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THE COMPARATIVE EFFECTS OF LSD, MESCALINE, & DMT ON PRIMATE SOCIAL & SOLITARY BEHAVIOR. R.F. Schlemmer, Jr.*, C.B. Tyler*, N. Narasimhachari*, J.M. Davis* (SPON: R.W. Morris) Ill. State Psychiatric Institute, Chicago, Illinois 60612

To study the effect of hallucinogens on primate behavior, 3 chemically diverse hallucinogens-d-LSD, mescaline (MESC), & dimethyltryptamine (DMT)-were administered chronically to 2 pairs of adult Stumptail macaque females housed in separate cages. Following a 5-day baseline observation period, MESC (17 mg/kg), DMT (2 mg/kg), or LSD (0.01 mg/kg) was administered daily i.m. to each of the 4 monkeys for 5 days. Only 1 monkey/pair received drug each wk & 1 wk elapsed between the different treatments. MESC, DMT & LSD were given 60, 5, & 15 min prior to observation respectively. Observation by a "blind" observer occurred for 1 hr daily for each group. MESC, DMT & LSD all induced dog-like "wet shakes" & involuntary limb jerks. There was evidence of tolerance to LSD & MESC, but not DMT, for each of these behaviors. Only DMT induced hypervigilance and this showed tolerance. All 3 drugs significantly decreased social & self grooming. Only MESC & LSD significantly increased resting scores. Wet shakes & limb jerks appear to be the most unique behaviors induced by hallucinogens in this species since 35 non-hallucinogenic psychoactive drugs tested did not induce these 2 behaviors. This study also demonstrates both similarities & differences in the behavioral changes induced by chemically diverse hallucinogens in monkeys. This paradigm may prove useful in the study of the psychopharmacology of hallucinogens.

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MODIFICATION OF BEHAVIORAL AND NEUROCHEMICAL EFFECTS OF COCAINE BY HALOPERIDOL. S.N. Pradhan, C.S. Aulakh,* A.K. Bhattacharyya,* S. Dose* and S.N. Roy.* Howard Univ. Coll. Med., Washington, D. C. 20059

Cocaine (10-20 mg/kg, i.p.) stimulated spontaneous motor activity (SMA) and facilitated self-stimulation (SS) behavior in rats with electrodes at the posterior hypothalamus (PH) or area ventralis tegmentum (A10 area); it also induced stereotyped behavior (ST). Cocaine increased the norepinephrine (NE) contents of the diencephalon-midbrain (DM) and pons-medulla (PM) at 10 min after its administration, but decreased them at 20 min onwards. It also increased dopamine (DA) contents in the DM and caudate nucleus (CN) at 20 min, and acetylcholine (ACh) content in the CN at 40 min. Haloperidol at 0.015 mg/kg, i.p. dose reduced or blocked cocaine-induced stereotypy and increase in SS of A10 area, whereas it did not affect, rather enhanced drug-induced increases in SMA and SS of PH area. At higher dose (0.03 mg/kg, i.p.) all behavioral effects were blocked. Haloperidol (0.03 mg/kg) itself reduced DA contents in the DM and CN but increased ACh content in the CN. Tested at 30 min after its administration along with cocaine, haloperidol reversed the cocaine-induced increase of DA, but further increased the ACh content in the CN; it also reduced decreases in the NE content in the DM and PM. It appears that haloperidol alters the behavioral actions of cocaine through its effects on the neurotransmitters in the respective brain areas.

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ANTAGONISM OF ACUTE COCAINE POISONING BY CHLORPROMAZINE IN THE CONSCIOUS DOG. I.W. Waters, J.D. Catravas,* M.A. Walz* and W.M. Davis. Department of Pharmacology, School of Pharmacy, Univ. of Mississippi, University, MS 38677.

Cocaine HCl was administered (0.5 mg/kg/min, i.v.) to conscious mongrel dogs (N=17) until death; the mean convulsive dose (MCD) was 14±1 mg/kg and the mean lethal dose (MLD) was 22±2 mg/kg. All animals exhibited significant increases in body temperature, arterial systolic, arterial diastolic, mean arterial and left ventricular pressures, heart rate, cardiac output, plasma glucose, blood lactate, plasma oxaloacetic transaminase, respiratory rate, minute volume, tidal volume and oxygen uptake; however, total peripheral resistance and arterial pH decreased significantly. Chlorpromazine pretreatment (12 mg/kg, i.v.) antagonized the cardiovascular, respiratory and biochemical responses induced by a cocaine challenge of 39.5 mg/kg (MLD+SSD); although mild convulsions (MCD 22±3 mg/kg) were evident, all animals (N=6) survived a 48-hr observation period. Animals (N=5) pretreated with propranolol (6-10 mg/kg, i.v.) prior to a similar cocaine challenge exhibited partial reduction of cocaine-induced cardiovascular changes; however, other parameters were relatively uninfluenced, and all animals experienced severe convulsions (MCD 9± 2 mg/kg) and failed to survive (MLD 20±1 mg/kg). (Supported in part by Research Institute of Pharmaceutical Sciences, University of Mississippi and GRS grant FRO 5594-01).

