distribution research. APA also acted as a central coordinator of the grassroots lobbying effort that was undertaken by the 65 NIDA-funded research sites across the country. Working with the White House, APA also proved instrumental in getting HHS to issue a statement of support for the program. This ultimately proved essential in turning the Senate around. The parliamentary effort involved a significant amount of fancy foot work. Although they had originally opposed the bleach distribution program at the outset by large margins, by the time the bill got back to the Senate for the last time, enough Senators had heard the educational message from the scientific community, and the supportive letter from HHS had arrived. These factors provided the needed political cover, and the funding of the bleach distribution programs was retained. Continued vigilance is critical in this area of AIDS policy. The IVDU community, unlike some of the other AIDS-affected populations, does not have an organized presence in Washington. Given this and their stigmatized and vulnerable position leaves them open to regular political attack. Without the help of the scientific community in this example, a major tool of AIDS prevention would have been lost.

SYMPOSIUM

The Current Status of Human Drug Discrimination Research
Chair: *Alison H. Oliveto*, University of Vermont, Burlington, VT
Discussant: *Donald Overton*, Temple University, Philadelphia, PA

DISCRIMINATIVE STIMULUS EFFECTS OF DRUGS IN HUMANS: STIMULANTS AND SEDATIVES. Stephen J. Heishman. Addiction Research Center, National Institute on Drug Abuse, Baltimore, MD; Richard J. Lamb. University of Medicine and Dentistry of New Jersey, Camden, NJ; Jack E. Henningfield. Addiction Research Center, National Institue on Drug Abuse, Baltimore, MD.

Much research has evaluated the discriminative stimulus effects of psychoactive drugs in animals. Recently, analogous drug discrimination paradigms have been developed for human testing. In two similar studies, subjects were trained to discriminate *d*-amphetamine 30 mg PO (Drug A) from placebo using a color tracking procedure with second-order scheduling. Daily experimental sessions tested one oral drug dose or placebo. All subjects readily acquired the discrimination and reported increased subjective ratings of drug liking, drug strength, and good drug effects after *d*-amphetamine compared to placebo. In the first study, subjects were then tested with *d*-amphetamine (3.75–30 mg), diazepam (5–40 mg), and methylphenidate (7.5–60 mg) to determine if the discriminative stimulus effects of these drugs would substitute for Drug A. In the second study, generalization testing involved the same doses of *d*-amphetamine and hydromorphone (2–12 mg). In both studies, *d*-amphetamine produced dose-related *d*-amphetamine-appropriate responding. Methylphenidate also substituted for the Drug A stimulus in a dose-dependent manner. In contrast, neither diazepam nor hydromorphone engendered Drug A-appropriate responding. These generalization data indicate that the learned drug discrimination was pharmacologically specific. Subjective drug effects collected concurrently with generalization testing revealed interesting data on the relationship between subjective and discriminative stimulus effects. In the first study, subjective effects produced by the drugs generally covaried with the discriminative stimulus effects. For example, *d*-amphetamine and methylphenidate, which substituted for Drug A, produced dose-related increases in ratings of drug liking and scores on the MBG, BG, and A scales of the Addiction Research Center Inventory, whereas diazepam did not. However, in the second study, *d*-amphetamine and hydromorphone dose-dependently increased reports of drug liking and scores on the MBG and A scales, although hydromorphone failed to substitute for the Drug A stimulus. These data indicate that drug discrimination procedures are useful for studying the discriminative stimulus effects of drugs in humans and that the subjective and discriminative stimulus effects of drugs do not necessarily parallel one another.

CAFFEINE AS A DISCRIMINATIVE STIMULUS IN HUMANS. Alison H. Oliveto, Warren K. Bickel, John R. Hughes, Stephen T. Higgins and Pam Shea. University of Vermont, Burlington, VT.

