

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

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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

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This study examined several durational and frequency