MARIHUANA, ethanol, and dextroamphetamine are three widely used social drugs with somewhat different actions. Marihuana is a sedative somewhat like ethanol, but also has perceptual effects resembling those of hallucinogens. Ethanol is primarily a sedative, while dextroamphetamine is a stimulant. As it has been seldom possible to compare these three drugs in the same subjects, using quantified doses, we measured their effects on mood and selected mental functions.

Methods

Twelve normal young volunteers were chosen primarily on the basis of their being in good physical and emotional health and intelligent and cooperative enough to carry out the required procedures. All but one were men. Although most subjects had had prior experience with small doses of marihuana and amphetamines, and all with alcoholic beverages, none were chronic or recent users of any of these drugs, except for mild use of beverage alcohol. Subjects were told that these three drugs were to be given, and that one might be given twice.

Four trials were run at weekly intervals, with random assignment of the following four treatments: (1) marihuana prepared as an extract and calibrated for 1-tetrahydrocannabinol (THC) content, 0.5 mg/kg; (2) 95% ethanol, 1 ml/kg; (3) dextroamphetamine sulfate, 0.2 mg/kg; and (4) a placebo made by reextracting marihuana from which all cannabinoids had previously been extracted. Subjects varied in weight from 66 kg (146 lb) to 91 kg (200 lb). Doses of drugs were as follows: marihuana as THC, median dose 32 mg, range 27 to 39 mg; dextroamphetamine, median dose 15 mg, range 13 to 18 mg; ethanol, median dose 57 gm, range 50 to 68 gm.

Doses of each drug were given orally in 180 ml of a flavored, noncaloric soft drink. To mask taste differences further, the subject was blindfolded and his nostrils occluded. To the greatest extent possible, double-blind control was exercised, although various circumstances (distinctive taste and effects of alcohol and marihuana) made this difficult.

Subjects were given the doses of drug at 8 AM, while in a fasting state. One hour later they were given a battery of tests which included the rod-and-frame test, the digit-symbol substitution test, and simple reaction time. These tests were repeated 3 1/2 hours after drug administration.

Rod-and-Frame Test
Marihuana, Ethanol, and Dextroamphetamine Mood and Mental Function Alterations

Written by Leo Hollister

This test used a portable, electrically operated apparatus (Model 12010, Stoelting). The subject looked into the enclosed box where he saw a white disk with a black rod inside a black square. The square was tilted first to the right then to the left, the rod being off vertical. The subject was allowed to direct movement of the rod until he saw it as vertical. Eight trials were done, with the setting of the frame to the right or left being equally divided but randomly ordered after the first two presentations. Deviation of the adjusted rod from vertical was recorded to the nearest 0.5 degree. All deviations were summed.

Digit-Symbol Substitution Test (DSST)

This test was part of the Wechsler-Bellevue Scale for Adults. After some explanation and practice, the subject was instructed to begin when signalled to match the appropriate symbol to each digit in order, working as rapidly as possible. A test period of 90 seconds was used. The score was the number of correct substitutions completed in the allotted time.

Simple Reaction Time

The subject was instructed to depress a telegraph key and keep it depressed until a tone which he would shortly hear stopped. A tone at 300 cycles per second at 70 dB was generated for periods of 2, 7, and 12 seconds randomly over 19 trials (7, 6, and 6, for each time period respectively). Reaction time was expressed as the mean time to release the key on the 19 trials.

Two hours and four hours after the drug was given, the following additional tests were done:

Adjective Checklist Mood Scale

The subject was given a checklist of 50 adjectives which describe different feelings or moods. He rated them on a four-point scale, ranging from "not a bit" to "extremely," based on his current feelings. Three factors, scores for "active," "stimulated," and "drowsy" were obtained by summing the ratings on 12 adjectives contributing to the "active" factor, 7 adjectives contributing to the "stimulation" factor, and 5 adjectives contributing to the "drowsy" factor.

Repetitive Psychometric Measures

Two tests were chosen from a series of psychometric tests designed for repeated measures, the Number Facility (NF) test and the Flexibility of Closure (FC) test. The NF test consists of a
series of 'simple arithmetic problems. The FC test consists of a task of retracing in a field of dots a figure drawn in a similar field, the point of origin being designated in the open field. Both tests were available in numerous variations equated for difficulty so that no subject received the same set of problems twice. The number of correct problems completed in a five-minute period was the basis for the score for each test.

Time Estimation.
—Subjects were instructed to pay close attention to the duration of a tone, try to conceive of a period of time exactly one half the duration of the tone and then, after a lapse of four seconds, to match that interval by depressing a telegraph key the appropriate length of time. The tones were the same as used above for the simple reaction time, once again being randomly presented. Each was separated by an interval during which the estimate of one half the time period was made. Thus, seven estimates of a 1-second interval, six of a 3.5-second interval, and six of a 6-second interval were required. Deviations from each time interval were summed algebraically and the mean score for each was calculated.

