label for sigma receptors will be presented. Finally we will present methods that allow solubilization of active sigma receptors and we will show that the novel probes described above are useful tools for characterizing the solubilized binding sites.

PHENCYCLIDINE DISCRIMINATION AND N-METHYL-D-ASPARTATE RECEPTOR STIMULATION AND ANTAGONISM IN RATS. Willetts, J. and R. L. Balster. Department of Pharmacology and Toxicology, Medical College of Virginia, Virginia Commonwealth University, Richmond, VA 23298.

Much evidence exists to suggest that phencyclidine (PCP) acts to inhibit excitatory amino acid (EAA) neurotransmission mediated by N-methyl-D-aspartate (NMDA)-sensitive EAA receptors: PCP and PCP-like drugs selectively antagonize NMDA-induced excitation of central neurons, PCP prevents NMDA-induced transmitter release and binding studies show that while PCP and NMDA receptor are distinct, they may be intimately associated. Evidence also suggests there is some overlap in the behavioral effects of PCP and NMDA-receptor blocking drugs (Koek *et al., Behav Brain Res* **19:** 257–259, 1986; Koek *et al., Life Sci* **39:** 973–978, 1986). We, therefore, decided to investigate whether the NMDA antagonist 2-amino-7-phosphonoheptanoate (APH) would produce PCP-like discriminative stimulus effects and whether NMDA could block the discriminative stimulus properties of PCP in rats. Male Sprague-Dawley rats were trained to discriminate between PCP (1.25 mg/kg IP) and saline on a two lever fixed-ratio 32 schedule of food reinforcement. During the last 10-minute segment of a 30-minute test session, intracerebroventricular (ICV, 0.375–30.0 μg), but not systemic (10–30 mg/kg IP), administration of APH produced greater than 80% PCP-lever responding in eight out of ten rats, though the dosage at which generalization occurred varied between rats. NMDA (0.05–0.30 μg ICV) was administered 10 minutes after PCP and immediately before test sessions. While the higher doses of NMDA produced modest reductions in PCP-lever responding during the first 10-minute segment of the 30-minute sessions, these were usually accompanied by large reductions in response rates. Brief convulsions also followed administration of the highest dose of NMDA. Thus, APH shares some discriminative stimulus properties with PCP in rats. However, since PCP-lever selection was not as consistent as it was following PCP administration, there may not be a complete overlap in the discriminative stimulus properties of PCP and APH. We also conclude that ICV administration of NMDA does not antagonize the discriminative stimulus properties of PCP. These results are in agreement with those of Leander *et al. (Excitatory Amino Acid Neurotransmission.* New York: Alan R. Liss Inc., 1987, pp. 197–204) who observed that NMDA does not antagonize behavioral suppressant effects of PCP in pigeons. (Research supported by NIDA Grant DA-01442.)

BEHAVIORAL SIMILARITY OF DI-ORTHO-TOLYL-GUANIDINE (DTG), A SELECTIVE LIGAND FOR A HALOPERIDOL-SENSITIVE SIGMA BINDING SITE, TO PHENCYCLIDINE (PCP) IN RATS, PIGEONS, AND RHESUS MONKEYS. Woods, J. H., W. Koek and E. Weber. University of Michigan, Ann Arbor, MI 48109; and Oregon Health Science University, Portland, OR 97201.

DTG is a highly potent ligand for a binding site in rat brain that also recognizes certain PCP-like substances, haloperidol, and 3-(3-hydroxy)-phenyl-N-propylpiperidine (Weber *et al., Proc Natl Acad Sci USA,* in press). An advantage of this ligand is its high affinity and selectivity for this site, when compared with the affinity and the selectivity of the other aforementioned compounds. DTG was compared to PCP in a number of behavioral preparations. In pigeons, intramuscular administration of DTG up to lethal doses failed to induce a PCP-like catalepsy. PCP-like discriminative stimulus effects in pigeons and in rhesus monkeys were neither induced nor potentiated or antagonized by behaviorally active doses of DTG. Up to lethal systemic doses, DTG failed to produce directly observable PCP-like behavioral effects (e.g., locomotion, sniffing, swaying and falling) in rats. In addition, while producing ataxia, DTG failed to produce PCP-type anesthesia, characterized by absence of eye closure and muscle relaxation, in rhesus monkeys. Thus, our preliminary data suggest that DTG does not share behavioral effects with PCP. DTG (10–10 mg/rat) when given intraventricularly in rats produces a dose-dependent forelimb extension and backward walking; perhaps, resembling some psychotomimetic opioids. The further characterization of behavioral effects unique to DTG is important to assess the relevance of its binding site. (Supported in part by USPHS Grant DA-00154.)

REGIONAL LOCALIZATION OF NMDA AND TCP BINDING IN MAMMALIAN BRAIN. Young, A. B., W. F. Maragos and J. B. Penney. Department of Neurology, University of Michigan, Ann Arbor, MI 48104.

Electrophysiological, behavioral and pharmacological studies suggest that dissociative anesthetics block the excitatory actions of N-methyl-D-aspartate (NMDA) in the CNS through an allosteric interaction at the channel linked to the NMDA receptor. Such an interaction would predict that the two receptors have identical regional distributions in brain and should be present in some fixed ratio. We have measured TCP and NMDA receptors in serial sections of rat and human brain using [3H]N-(1-[2-thienyl]cyclohexyl) 3,4-piperidine (TCP) and [3H]glutamate as previously described (Maragos *et al., Eur J Pharmacol* **123:** 173–174, 1986). There was a marked correlation between the regional localization of NMDA receptors and TCP receptors in rat and human brain. In 52 regions of rat brain, NMDA receptor density correlated with TCP receptor density ($r=0.95$; $p<0.001$). Binding was highest in stratum radiatum of hippocampus.