

to perturbations of its environment. Current evidence suggests that the release of corticotropin-releasing factor (CRF) within the brain may permit the coordination of a whole body response in stress, thus reinforcing Selye's global stress concept. The evidence supporting such a role for CRF is summarized below. CRF administered intracerebroventricularly (ICV) elicits a number of behavioral, physiological, and neurochemical responses characteristic of stress. Behavioral effects include effects on locomotor activity, increased grooming, decreased feeding and sexual activity, decreased exploratory behavior and social interaction, an increased acoustic startle response and shock-induced fighting, and "anxiogenic" actions in conflict tests, and in the elevated +-maze. ICV CRF activates the sympathetic nervous system and the adrenal medulla, and has several effects on gastrointestinal function. Endocrine factors affected include an increase in ACTH secretion, and decreases in LHRH and growth hormone secretion. There is increased firing of noradrenergic neurons in the locus coeruleus, and increased production of the metabolites of norepinephrine (NE) and dopamine, suggesting increased release of these catecholamines. Where tested, these effects are independent of the pituitary, and hence ACTH or glucocorticoid secretion. Each of these effects could indicate merely that ICV administration of CRF is stressful. However, intracerebral administration of a CRF antagonist,  $\alpha$ -helical CRF<sub>9-41</sub> (ahCRF) has been reported to reverse or attenuate the effects of various stressors on LHRH secretion, plasma NE, feeding, exploratory behavior, and aggression. These observations may provide an explanation for the rather widespread distribution throughout the brain of CRF-like immunoreactivity, bioactivity, and CRF-binding sites. The demonstration that CRF can be released from excised brain regions by stimulation with high K<sup>+</sup> in a Ca<sup>2+</sup>-dependent manner suggests that CRF may act as a neurotransmitter in the brain. Changes in the cerebral concentration of CRF in various brain regions during stress reinforce this idea. The above discussed results support the hypothesis that release of brain CRF may be both necessary and sufficient to characterize stress.

## POSTER SESSION

### *Biological Bases of Behavior*

**THE CONTRIBUTION OF SUBJECT EXPECTATION ON ANALGESIC EFFICACY FOR CLINICAL AND EXPERIMENTAL PAIN.** Manon Houle, S. Kogon, P. A. McGrath and G. Moran. University of Western Ontario, London, Canada.

The study aims to quantify the contribution of expectation for pain relief on analgesic effectiveness for both experimental and clinical pain. One hundred patients scheduled for extraction of impacted third molars used visual analogue scales to rate the intensity and the unpleasantness of experimental pain (thermal stimuli 45–51°C) before and after double-blind administration of Tylenol 3 or placebo. Subjects were divided into four groups of a balanced placebo design in which the traditional placebo design—expect analgesic/receive placebo and expect analgesic/receive analgesic is complemented with two groups—expect placebo/receive analgesic and expect placebo/receive placebo. These expectancy manipulations allow for the determination of what portion of the overall experimental pain reduction (both intensity and unpleasantness) is due to the independent effects of the expectation of receiving an analgesic and what portion is due to the pharmacological effect of the analgesic. Subjects also used visual analogue scales to rate the intensity and unpleasantness of post-surgical dental pain both before and after treatment administration. Although all subjects received the analgesic for postsurgical pain,

expectancy was manipulated by telling subjects that they received the same drug as they had received during the experimental session. It is expected that subjects' expectancy will be a major determinant of subjects' analgesic responses to placebo and significantly modulate subjects' ratings of the efficacy of the analgesic.

**SENSORIMOTOR REPLACEMENT AS A STRATEGY FOR SMOKING CESSATION.** Jed E. Rose, F. Behm, C. Schur, N. Comfort, E. D. Levin and D. P. Tashkin. University of California, Los Angeles, CA.

In a three-week smoking cessation program, we tested an inhaler that delivered an aerosol containing citric acid and smoke flavor. The goal was to simulate the taste and tracheobronchial sensations produced by cigarette smoke. The active inhaler was compared with a placebo inhaler in a randomized double-blind design. Relative to placebo, this treatment significantly reduced smoking and self-reported craving for cigarettes in subjects with baseline CO values higher than the mean. These results suggest that sensorimotor replacement, alone or in combination with nicotine replacement treatments, may be useful as a smoking reduction or cessation aid.