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BEHAVIORAL INTERACTIONS OF PHENCYCLIDINE AND PENTOBARBITAL. L.D. Chait* and Robert L. Balster* (SPON: L.A. Woods). Dept. of Pharmacology, Med. Col. of Va., Va. Commonwealth Univ., Richmond, Va. 23298

A previous operant study in squirrel monkeys failed to confirm the reported enhancement of pentobarbital (PB) induced surgical anesthesia by phencyclidine (PCP) pretreatment in rhesus monkeys. Therefore, several studies were performed in different species to more fully characterize the interaction between these two drugs. In mice, 3.0 and 30.0 mg/kg PCP (i.p.) significantly lowered the LD 50 of i.p. PB from a control value of 110 mg/kg to 80 and 53 mg/kg, respectively. Using a behavioral rating scale, an inactive dose of PCP (0.2 mg/kg i.m.) combined with only a moderately depressant dose of PB (25.0 mg/kg i.m.) produced surgical anesthesia in rhesus monkeys, confirming our original observations. Employing an equivalent rating scale for squirrel monkeys, it was found that combining 0.16 mg/kg PCP i.m. with 12.5 mg/kg PB i.m. failed to produce surgical anesthesia, despite the fact that these two doses by themselves had a greater effect than the two doses used in the rhesus monkeys. These studies demonstrate that the interaction observed between PCP and PB depends upon 1) the species employed, even when species differences in sensitivity to the interacting drugs are accounted for, and 2) the nature of the response being measured. (Supported by research Grant DA-01442 and training Grant DA-07027)

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EFFECTS OF LEVO-ALPHA-ACETYL METHADOL ON LOCOMOTOR ACTIVITY AND OPERANT BEHAVIOR IN THE RAT. W.T. McGivney* and D.E. McMillan, Department of Pharmacology, University of North Carolina, School of Medicine, Chapel Hill, N.C. 27514.

Levo-alpha-acetyl methadol (LAAM) produced increases in locomotor activity in rats when the drug was given intraperitoneally (i.p.) at doses of 1 mg/kg and 3 mg/kg. An i.p. injection of 10 mg/kg LAAM decreased motor activity over the ten-hour period. The largest increases and decreases in locomotor activity after LAAM occurred approximately 7 to 8 hours after administration. In addition, rats were trained to lever press for food pellets under a fixed-interval 90 sec., fixed-ratio 10 multiple schedule. In contrast to the increased locomotor activity produced by LAAM, it only decreased rates of responding under the multiple schedule. Marked decreases in rates of responding under both components of the schedule occurred when LAAM was administered i.p. either 3 or 6 hours prior to the session at doses of 3 mg/kg and 10 mg/kg. The greatest rate-decreasing effect of LAAM occurred when the session was initiated 6 hours after administration of the drug. Chronic administration (i.p. and oral) of LAAM for 21 days produced physical dependence in rats as demonstrated by weight loss during naloxone-induced withdrawal. Oral administration of LAAM appeared more toxic in that a 33% mortality rate was observed during the chronic oral administration of 10 mg/kg as opposed to no deaths when the drug was given i.p. (Supported by NIDA DA-00570 and NIGMS 5-T32 GM-07040.)

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RELATIVE BEHAVIORAL POTENCIES OF d-N-ALKYLATED AMPHETAMINES. W.L. Woolverton* and C.R. Schuster. The University of Chicago, Chicago, Illinois 60637

d-N-Alkylated amphetamines were synthesized in a series up to and including d-N-butylamphetamine (NBA) and potencies were compared in 1) rats allowed to drink milk for 15 min/day and 2) rhesus monkeys allowed to respond for intravenous infusions of the drug. In the milk drinking procedure, all drugs produced dose-related decreases in intake. Drugs fell into 2 groups in terms of potency. d-Amphetamine (A), d-N-methylamphetamine (MMA), and d-N-ethylamphetamine (NEA) were approximately equipotent and four times as potent as d-N-propylamphetamine (NPA) and NBA. In the self-administration procedure, A, MMA and NEA were self-administered above saline levels by all animals. Response rates were similar for these 3 drugs across a broad range of doses. NPA was self-administered above saline levels by 3/4 animals at least at one dose. Peak response rates, however, were only 1/2 of those maintained by the smaller compounds and the potency was about 1/4. NBA maintained self-administration responding above saline control levels in only one of four animals. It may be concluded that potency of alkyl substituted amphetamines in disrupting milk intake in rats or maintaining drug self-administration responding in monkeys is inversely related to the substituent size. (Supported by USPHS NIDA Grants DA-00047, -00250, -00024 and USPHS 1-T32 MH-14274)