Although caffeine is the most widely used psychoactive compound in the world, its behavioral effects have not been investigated extensively. The present study examined the ability of caffeine to serve as a discriminative stimulus in humans. Briefly, 8 healthy male and female subjects (aged 18–45 years) having some prior experience with caffeine were employed. During the experiment, subjects were required to abstain from alcohol and caffeine for 12 hr and solid food for 4 hr prior to each session. The following procedure was used to determine whether subjects could learn to discriminate between 320 mg/70 kg of caffeine (e.g., drug A) and placebo (drug B): During the first 4 daily sessions (Training Phase), drug A and drug B were administered orally in capsule form 90 min prior to the session on alternate days and subjects were informed of the drug label at the time of drug administration. Over the next 20 sessions (Test of Acquisition Phase), drug A and drug B were administered in a randomized-block fashion, such that each drug was administered twice every four days, and subjects were informed of the drug label after the session terminated. Discrimination was assessed by measuring: 1) percentage of points accumulated using the appropriate drug label manipulandum under a concurrent fixed-interval 1-sec schedule; 2) identification of the appropriate drug label under a discrete choice procedure; and 3) number of points out of 100 placed on the appropriate drug label. Thus far, 2 of 3 subjects learned the discrimination within 20 sessions. A caffeine stimulus generalization curve was obtained, such that caffeine at doses of 56 and 100 mg/70 kg generally produced placebo-appropriate responding, whereas caffeine at doses of 180, 240 and 320 mg/70 kg generally produced caffeine-appropriate responding. Triazolam (0.10–0.56 mg/70 kg) produced predominantly placebo-appropriate responding. These preliminary results indicate that the caffeine stimulus is discriminable and has pharmacological specificity.

DISCRIMINATIVE STIMULUS PROPERTIES OF DIAZEPAM IN HUMANS. Chris E. Johanson. Uniformed Services University of the Health Sciences, Bethesda, MD.

Nineteen normal human volunteers participated in an experiment designed to investigate the discriminative stimulus properties of 10 mg diazepam. On each experimental session, participants filled out a series of mood questionnaires, ingested a capsule, and then were free to leave, i.e., they returned to their normal daily activities. At 1, 3 and 6 hr after leaving, subjects filled out additional sets of the mood questionnaires. During phase 1, the participants were trained to discriminate between 10 mg diazepam and placebo by identifying the capsule to the participant prior to ingestion using letter codes (A or B). Each subject received two sessions with diazepam and two with placebo under single-blind conditions. During phase 2, subjects were not told which capsule they received prior to ingestion and were asked to telephone the experimenter 6 hr after ingestion to report their discrimination

using the letter codes. If they were correct, they were so informed and also received bonus money. This phase consisted of 7 sessions with drug and placebo administered randomly approximately an equal number of times. If a subject correctly identified the capsules on 5 of these 7 occasions, they participated in a third phase consisting of 12 sessions. On 6 of these sessions, the procedure was identical to phase 2 with diazepam and placebo each administered on 3 occasions. Randomly intermixed with these training sessions were 6 test sessions. During these test sessions, subjects received 2 mg DZ, 5 mg DZ, 1 mg lorazepam, 2 mg lorazepam, 50 mg pentobarbital, or 10 mg *d*-amphetamine. Order of presentation was random across subjects. Subjects were not aware that a test session was scheduled until they telephoned the experimenter and they received bonus money regardless of their response (i.e., there was not a correct answer by definition). Sixteen of the 19 subjects learned the discrimination with overall accuracy of 90% during phase 2 which was maintained at a level of 85% during phase 3 training sessions. When 2 and 5 mg diazepam were administered drug-appropriate responding was 7% and 64%, respectively. Drug-appropriate responding increased from 29% at 1 mg lorazepam to 86% at 2 mg. Sixty-four percent of the subjects called 50 mg pentobarbital drug, whereas only 21% discriminated amphetamine as diazepam. The subjective effects of diazepam were typical of benzodiazepines. These results indicate that it is possible to train humans to discriminate diazepam and this discrimination is sensitive to differences in dose and appears specific to sedative-like drugs.

OPIOID DRUG DISCRIMINATIONS IN HUMANS. George E. Bigelow and Kenzie L. Preston. The Johns Hopkins University School of Medicine, Baltimore, MD.

