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METHYLPHENIDATE(M) EFFECTS ON WHIRLER MICE(W). A.M. Sackler*, A.S. Weltman, L. Johnson*, P. Tsai* and P. Steinglass,* Labs. Therapeutic Res., Goldwater Mem. Hosp., N.Y., N.Y. 10044

Methylphenidate, a CNS stimulant has been used therapeutically to treat hyperkinesis in children. Possible parallelisms between MBD & the waltzing syndrome of mutant mice suggested use of the whirlers as animal models. This study reports effects of (M) on circling activity of male (W) mice (B.W. 21gm). On the basis of activity scored in an open-field for 20 min., test & control (W) were divided into equal groups. During the 1st wk, test mice received orally single doses of 2.5mg/kg of (M). Afterwards the dose was increased to twice/day given on week days. Controls received tap water. After ½, 4½, 12, 17 & 21 wks, circling levels scored 1 hr after (M) showed significant decreases in the rotations of the test group except at 4½ wks. To test permanence or reversibility of (M) effects treatment was stopped after 23 wks. Although circling remained significantly lower at the 2nd wk, differences between the former test & control groups gradually diminished at wks 5, 8 & 13 until no apparent diff. was noted between the 2 groups. A single, oral dose given 18 wks after cessation of (M) induced a 37.8% increase (P=0.10) in activity, indicating that an apparent stimulatory effect of a single dose still existed. The data demonstrated that (M) at 5 mg/kg/day decreased hyperactivity of whirler mice & the effects were reversible. The similarities between effects on the whirler mice & hyperactive children suggest the possible use of the waltzing mice as animal models for MBD studies.

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STRAIN SPECIFIC ALTERATION OF CHOLINERGIC FUNCTION IN DISCRETE BRAIN REGIONS OF RATS IN RESPONSE TO SHOCK STRESS. D.E. Schmidt, D.O. Cooper* and R.J. Barrett. Tennessee Neuropsychiatric Institute, Nashville, TN, 37217.

It has been demonstrated that a random bred strain of Sprague-Dawley rats from Zivic Miller Labs (ZM) show behavioral suppression in response to shock stress, while an inbred Fisher strain (F-344) becomes behaviorally aroused (Barrett et al., Behav. Biol. 11, 189, 1975). Furthermore, the suppression in ZM rats is blocked by microinjection of scopolamine into dorsal hippocampus (Barrett et al., Psychopharmacologia 25, 321, 1972). Measurement of cholinergic function has shown that in ZM rats shock stress elicits a 25.3% increase ($p < .05$) in high affinity choline uptake (HACU) and a 43% increase ($p < .05$) in ACh turnover in dorsal hippocampus. However, no significant change in HACU or ACh turnover was observed in ventral hippocampus or striatum. In contrast, measurement of ACh turnover in dorsal hippocampus of F-344 rats showed no change, while there was a small decrease (13.3%) in HACU. These data support the hypothesis that the strain specific suppression seen in ZM rats in response to shock is mediated via activation of a suppressive hippocampal cholinergic pathway, and that this system does not respond to shock stress in a similar fashion in F-344 rats. (This work was supported by USPHS grant MH-29189 and the Tenn. Dept. of Mental Health and Mental Retardation).

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EFFECTS OF ANTICHOLINERGICS ON PRIMATE EQUILIBRIUM. C. T. Bennett *, D. N. Farrer*, D. J. Barnes*, J. A. Bachman* and N. E. Lof* (SPON: F. R. Sidell). USAF School of Aerospace Medicine, Brooks AFB TX 78235.

Eight rhesus monkeys were trained to maintain a horizontal position of a "flight simulator" by means of a control stick. The platform was driven off horizontal by a random input signal. The principal dependent variable was root mean square (RMS) error about the average platform position. This measure reflected the subject's ability to "track" input signals, thereby maintaining a relatively stable platform position. In a counter-balanced design, four animals each received either benactyzine (0.054, 0.17, 0.54 or 1.7 mg/kg) or atropine (0.014, 0.044, 0.14 or 0.44 mg/kg) IM. A buffered saline solution was used for control injections. Injection of either atropine or benactyzine resulted in a dose related increase in average RMS error indicating a disruption in the ability of the subjects to track the random movement of the simulator. These data indicate anticholinergics disrupt the ability of rhesus monkeys to follow motion-related input. Even though the sensory-motor skills required to satisfactorily operate the simulator are extremely complex, the effects reported here suggest that anticholinergics disrupt primate equilibrium.

