 60 s, prompting a high rate of US. During the protected encounter morphine (1-10 mg/kg SC) dose-dependently decreased the rate and duration of US, paralleling its analgesic effects and increases in submissive behavior. These effects were antagonized by naltrexone (0.1 mg/kg IP; 3-5-fold rightward shift), which by itself modestly increased the rate and duration of US. In separate groups of defeat experienced or socially inexperienced male rats, morphine (1-30 mg/kg IP) produced only a slight attenuation of the startle reflex. The suppression of US and pain sensitivity, but not the startle reflex, may reflect specific opioid actions on affective components of social stress reactions.

COMPARISON OF OPIOID AGONISTS IN ANALGESIA AND DRUG DISCRIMINATION ASSAYS. Ellen A. Walker and Al-