BEHAVIORAL ANALYSIS OF MARIJUANA EFFECTS ON FOOD INTAKE IN HUMANS. Richard W. Foltin and Marian W. Fischman. The Johns Hopkins University School of Medicine, Baltimore, MD.

Fifteen adult male research volunteers, in five groups of three subjects each, lived in a residential laboratory for up to 25 days. All contact with the experimenter was through a networked computer system, and subjects' behaviors, including food intake, were continuously recorded. During the first part of the day, subjects remained in their private rooms doing assigned work activities, and during the remainder of the day, they were allowed to socialize. In the first three experiments, a single cigarette containing active marijuana (1.84% Δ^9-THC, w/w) or placebo was smoked prior to the work period, and two or three cigarettes were smoked during the social access period. There was no effect of marijuana on food intake during the private period, but cigarettes smoked during the social access period increased total daily caloric intake by 20%. This increase was due to an augmentation of calories consumed as between-meal snack items rather than an increase in meal size per se. In the remaining two experiments, the type and variety of snack foods were increased, and the dose of marijuana was increased by having subjects smoke two cigarettes containing active marijuana (2.7% Δ^9-THC, w/w) or placebo during both the private work period and the social access period. Smoked active marijuana significantly increased total daily caloric intake by 40%. Once again, the increase in caloric intake was due to an increased consumption of snack foods rather than meals, but in this case increased food intake was evident during both private and social periods. The principal increase within the category of snack foods was in the intake of sweet solid items (e.g., candy bars) compared to sweet fluids (e.g., carbonated beverages), or savory solid items (e.g., potato chips). Increases in body weight during periods of active marijuana smoking were greater than predicted by caloric intake alone.

PRESIDENTIAL ADDRESS

Drug Reinforcement and Drug Abuse: From Laboratory to Clinic

George E. Bigelow, The Johns Hopkins University School of Medicine, Baltimore, MD

Chair: *Donald A. Overton,* Temple University, Philadelphia, PA

SYMPOSIUM

Opioid Agonists/Antagonists: Laboratory and Clinical Aspects

Chair and Discussant: *Linda A. Dykstra,* University of North Carolina at Chapel Hill, NC

INTRODUCTION. Linda A. Dykstra. University of North Carolina at Chapel Hill, Chapel Hill, NC.

In the last decade, a considerable amount of research has been devoted to developing opioid analgesics with a lower incidence of side effects such as respiratory depression, sedation and physical dependence. In this regard, the newly developed agonist/antagonists are of considerable interest due to their unique behavioral effects. For example, many of them produce analgesia, but have a reduced dependence potential when compared to morphine. In addition, investigations in man suggest that these compounds have potential in the treatment of chronic pain as well as in the treatment of opioid dependence. This symposium considered the behavioral pharmacology of some of these agents in nonhumans by presenting data about their effects in at least three different behavioral assays. These include (1) analgesic assays, (2) drug self-administration assays for examining reinforcing properties and (3) drug discrimination assays for examining a drug's stimulus properties. In addition to reviewing existing knowledge about the behavioral effects of opioid agonists/antagonists in animals, investigations about the behavioral effects of these agents in heroin-dependent individuals were discussed. Moreover, the use of opioids in the treatment of chronic pain was discussed with special emphasis on their potential for abuse in these situations.

REINFORCING AND DISCRIMINATIVE EFFECTS OF MU AGONISTS-ANTAGONISTS. Alice M. Young and Maureen A. Walton. Wayne State University, Detroit, MI; and Gail Winger. University of Michigan, Ann Arbor, MI.

The agonist-antagonist opioids are a heterogeneous group of compounds that display dissimilar constellations of agonist and antagonist effects. The behavioral pharmacology of agonist-antagonist opioids that exert mu agonist actions can be described in terms of the reinforcing and discriminative stimulus profiles of these compounds, with special emphasis on how these profiles may allow discrimination among compounds that differ in their efficacy as agonists. Studies of the reinforcing characteristics of selected mu agonists and agonist-antagonists have provided new evidence that maintenance of behavior under progressive-ratio procedures may require compounds with higher efficacy as agonists than does maintenance of behavior under fixed-ratio procedures. Specifically, full agonists such as codeine and alfentanyl can maintain performance under both procedures, whereas certain agonist-antagonists such as nalbuphine and buprenorphine maintain behavior under the fixed-ratio procedure but do not generate breaking points higher than those generated by saline under the progressive-ratio procedure. In addition, the discriminative profiles of selected agonist-antagonists provide evidence that generalization of stimulus control to different training doses of morphine can be indicative of agonist efficacy. Specifically, generalization to a higher morphine training dose may require greater efficacy than does generalization to a lower training dose. For example, a full agonist will generalize to both a lower and a higher morphine training dose, whereas certain agonist-antagonists will generalize only to the lower training dose, acting instead to antagonize control by the higher dose. Taken together, information about the discriminative and reinforcing characteristics of opiate agonist-antagonists may provide new leads in the search for analgesics with lowered abuse liability. (Supported by DA-03796 and DA-00254.)

ANALGESIC EFFECTS OF OPIOID AGONISTS AND PARTIAL AGONISTS IN MONKEYS. Charles P. France. University of Michigan School of Medicine, Ann Arbor, MI.

A tail withdrawal procedure similar to that described by Dykstra and Woods (1986) was used to study the analgesic effects of opioids in rhesus monkeys. The latency for monkeys to remove tails from 40°, 50° and 55°C water was compared among opioids that vary widely in receptor selectivity and efficacy. Some opioid agonists (e.g., alfentanyl, bre-