**SMOKELESS TOBACCO DEPRIVATION, NICOTINE AND PERFORMANCE.** Dorothy K. Hatsukami, Robert M. Keenan and Deborah J. Anton. University of Minnesota, Minneapolis, MN.

The purposes of this study were to 1) examine the effects of smokeless tobacco deprivation on performance, and 2) determine the effects of nicotine gum dose on performance during deprivation. Male Copenhagen smokeless tobacco users underwent 3 days of baseline measurement while continuing to use smokeless tobacco ad lib. They were then randomly assigned to one of five groups for the next five days: 1) continuous smokeless tobacco users; 2) discontinuous users; 3) 0 mg nicotine gum; 4) 2 mg nicotine gum; or 5) 4 mg nicotine gum. All groups except the continuous smokeless tobacco users were asked to quit using smokeless tobacco during this experimental period. The results were as follows: 1) There were significant increases in reaction time and variability of reaction time (S.D.) during the experimental period among the discontinuous users when compared to the continuous users group. 2) There were no nicotine gum dose-related effects on reaction time performance after smokeless tobacco deprivation. 3) There were significant increases in reaction time and variability of reaction time (S.D.) among the discontinuous users when compared to the placebo group. Those findings replicate previously published results regarding the effects of smokeless tobacco deprivation on performance. They also indicate that among smokeless tobacco users, there is a significant placebo effect which masks the effects of nicotine gum.

**EFFECTS OF SMOKING AND SMOKING ABSTINENCE ON FINE MOTOR PERFORMANCE.** Michael J. Klitzke, Thomas W. Lombardo and Stephen C. Fowler. University of Mississippi, University, MS.

Data regarding the effect of smoking and abstinence from smoking on fine-motor task performance are rarely encountered in the literature. However, precise spatio-temporal force regulation is important for professionals such as pilots and surgeons. In a laboratory setting, the performance of nonsmokers, abstinent

smokers, and smokers who smoked before a discriminative force-time emission task, was measured in terms of peak force, response duration, and response latency. Abstinent smokers exhibited significantly greater variability in both force emission and response latency compared to either nonsmokers or smokers who smoked. Abstinent smokers' greater response variability may reflect withdrawal from nicotine and a decreased ability to regulate force emission and time estimation.

**PHYSIOLOGICAL AND VERBAL MANIFESTATIONS OF SMOKING URGES PRODUCED THROUGH IMAGERY.** Stephen T. Tiffany, Denise M. Hakenewerth, David J. Drobos and Peg M. Maude-Griffin. Purdue University, West Lafayette, IN.

The results of two studies will be reviewed showing that smoking urges can be elicited in the laboratory through a procedure in which smokers are instructed to vividly imagine scripts presented by audiotape. The data indicate that the magnitude of self-reported urges and cravings produced through imagery can be manipulated by the urge and affective content of the imagery scripts. Furthermore, urge-eliciting scripts also produce somato-visceral changes during imagery trials, e.g., increases in heart rate and decreases in skin conductance habituation. The potential applications of the imagery paradigm in the study of the structure and function of drug urges will be discussed.

**NICOTINE ALTERS INSULIN LEVELS IN RAT HYPOTHALAMI.** Margarita Raygada, Stephanie M. Nespor and Neil E. Grunberg. Uniformed Services University of the Health Sciences, Bethesda, MD.

Effects of nicotine administration and cessation on insulin levels in hypothalami of rats were examined. Subjects were 63 rats that received 12, 8, 6, 4, or 0 mg nicotine/kg body weight/day by osmotic minipumps for 14 days. Hypothalami were assayed for insulin at the end of the drug administration period or 7 days after drug cessation. Nicotine administration was related to hypothalamic insulin values by a U-shaped function. Cessation of nicotine was accompanied by a dose-related decrease in hypothalamic insulin levels. These changes in hypothalamic insulin may underlie actions of nicotine on energy intake and expenditure.

