ABSTRACTS

THURSDAY P.M.

Executive Committee Meeting

FRIDAY A.M.

SYMPOSIUM

Excitatory Amino Acids: Agonists, Antagonists, and Function

Chair: *James H. Woods*, University of Michigan, School of Medicine, Ann Arbor, MI

INTRODUCTION. James H. Woods. University of Michigan, School of Medicine, Ann Arbor, MI.

Excitatory amino acids are major neurotransmitters throughout the brain and spinal cord. Neuropharmacological advances have led to a division of their actions upon neurons through a characterization of different receptors. These receptors can now be assessed through the use of agonists and antagonists and inferences drawn about function through the selective actions that agonists and antagonists evoke. This symposium will demonstrate the various ways that behavioral pharmacology can play an important role in describing and analyzing these functions.

DRUG DISCRIMINATION OF COMPETITIVE (CGS-19755) AND NONCOMPETITIVE (PHENCYCLIDINE) N-METHYL-D-ASPARTIC ACID ANTAGONISTS IN PIGEONS. J. David Leander. Lilly Research Laboratories, Eli Lilly and Co., Indianapolis, IN.

Pigeons were trained to discriminate 0.64 mg/kg IM of phencyclidine vs. vehicle or 1.25 mg/kg IM of CGS-19755 vs. vehicle under fixed-ratio 40-response schedules of reinforcement. The pretreatment times before the sessions began were 15 min for phencyclidine and 90 min for CGS-19755. The doses of the two training drugs have previously been shown to antagonize the behavioral suppressant effects of 10 mg/kg of N-methyl-D-aspartic acid in pigeons responding under a multiple FR-FI schedule of reinforcement. When competitive NMDA antagonists (AP-5, AP-7, etc.) were tested in birds trained to discriminate phencyclidine, there was no generalization to the phencyclidine cue, although noncompetitive antagonists (phencyclidine, MK-801, etoxadrol, dexoxadrol, etc.) were generalized. In birds trained to discriminate CGS-19755, both competitive and noncompetitive antagonists were generalized to the CGS-19755 cue in a dose-related fashion. These results suggest that noncompetitive antagonists (i.e., phencyclidine) have subjective, discriminative effects that are not shared by competitive NMDA antagonists. However, the subjective, discriminative effects of competitive antagonists can be detected within the complex of discriminative effects produced by noncompetitive antagonists.

EFFECTS OF EXCITATORY AMINO ACIDS ON ACQUISITION, RETENTION AND PERFORMANCE. J. M. Moerschbaecher, C. W. Berthold, P. Stevens, L. LaMotte and M. Pierson. Louisiana State University Medical Center, New Orleans, LA; and J. H. Woods. University of Michigan School of Medicine, Ann Arbor, MI.

The effects of various excitatory amino acid agonists and antagonists were investigated in rats and monkeys responding under various discrimination procedures. In rats, NMDA produced a dose-dependent decrease in response rate, but had no effect on accuracy of the performance. In general, the noncompetitive antagonist phencyclidine (PCP) failed to antagonize the effects of NMDA. Similarly, the glycine analog *d*-cycloserine failed to antagonize the effects of PCP. Across a wide range of doses NMDA failed to enhance acquisition in either rats or monkeys responding under repeated acquisition procedures. Rather, at high doses, NMDA produced decreases in overall response rates which were antagonized by the competitive antagonist CGS 19755 in a dose-dependent manner. In monkeys, NMDA failed to enhance retention of a discrimination following either a 1-hr or 24-hr delay. At higher doses, however, NMDA decreased response rate and produced amnestic effects as evidenced by a decrease in percent savings. The amnestic effects of NMDA were antagonized by CGS 19755 at doses lower than those required to antagonize the rate-decreasing effects.

N-METHYL-D-ASPARTATE AND KAINATE ARE POWERFUL DIPSOGENS IN PIGEONS. S. P. Baron and J. H. Woods. University of Michigan, Ann Arbor, MI.

During a previous study in which pigeons were trained to discriminate 5.6 mg/kg N-methyl-D-aspartate (NMDA) IM from saline it was observed that subjects that had received NMDA drank water more often than those that had received saline injections. A dose response to NMDA was then determined in six pigeons. Drinking over one hour reached a maximum following 10.0 mg/kg NMDA followed by a decrease after 18.0 mg/kg. Drinking after saline was considerably less than that produced by NMDA. Kainate was ten times more potent than NMDA in producing drinking. Water consumption reached a maximum at 1.0 mg/kg and was also followed by a slight decrease following 3.2 mg/kg kainate. Water consumption following NMDA or kainate administration is approximately equivalent to that produced by 48-hour water deprivation. The proposed competitive NMDA antagonist CGS 19755 (Lehmann *et al.*, J. Pharmacol. Exp. Ther. 245: 65–75; 1988), when given as a 10-minute pretreatment (1.0 and 3.2 mg/kg), modified the drinking-dose-response for both kainate and NMDA while producing no effect on deprivation-induced drinking. The changes in agonist-induced drinking by CGS 19755 were different for NMDA and kainate. CGS 19755 produced an apparent antagonism of NMDA-induced drinking, but a marked increase (approximately 2-fold) in high-dose kainate-induced drinking. (This research was supported by NIDA grant DA-05325.)