A1

NICOTINE: BEHAVIORAL AND PHYSIOLOGICAL EFFECTS AND SELF-ADMINISTRATION IN HUMANS. Jack E. Henningfield, Katsumasa Miyasato, Rolley E. Johnson, and Donald R. Jasinski, NIDA Addiction Research Center, P.O. Box 5200, Baltimore, MD 21224

Results from 3 experiments are reported in which nicotine was investigated using both the clinical pharmacologic methods of the Addiction Research Center as well as the more recently formulated methods of behavioral pharmacology. In Experiment 1, intravenous injections of nicotine tartrate were administered to 8 cigarette smokers (8 hr cigarette deprived) according to a latin square design whereby each subject received each of 4 doses (0.0, 0.75, 1.5, 3.0 mg) at 1 hr intervals on each of 4 test days. Behavioral and physiologic changes were monitored for 10 minutes preceding and 30 minutes following injections. These same subjects were also tested in an identical paradigm but nicotine dosing (at similar dose levels) was accomplished by having the subjects smoke research cigarettes. Nicotine produced dose-related changes in magnitude and duration of responses on dependent variables. For instance, highly discriminable subjective effects occurred within about 30 seconds and dissipated within 2–3 minutes. Certain physiologic measures (e.g., heartrate) showed a similar temporal pattern of change. In the second experiment, the profile of subjective effects produced by intravenous nicotine were characterized in persons with histories of polydrug abuse. The ARC Inventory revealed a profile most similar to that produced by either morphine or stimulant drugs. Drug identification responses by the subjects were most frequently of cocaine. Drug dose strength and drug liking scores were directly related to dose. In the third experiment, subjects were permitted to self-administer nicotine via an automatic intravenous infusion system. Drug infusions were available during 3 hr test sessions on a fixed-ratio 10 (FR 10) reinforcement schedule with a 1 or 2 minute time-out following each injection. The subjects were not allowed to smoke cigarettes during sessions. Preliminary results showed that nicotine can serve as a positive reinforcer with infusions occurring at fairly even temporal intervals. Nicotine intake was directly related to unit dose while number of infusions and desire to smoke cigarettes were an inverse function of nicotine dose.

A2

PENTOBARBITAL-MAINTAINED PROGRESSIVE-RATIO PERFORMANCE BY HUMANS. D. R. McLeod and R. R. Griffiths, Department of Psychiatry, Baltimore City Hospitals and Department of Psychiatry and Behavioral Sciences, The Johns Hopkins University School of Medicine, Baltimore, MD 21224.

Within a residential research ward, five human volunteers with histories of sedative drug abuse were exposed to progressive-ratio schedules of pentobarbital (200, 400, 600 mg) or placebo self-administration. All doses were letter-coded and administered under double-blind conditions. The letter-coded drugs could be earned by pressing a pair of buttons (three subjects) or by riding a stationary bicycle (two subjects). Only one dose of drug could be obtained per day. The response requirement to obtain each drug was systematically increased over successive sessions until the subject failed to meet the response requirement for the drug (i.e. the subject chose not to work for the drug). Two hours after drug ingestion, subjective effects of the drug were assessed by a questionnaire drawn from the Addiction Research Center Inventory (LSD, AG, BG, MBG, and PCAG scales). The magnitude of drug effect also was measured by subject and staff drug-effect rating scales and by a subject liking scale. Following completion of these questionnaires, two of the five subjects completed a battery of psychomotor performance tasks. The psychomotor performance of two additional subjects also was assessed following administration of pentobarbital during the course of other studies. Analysis of the results showed that pentobarbital maintained dose-related increases in the maximum ratio completed under the progressive-ratio schedule. Pentobarbital also produced dose-related increases in the subject and staff ratings of drug-effect, in the subject ratings of drug liking, and in the scores on the PCAG scale of the Addiction Research Center Inventory. Doses of pentobarbital had no systematic effect on the LSD, AG, BG or MBG scales. Finally, pentobarbital produced dose-related decrements in psychomotor performance. The covariance of these data with those of other studies suggests that a unifying construction, such as relative reinforcing efficacy, can provide a useful framework within which to compare the effects of pharmacological agents.