Results

The clinical effects of the drugs were about what might be expected, and to some extent were recognized by the subjects. Ethanol ingestion, in the large amounts given in the fasting state, had an immediate and profound effect, readily recognized as alcoholic intoxication. Most subjects were also able to distinguish the effect of marihuana, which occurred more slowly and was characterized by euphoria and sleepiness. The effects of dextroamphetamine were less readily evident and the placebo had no discernible effect, other than its noxious taste which resembled the active marihuana extract.

Mean scores from the three mood-scale factors were compared for the three drugs and placebo two and four hours after the dose was given. Treatments were shown by two-way analysis of variance to differ in regard to drowsiness at two hours (F = 5.54, df 3, P < 0.005), due to less drowsiness from dextroamphetamine than from the other treatments (Table 1). Although this relationship held at four hours, differences between treatments just missed being significant. Stimulation is not necessarily the converse of drowsiness, and all three drugs tended to increase this factor as compared with placebo. Analysis of variance again revealed a significant difference between treatments after two hours (F = 3.00, df 3, P < 0.05), due to the greater degree of stimulation from dextroamphetamine at both time intervals. The activity factor was differently affected by treatments, both after two hours (F = 5.68, df 3, P < 0.005) and after
four hours (F = 6.04, df 3, P < 0.005). After two hours, the difference was due to increased activity from dextroamphetamine, while at four hours it was due to decreased activity from alcohol and marihuana. All changes in mood-scale factors were in directions postulated from known actions of the drugs.

The Repetitive Psychometric Measures revealed differences between treatments (Table 2). Differential effects on the FC test were observed after two hours (F = 5.10, df 3, P < 0.01) due to improved performance following dextroamphetamine. After four hours, this difference was lost. A relative decrease in performance from marihuana was noted, although not statistically significant. The NF test revealed differences between treatments at both two hours (F = 5.33, df 3, P < 0.005) and four hours (F = 3.90, df 3, P < 0.025). Although dextroamphetamine also increased performance on this test, it did not account for the treatment differences. Rather it was marihuana, which decreased performance at both times. After two hours alcohol also decreased performance, to a degree which was not quite significant.

The treatments differed on their effects on time estimate only on that for the 3.5-second interval (Table 3). The difference between treatments was significant both at two hours (F = 3.64, df 3, P < 0.025) and at four hours (F = 6.05, df 3, P < 0.005). In both instances it was marihuana which accounted for the differences in two distinct ways: toward a longer estimate of time and a closer approximation of the actual time interval. This marihuana effect was rather consistent, regardless of the time interval being estimated or the time of testing.

No differences between treatments were observed in the amount of error on the rod-and-frame test, either by analysis of variance (F = 1.45, df 3, NS) or by comparing each drug with placebo (Table 4). The digit-symbol substitution test revealed a difference between treatments after 1 hour (F = 3.15, df 3, P < 0.05), but not at 31/2 hours (F = 1.27, df 3, NS). This early difference was attributable to an increase in performance following dextroamphetamine. Differences between treatments were observed on the simple reaction time at both 1 hour (F = 8.62, df 3, P < 0.0005) and 31/2 hours (F = 4.94, df 3, P < 0.01). Alcohol significantly increased reaction time at both testing intervals, while the effects of marihuana in increasing reaction time were not apparent until the 31/2-hour time interval.
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Table 2: Mood Alteration

<table>
<thead>
<tr>
<th>Drug</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marihuana</td>
<td>75%</td>
<td>80%</td>
</tr>
<tr>
<td>Ethanol</td>
<td>60%</td>
<td>70%</td>
</tr>
<tr>
<td>Dextroamphetamine</td>
<td>50%</td>
<td>60%</td>
</tr>
</tbody>
</table>

Comment

Dextroamphetamine produced the greatest changes in mood, with an increase in stimulation and activity factors of the present scale.4 In another, synthetic TI-IC decreased "friendly," "aggressive," and "unhappy" scores, while increased "stimulated" and "alert" scores. This is consistent with earlier studies and expectations for all three drugs.

Summary

Simple reaction time has usually been impaired by ethanol, although results have varied due to different conditions.8 Although dextroamphetamine has been reported to decrease visual reaction time, and especially to increase variability in performance due to occasional complete lapses of attention.8 Although dextroamphetamine has been reported to decrease visual reaction time, and especially to increase variability in performance due to occasional complete lapses of attention.8

Subjective responses based on a mood scale revealed increased stimulation and activity, as well as decreased drowsiness from dextroamphetamine as compared with placebo; ethanol and marihuana increased simple reaction time.

This study was supported in part by Public Health Service grant MH 03030.