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DISRUPTION OF LEARNING PERFORMANCE BY CHRONIC ETHOSUXIMIDE ADMINISTRATION IN THE BABOON. Merle G. Paule* and Eva King Killam. Department of Pharmacology, School of Medicine, University of California, Davis, CA 95616

Experiments were designed to assess the effects of chronic Ethosuximide (ESX) administration on acquisition of learning in the epileptic baboon, Papio papio. The behavioral task involved learning new 2, 3, 4 and 5 lever sequences each day to obtain banana pellet rewards. Studies using three adolescents and one young adult were carried out before, during and after an eight week period of ESX administration at doses ranging from 15-60 mg/kg/day I.M. A dose related decrease in learning performance was seen especially in the acquisition of the longer chains of lever pressing. Performance deficits did not appear to be related to motor difficulties nor to loss of motivation for their banana pellet rewards, but were manifested by decreased efficiencies, increased times to criteria performance, and often, refusal to attempt the task. Some tolerance to ESX was noted but results were inconsistent. Disruption of learning performance was evident for up to 4 months after cessation of ESX administration. The young animals used in this study showed minimal sensitivity to the seizurogenic properties of intermittent light stimulation and were not changed in seizure susceptibility during the course of daily drug administration. In two animals, however, seizures intensified for 1-2 weeks after withdrawal of chronic ESX administration. (Supported by Epilepsy Foundation of America)

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HISTAMINE AS A PUNISHER: EFFECTS OF H_1 and H_2 RECEPTOR ANTAGONISTS ON BEHAVIOR AND CARDIOVASCULAR RESPONSES. Steven R. Goldberg. NERPRC, Harvard Medical School, One Pine Hill Drive, Southborough, MA 01772

Histamine can function as a punisher to suppress food-maintained responding by squirrel monkeys (S.R. Goldberg, Fed. Proc. 37, 828, 1978). In the present study, three squirrel monkeys pressed a key under a two-component, 30-response fixed-ratio schedule of food presentation. In the nonpunishment component, only food was presented. In the punishment component, the 11th and 22nd response in each fixed ratio also produced a 200 msec i.v. injection of 30 to 100 µg/kg histamine, which resulted in about an 80% suppression of responding. Another three squirrel monkeys, with arterial catheters for continuous monitoring of blood pressure and heart rate, received automatic i.v. injections of 30 and 100 µg/kg of histamine; mean arterial blood pressure decreased by 5-20 mm Hg and heart rate increased by 60-120 bpm. Presession treatment with 1 to 3 mg/kg of the H_1 receptor antagonist, diphenhydramine, reversed the punishment effects of histamine but only enhanced its cardiovascular effects. In contrast, 10 to 30 mg/kg of the H_2 receptor antagonist, cimetidine, failed to reverse histamine's punishment effects but markedly attenuated its cardiovascular effects. Thus, histamine's suppression of responding appears to be an H_1 effect and does not appear to be related to its effects on blood pressure and heart rate. (Supported by USPHS Grants DA 01505, MH 07658, DA 00499 and RR 00168).

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EVIDENCE FOR SEROTONIN MEDIATION OF LSD-INDUCED ABNORMAL BEHAVIOR IN MONKEYS. R.F. Schlemmer, Jr.*, W.J. Heinze*, & J.M. Davis* (SPON: R.W. Morris). Ill. State Psychiatric Institute, Chicago, IL 60612

This study examined the effect of the serotonin (5-HT) antagonist cinanserin (CIN) on LSD-induced behavior in monkeys. The subjects were 4 adult Stumptail macaque females housed as 2 pairs. Following a baseline observation period, each monkey received 2 treatment regimens: 1) d-LSD 10 ug/kg alone, once daily for 5 consecutive days & 2) CIN HCl 5 mg/kg + LSD for 2 days, then LSD alone for the next 3 days. CIN was given 2.5 hrs & LSD 15 mins prior to observation. Both drugs were given i.m. Only 1 monkey/pair received drug during any given wk & at least 4 wks separated the respective drug regimens. Behavioral observation by a "blind" observer occurred for 1 hr/day/pair, 5 days/wk. LSD alone induced 2 abnormal behaviors, body shakes (wet shakes) & limb jerks. Partial tolerance appeared with both behaviors within 3 days. CIN prevented the appearance of LSD-induced body shakes & limb jerks but failed to antagonize LSD-induced changes in social behavior. CIN delayed the development of tolerance to body shakes in all monkeys & to limb jerks in 2 of 4 monkeys. These results demonstrate that 1) LSD-induced abnormal behavior in monkeys appears to be mediated thru 5-HT systems & 2) LSD interaction with 5-HT systems appears to be a necessary component for the development of tolerance to body shakes & perhaps limb jerks.