clazocine and ketocyclazocine. The results indicate that the kappa opioid agonists, as a group, generated less drug-appropriate responding in rats trained to discriminate a high dose of morphine (10 mg/kg) than in rats trained to discriminate a low dose of morphine (3.0 mg/kg).

ENHANCED SENSITIVITY TO MIXED-ACTION OPIOIDS IN MORPHINE-TOLERANT SQUIRREL MONKEYS. Alison H. Oliveto, Linda A. Dykstra and Mitchell J. Picker. University of North Carolina at Chapel Hill, Chapel Hill, NC.

Various opioid compounds were examined in squirrel monkeys responding under a fixed-ratio 30 schedule of food presentation. Dose-effect curves were obtained prior to and during a chronic regimen in which monkeys received 6 mg/kg/day of morphine. During chronic morphine, the dose-effect curves for the mu agonists morphine and *l*-methadone shifted 1 and ½ log units to the right, respectively; whereas those for the kappa agonist U50,488 did not change. The dose-effect curves for the opioid antagonist naloxone and the mixed-action opioids nalorphine, nalbuphine, and butorphanol shifted approximately 3, 2, 2, and ½ log units to the left, respectively; whereas those for the mixed-action opioid pentazocine were unaltered.

DISCRIMINATIVE STIMULUS REINFORCING AND PHYSICAL DEPENDENCE PROPERTIES OF ACETORPHAN. Janet S. Knisely. Medical College of Virginia, Richmond, VA; Patrick M. Beardsley. G. D. Searle and Company, Skokie, IL; and Mario D. Aceto, Robert L. Balster and Louis S. Harris. Medical College of Virginia, Richmond, VA.

Drug discrimination, self-administration and physical dependence procedures were employed to assess the abuse potential of acetorphan, a parenterally-acting enkephalinase inhibitor. Rats trained to discriminate 2 mg/kg morphine from saline did not generalize to acetorphan at any dose tested (5–50 mg/kg). Also, acetorphan did not reliably serve as a reinforcer in rhesus monkeys trained to lever press for intravenous delivery of cocaine. In physical dependence studies, acetorphan also failed to produce opioid-like effects. No overt withdrawal signs were observed in rats following chronic administration of acetorphan and acetorphan did not prevent withdrawal in morphine-dependent rats and rhesus monkeys. Collectively, these results indicate that acetorphan does not produce opioid-like effects using these procedures and has minimal abuse potential.

TOLERANCE TO AN AMPHETAMINE DISCRIMINATIVE STIMULUS. Elizabeth S. Steigerwald and Alice M. Young. Wayne State University, Detroit, MI.

Tolerance to an amphetamine discriminative stimulus was examined as a function of the dose and duration of repeated amphetamine treatment. Rats (N = 12) were trained to discriminate saline and 0.8 mg/kg *d*-amphetamine under FR schedules of food delivery. Amphetamine stimulus control was examined before, during, and after repeated treatment with saline or amphetamine. During each treatment phase, training sessions were suspended and each rat received daily injections of either saline or a total dose of 6.4 or 12.8 mg/kg amphetamine for 3 or 18 days. Treatment with saline produced no change in the dose of amphetamine required to evoke generalization or alter response rates. Treatment with 6.4 mg/kg amphetamine for 3, 7 or 14 days increased the dose of amphetamine required for stimulus control by 2- to 3-fold and that required to suppress response rates by more than 2-fold. In contrast, treatment with 12.8 mg/kg amphetamine for 3 or 7 days produced lesser tolerance, and in 4 of 12 animals treatment for 14 days produced evidence of sensitization. Thus, repeated treatment with amphetamine may produce biphasic changes in amphetamine stimulus control, with lower treatment doses or shorter durations yielding tolerance, and higher doses producing sensitization. (Supported by DA-03796.)

DISCRIMINATIVE STIMULUS PROPERTIES OF ANTIHISTAMINES MAY INVOLVE MEDIATION BY SEROTONIN. Tammy A. Winters and Barbara L. Slifer. University of New Orleans, New Orleans, LA.

Although histamine H1-receptor antagonists are among the most widely taken drugs, their behavioral effects in animals have not been studied extensively. The most common side effects of antihistamines are drowsiness and sedation, however, more recently their stimulant-like properties have been reported. Besides antagonism of histamine receptors, antihistamines are known to exert their effects on other neurotransmitter systems as well, including serotonin. A drug discrimination study was conducted to further examine serotonergic involvement in the discriminative stimulus properties of antihistamines using cyproheptadine (CYP), an effective H1-receptor blocker that has prominent serotonergic blocking activity. Rats were trained to discriminate IP injections of CYP (3 mg/kg) from saline under a two-lever fixed-ratio 30 schedule of food presentation. Doses of select antihistamines were tested. Neither tripelennamine (0.3–10 mg/kg) nor chlorpheniramine (1.0–30 mg/kg) substituted for CYP at any dose tested. A dose-related substitution was achieved with diphenhydramine (1–20 mg/kg) with >90% drug lever responding at doses of 17.5 and 20 mg/kg. Promethazine (1–10 mg/kg) also substituted in a dose-related manner for CYP with >95% drug lever responding at doses of 5.6 and 10 mg/kg. Thus, the discriminative stimulus properties of some antihistamines appear to involve a serotonergic component. (Supported by DA-03838 and DA-04851.)

EFFECTS OF H_1 ANTAGONISTS ON PUNISHED RESPONDING IN THE RAT. Paul A. Gore, Jr. and Barbara L. Slifer. University of New Orleans, New Orleans, LA.

In addition to the well known therapeutic effects of the antihistamines in treating allergic reactions and cold symptoms, these drugs may occasionally be prescribed for anxiety. The present study investigated the possible anxiolytic activity of antihistamines in rats trained to respond under a multiple FI3 minute FR10 (food + shock) punishment schedule. The H_1 antagonists tested [tripelennamine (0.3–10 mg/kg), diphenhydramine (1–20 mg/kg), chlorpheniramine (0.3–17.5 mg/kg), and hydroxyzine (1–20 mg/kg)] resulted in nonselective increases followed by decreases in overall rates of responding, whereas diazepam (0.3–10 mg/kg) selectively increased rates of responding during punished components. Additionally, the effects of the antihistamines on local rates of nonpunished responding differed from those of diazepam. While the latter produced significant rate-dependent effects, the antihistamines' effects on local rates of responding were not consistently related to control rates of responding. These data replicate previous findings and suggest that although the antihistamines may occasionally be prescribed as anxiolytics, their effects on responding suppressed by punishment in the rat differ from those of the CNS depressants. (Supported by NIDA Grant DA-03838.)