**NICOTINE AND BODY WEIGHT: EXAMINING THE ROLE OF ENDOGENOUS OPIOIDS.** Elizabeth C. Sibolboro and Neil E. Grunberg. Uniformed Services University of the Health Sciences, Bethesda, MD.

To determine whether effects of nicotine on body weight and food consumption are mediated by opioid mechanisms, rats received nicotine, naltrexone, nicotine and naltrexone, or saline. Nicotine or naltrexone alone had similar suppressive effects on body weight and sweet food consumption. Together, these drugs suppressed body weight additively, but suppressed food consumption similar to each drug alone. After drug cessation, subjects gained more weight than controls. These results indicate that effects of nicotine on body weight and food consumption are not mediated by the endogenous opioid peptides. Effects of nicotine and naltrexone on body weight involve energy intake and expenditure during, and energy intake after drug administration.

**THE EFFECT OF TRIAZOLAM ON COGNITIVE PERFORMANCE.** Rosemarie L. Duncan. Walter Reed Army Institute of Research, Washington, DC; Lisa M. Simon. National Institute of

Drug Abuse, Rockville, MD; and Vincent M. O'Donnell, Robert K. Winegar, Debra S. Friedman and Gregory L. Belenky. Walter Reed Army Institute of Research, Washington, DC.

The objective of this study was to determine the effects of a low dose of triazolam on cognitive performance on a variety of tasks across time. Subjects (151 males) were randomly administered either a 0.125 mg dose of triazolam or placebo and began a series of cognitive performance tasks forty minutes postdrug administration. Mean data were statistically evaluated using analyses of variance. Significance level was set at  $p < 0.05$ . A treatment effect was found for a high memory load letter search task. The triazolam group attempted fewer items, scored fewer hits, and recorded fewer correct rejects than did the placebo group. To our knowledge, this study was the first to find cognitive impairment with the 0.125 mg dose of triazolam. These results suggest that the effects of the 0.125 mg dose on performance are strongest within the first hour postdrug and that in normal subjects, this dose of triazolam will only impair performance when the task taxes the ability of the subject.

**INDIVIDUAL DIFFERENCES IN THE EFFECTS OF TRIAZOLAM ON COGNITIVE PERFORMANCE.** Debra S. Friedman. Walter Reed Army Institute of Research, Washington, DC; Lisa M. Simon. National Institute of Drug Abuse, Rockville, MD; and Vincent M. O'Donnell, Rosemarie L. Duncan, Robert K. Winegar and Gregory L. Belenky. Walter Reed Army Institute of Research, Washington, DC.

The purpose of this study was to determine if the cognitive effects of triazolam, a benzodiazepine hypnotic, are dependent on the baseline personality of the subject. One hundred fifty-one subjects were given the Eysenck and Freiburg Personality Inventories and, the State-Trait Anxiety Inventory, in order to determine personality type. Each subject was then administered either placebo or a 0.125 mg dose of triazolam. The subjects performed a series of cognitive tasks during periodic testing from 40 minutes to 5 hours postdrug administration. On each of the personality dimensions, subjects were divided into high and low trait groups using a median split of their scores. Two-way analyses of variance were conducted to determine if interaction effects were present. Many of the cognitive tests were differentially affected by treatment (triazolam vs. placebo) depending on subject personality type. Portions of the Differential Aptitude Tests (DAT), the Symbol Digit Modalities Test, and a letter search task revealed a significant ( $p < 0.05$ ) drug by personality interaction. Dimensions of personality interacting with drug included anxiety, sociability, neuroticism, impulsivity, and stability. This is the first study to demonstrate interactive effects of triazolam and personality on cognitive performance.

**THE EFFECTS OF TRIAZOLAM (HALCION) ON HUMAN MULTI-OPERANT RESPONDING.** Ralph Spiga, Don R. Cherek, Richard A. Meisch and John D. Roache. University of Texas Health Science Center at Houston, Houston, TX.

The acute effects of triazolam on multi-operant responding were studied under controlled laboratory conditions. Three response options were provided: 1) lever A responding maintained by the presentation of points exchangeable for money, 2) lever B responding which ostensibly subtracted points from another person, i.e., aggressive responding, and 3) lever C responding which protected the subject's counter from point subtractions for some period of time, i.e., escape responding. Aggressive and escape