In the animal laboratory use of behavioral drug discrimination procedures has proven quite useful in permitting characterization and categorization of the stimulus effects of drugs. The stimulus effects produced by drugs are thought to be related to subjective drug effects, which are, in turn, thought to be related to the likelihood of their being abused. The drug discrimination method has been especially useful in the study of opioid drugs; opioids with different receptor activites have been found to differ in their stimulus properties, and this has made it possible to use the drug discrimination procedure to infer differential receptor activity and differential abuse liability of different drugs. This presentation will provide an overview and summary of a number of different studies from our laboratory in which the drug discrimination procedure has been adapted and utilized with human volunteers to study the comparative clinical pharmacology of various opioid agonists, antagonists, and mixed agonist-antagonists, and to study features of the drug discrimination procedure itself. These studies have been conducted in a residential laboratory setting with experienced opioid-abuser volunteers; in some studies participants have been opioid-dependent methadone-maintained volunteers, while in other studies participants have been currently nondependent postaddict volunteers. With both populations opioid drug discriminations have been trained using either a three-choice procedure (Drug A vs. Drug B vs. Drug C) or a two-choice procedure (Drug A vs. Drug B), with one alternative being placebo. Subjects have then been tested under double blind conditions with a range of doses of the training drugs and a range of doses of various opioid mixed agonist-antagonists. Mixed agonist-antagonists were sometimes discriminated as agonist-like and sometimes as antagonist-like, sometimes as similar to one another and sometimes as dissimilar. The presentation will describe the profiles of effects observed, as well as the effects of subject characteristics, and the effects of training procedures. It is concluded that the drug discrimination methodology is adaptable to and readily learned by humans, and that the methodology is of substantial value in making subtle distinctions among compounds with overlapping profiles of activity.

SYMPOSIUM

The Analysis of Social Behavior: Drug Effects and Related Issues
Chair: *Thomas H. Kelley*, The John Hopkins University School of Medicine, Baltimore, MD
Discussant: *Larry D. Byrd*, Emory University, Atlanta, GA

AGGRESSION AND ANXIETY IN ANIMALS: BENZODIAZEPINES AND 5-HT RECEPTORS. Klaus A. Miczek and Alice Weerts. Tufts University, Medford, MA.

In preclinical experimental preparations, benzodiazepine-type anxiolytic drugs and 5-HT receptor antagonists may restore behavior that has been suppressed by punishment and attenuate distress calls in infants and adult submissive rodents and monkeys. Benzodiazepines as well as alcohol, but not anxiolytics acting on 5-HT receptors have proaggressive effects in male resident rats and dominant monkeys; at higher doses, all these drugs decrease aggressive behaviors. Beta-carboline derivatives and imidazobenzodiazepines antagonize the punishment- and distress-attenuating as well as proaggressive effects of alcohol and benzodiazepines. The selective and antiaggressive and distress-attenuating effects of 5-HT_{1a} agonists represent a most promising novel profile of effects.

ACUTE EFFECTS OF MARIJUANA SMOKING ON AGGRESSIVE, ESCAPE AND POINT-MAINTAINED OPERANT RESPONDING. Don R. Cherek, Ralph Spiga and Robert H. Bennett. University of Texas Health Science Center at Houston, Houston, TX.

Male subjects with histories of marijuana use were recruited for research. Marijuana cigarettes containing 0.00, 1.75, 2.57, 3.55 w/w delta-9-tetrahydrocannabinol were smoked using a paced puffing procedure. Signalled by stimulus lights, subjects took ten inhalations of two-second duration every thirty seconds, followed by a ten-second breath hold prior to exhaling. During each experimental day, subjects participated in six twenty-five-minutes sessions. The first session was conducted at 0830 prior to smoking, and the remaining sessions were conducted 0.0, .5, 2.0, 4.0 and 6.0 hr after smoking. Three distinct nonreversible response options levers A, B, C were provided. Responding on lever A was maintained by a fixed-ratio (FR) 100 schedule of point presentation (1 pt = 10 cents). Responding on levers B and C was engendered by subtracting points for the subject's counter. Point subtractions were attributed to a fictitious person ostensibly paired with the subject. Following a point subtraction, completion of a FR 10 on either lever B or C initiated a 125-sec interval during which point subtractions were not presented. Subjects were instructed that responding on lever B (FR 10) resulted in the subtraction of one point from their partner. Such responding was termed "aggressive" since it resulted in the presentation of an aversive stimulus to another person. Subjects were instructed that responding on lever C (FR 10) protected their counter for some period of time. Lever C responding was termed "escape" responding. Acute marijuana smoking resulted in slight decreases in point-maintained responding. Aggressive and escape responding were only clearly suppressed postintoxication (i.e., 2–4 hr after smoking). During intoxication (0–0.5 hr), some subjects increased