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Marijuana users can adjust the delivered dose of THC by altering their smoking patterns as has been observed in tobacco smokers, but evidence for THC dose regulation is sparse. We (Herning *et al.*, 1986) reported that marijuana users adjusted their smoking patterns in response to the potency of the marijuana. To investigate further how users might regulate the delivered dose, two additional studies were performed. In the first study, 32 subjects smoked four marijuana cigarettes with different THC potencies (0.0, 1.2, 2.9 and 3.9% by weight) on separate days. Smoking patterns and expired carbon monoxide (CO) as well as the subjective and cardiovascular effects of marijuana were measured. Subjective intoxication ratings and heart rate increased with potency, but expired CO did not. Puff and inhalation measures differed across THC potency. In the second study, 6 frequent (57.8 marijuana cigarettes/month) and 6 infrequent (2.4 marijuana cigarettes/month) smoked a 1.8% THC cigarette. Smoking patterns, subjective and cardiovascular effects were measured. Expired CO and THC plasma levels were also monitored. Both groups had similar cardiovascular and subjective changes after smoking. The frequent users' puff volumes and expired CO levels were more than double those of the infrequent users. Marijuana users can regulate the delivered dose of THC from a marijuana cigarette by modifying their smoking patterns. Frequent users inhale larger amounts of THC smoke to obtain the same subjective and cardiovascular effects as infrequent users. Potency-adjusted dosing patterns and acquired tolerance may account for discrepancies in dose-response relationships observed in marijuana studies.

SMOKING TOPOGRAPHY AND PERFORMANCE EFFECTS OF MARIJUANA IN HUMANS. Stephen J. Heishman and Maxine L. Stitzer. The Johns Hopkins University School of Medicine, Baltimore, MD.

Smoking is an efficient means of marijuana administration, producing rapid onset of pharmacological effects. However, it is difficult to control dosages via the inhalation route. To examine the effects of marijuana across a range of physiological, subjective and performance measures, six subjects smoked two marijuana cigarettes each containing 0, 1.3 or 2.7% Δ^9 -THC on separate days. Dosing was accomplished using a standardized smoking procedure which controlled number of puffs, breath hold duration and inter-puff interval, but not puff volume. Both active doses produced significant increases in heart rate and drug "high" ratings over placebo; however, there was no differentiation between the two active marijuana doses. Of three psychomotor tasks, circular lights, tracking and digit-symbol substitution (DSST), marijuana only slowed DSST performance; again, the active doses did not differ. Thus, orderly physiological, subjective and performance dose-response relationships were not achieved. One possible explanation is that subjects alter their smoking pattern (e.g., puff volume) of different potency cigarettes, thereby adjusting the delivered marijuana dose. Additionally, the lack of performance decrements may be explained by insensitive tasks. To investigate these issues, a second study was conducted in which

subjects smoked ad lib one cigarette containing 0, 1.3 or 2.7% Δ^9 -THC. Similar to the first study, both active marijuana doses significantly increased heart rate and subjective effects over placebo, but were not different from each other. Significant impairment was observed on a reverse digit span task, but not on forward digit span, divided attention (tracking and visual search) or DSST. Smoking topography measures indicated a trend toward smaller puff and inhalation volumes and shorter lung exposure duration for the high marijuana dose compared to the low dose. Expired air carbon monoxide (postsmoking-presmoking levels) for the high dose was significantly less than that for the low dose, indicating less smoke inhalation. The data suggest that marijuana smokers can adjust their delivered dose, thereby minimizing the likelihood of observing clear dose-response relationships.

UNIQUE BEHAVIORAL-PHARMACOLOGICAL PROFILES OF MARIJUANA EFFECTS IN HUMANS. John D. Roache. The University of Texas Health Science Center, Houston, TX; George E. Bigelow. The Johns Hopkins University School of Medicine, Baltimore, MD; and Warren K. Bickel. University of Vermont College of Medicine, Burlington, VT.

The effects of smoked THC-containing or placebo marijuana were compared with those of diazepam, secobarbital and amphetamine in 80 healthy adult male volunteers with recreational marijuana use histories. As a previous report described (NIDA Res. Monogr. 67:492, 1986), subjects were evaluated for intoxication by four members of the Los Angeles Police Department (LAPD) and also completed subjective ratings and objective performance tasks. Using a double-blind, triple-dummy, placebo-controlled design, all subjects smoked placebo or THC-containing marijuana cigarettes and ingested placebo or other drug-containing capsules; 10 subjects in each of three groups finally received 8 puffs (1 puff/30 sec) from each of two cigarettes containing either placebo, 1.2% or 2.8% THC. Marijuana did not significantly impair performance on any of the tasks, in contrast to diazepam and secobarbital which did impair circular lights (a saccadic hand-eye coordination test), DSST (computerized digit-symbol substitution), tracking (computer video) and 8-digit number recall (computer video) tasks. In contrast to the lack of marijuana effects on objective performance tasks, the blind observers (LAPD members) were surprisingly accurate in identifying and distinguishing the THC marijuana-treated subjects from those treated with placebo, amphetamine, diazepam or secobarbital. The four observers independently evaluated each of the subjects resulting in a total of 40 judgements for each dose. There was a dose-related increase in "marijuana intoxication" judgements from 0-11-28 across the placebo, 1.3% and 2.8% marijuana dose conditions; only 2 "stimulant" and 3 "depressant" judgements were made for the marijuana-treated subjects, and the remainder were identified as "not intoxicated." Analyses of the individual items which observers used to evaluate the subjects indicated observations of marijuana-specific effects in subjects' attitude, speech, physiological signs and motor function. Subject ratings on a checklist of 52 target symptoms indicated that marijuana produced some specific effects but also produced a mixed profile of "sedative" and "stimulant" symptoms. These results demonstrate a uniqueness in the profile of behavioral effects of marijuana as compared to other drugs.