logic effects of fenfluramine and amphetamine were compared by using methods previously described by Martin and associates[18] and Jasinski, Nutt, and Griffith.[13]

Methods

Participants were 8 men detained for federal crimes committed in connection with their narcotic use. They ranged in age from 31 to 44 and were in good health, as evidenced by medical history, physical examination, and appropriate laboratory studies, and exhibited no psychiatric impairment beyond drug abuse and concomitant antisocial behavior. All had used narcotics for an average of 18 yr before incarceration; in addition, 7 had also used amphetamine or cocaine, and 4, LSD-like hallucinogens. Participation was voluntary.

The doses of *dl*-fenfluramine hydrochloride (60, 120, 240 mg) and *d*-amphetamine (20, 40 mg) were selected following a dose run-up and on the basis of prior studies,[18] respectively. During dose run-up, 1 subject given 270 mg of fenfluramine reported transient, paranoid thoughts just prior to a euphoric episode. For this reason, and because a demonstration of psychotomimetic effects was not a purpose of this study, the largest dose of fenfluramine used in the crossover was 240 mg, an amount also well tolerated in toxicity studies done elsewhere. A cherry syrup with a trace of quinine added served as both the vehicle for the drugs and as a placebo. Each treatment was administered orally in random sequence at weekly intervals under double-blind conditions.

Subjects were admitted to the ward the evening before their test day and examined to rule out intercurrent illnesses. On the test day, they were awakened at 6:30 A.M., and baseline physiologic observations were made at 7:00 and 7:30 A.M. Treatments were given at 8:00 A.M. Physiologic observations would then be repeated at 0.5, 1, 2, 3, 4, 5, 6, 12, and 24 hr postdrug. These were: (1) duplicate 10-min supine blood pressures as determined by calibrated sphygmomanometer and auscultation; (2) pulse rate; (3) respiratory rate; (4) rectal temperature; and (5) pupil diameter (determined photographically; eye 11 inches from a back-illuminated opal glass screen and target transilluminated to 300 ft-lamberts). Two-min standing blood pressures and pulse rates were obtained at 3 and 24 hr and compared to the immediately preceding supine values. Urine pH was not controlled in this acute study.

At these postdrug intervals, subjective effects were measured by a group of questionnaires completed by both subjects and observers. These were the Single Dose Opiate Questionnaire for subjects and observers[6] and a special questionnaire for subjects that consisted of items from the following scales of the Addiction Research Center Inventory[10]: MBG (Morphine-Benzedrine Group Scale), a general measure of drug-induced euphoria; LSD (Lysergic Acid Diethylamide Group Scale), a measure of dysphoric and somatic symptoms elicited by graded doses of LSD and certain narcotic antagonists[11, 17]; and an 11-item Amphetamine Scale, a measure specific for the dose-related effects of *d*-amphetamine.[18] The Amphetamine Scale contains items that relate mainly to concepts of self-confidence and personal assertiveness.

The effects of drugs on food intake were estimated by calculating the caloric value of food actually eaten at the noon, evening, and breakfast meals (using weighed portions and standard tables). Except for noncaloric beverages, including coffee, subjects fasted from midnight until the noon meal and then again until the evening meal (5:00 P.M.).

The morning following the test day, subjects estimated their time asleep to the nearest half-hour. Sleep time was also estimated by observers who inspected subjects at half-hour intervals during the evening and night (6:00 P.M. to 6:00 A.M.).

Dose-effect relationships were determined by partitioning the treatment sums of squares from the analysis of variance for a randomized block design into components to test the significance of the regression mean square of measured total 6-hr response on each measure against dose of amphetamine and fenfluramine. In addition, mean placebo responses and 95% confidence limits of mean placebo response were calculated for each measure to allow dif-