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Human Tonal Preferences As A Function of Frequency Under Δ^8-Tetrahydrocannabinol

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SOUZA, M. R. C., I. G. KARNIOL AND D. F. VENTURA. *Human tonal preferences as a function of frequency under Δ^8-tetrahydrocannabinol.* PHARMAC. BIOCHEM. BEHAV. **2**(5) 607–611, 1974. – Tonal preference distributions were measured in volunteers, before and after the ingestion in double-blind conditions, of 5, 10, 20, and 40 mg of Δ^8-tetrahydrocannabinol (Δ^8-THC), an active constituent of marihuana, and placebo. Placebo and 5 mg of Δ^8-THC did not change the typical inverted U-shaped distribution of preferences as function of sound frequency. At higher dosages there was a reliable tendency towards preference for the highest pitched tones, and in a few cases, a disruption of the responses. Increase in pulse rate, alterations in time production tasks and subjective effects were other actions of the higher dosages of the drug. Those data confirmed previous reports.

Δ^8-THC Marihuana Tonal preference

PERCEPTUAL disturbances induced by marijuana in several sensory modalities are frequently reported by drug users [15]. Reference to these alterations is widely found in the literature, both in general review studies [12,16], as in studies in which other aspects are investigated and where reports of perceptual alterations appear as incidental observation [4]. More detailed descriptions of perceptual effects of cannabis are available in studies in which perceptual and other effects are listed, as in Tart's work [15]. He did an extensive survey by submitting questionnaires to experienced marijuana users. His finding was that "the most characteristic effect of marijuana is an auditory one . . . which is experienced very often or usually by almost all users and occurs at a low level of intoxication . . ." This effect is described as an ability of the subject for hearing "more subtle changes in sounds; e.g., the notes of music are purer and more distinct, the rhythm stands out more."

Even though the importance of cannabis effects on perception has been emphasized, there are relatively few systematic studies of its effects in man. Most of the studies that make use of psychophysical or psychophysiological procedures have investigated visual variables [13]. Fewer studies have dealt with auditory effects. Among those, a psychophysical work on intensity thresholds showed that marijuana smokers presented a higher intensity differential threshold, as compared with the placebo group, but failed to show any differences in absolute threshold [3]. Other authors [5], however, working with frequency discrimination, reported no effect. From these reports, the conclusion is that at least some of the basic auditory functions, e.g., absolute threshold and frequency discrimination are unaffected by marijuana. Accounts from drug users, on the other hand, suggest strong effects, with relation to music listening, as described by Tart [15]. In addition, improvement of artistic performance under the effect of marijuana has been reported by jazz musicians [2,16]. The obvious suggestion is that the effect of marijuana in audition, if not found in basic auditory functions, should be searched in more complex perceptual functions.

The present work was therefore undertaken with the purpose of determining the effect of an active component of marijuana on tonal preference as a function of frequency. The psychophysical procedure of paired-comparisons used by Vitz [17] for the investigation of tonal preferences in humans offered a simple and objective method, that was convenient for drug studies, since session length was short and the subject's task easy. The drug used was Δ^8-trans-tetrahydrocannabinol (Δ^8-THC), had been previously shown [8,9] as capable of mimicking the effects of Δ^9-trans-tetrahydrocannabinol, the major active principle of marijuana [11], although with lower pharmacological potency.

METHOD

Subjects

The subjects used were 25 male graduate and undergraduate students, selected after physical examination and

psychiatric interview. This precaution was taken in order to insure that the volunteers were in apparent good mental and physical health. All subjects reported that to their knowledge they had normal hearing. They were distributed in 5 groups of 5 subjects each, balanced for age, weight, and previous experience with marijuana. Eleven of the volunteers reported previous occasional use of the drug.

Drug Administration

Δ^8-THC as an alcoholic solution kept in dark ampoules was kindly provided by NIMH.

Each of the 5 groups of subjects was given, in double-blind conditions, respectively, placebo and 5, 10, 20, and 40 mg of Δ^8-THC. The drugs were previously dissolved in 1 ml of ethanol and added to 200 ml of orange juice. A solution of 1 ml of ethanol in 200 ml of orange juice was used as placebo. Subjects ingested the selected dose at 9:00 a.m., having had only a light breakfast (coffee, milk, and one toast) about 2 hr before. They were instructed to refrain from alcoholic beverages for 24 hr before the experimental day.

Oral route was preferred to prevent the great loss of drug when smoke is employed, and to avoid the problem of different styles of smoking [4]. In support of this, a demonstration made by Rafaelson [14] that cannabis metabolites in urine were more consistently found after oral intake than after smoke favors the assumption that dosage is more constant intra and inter individually by this route.

Overall Testing Procedure

The method employed by Karniol *et al.* [10] was used with slight modifications. In short, subjects were admitted in a partially soundproof laboratory and given a description of the experimental sequence. Initially, pulse rate was measured 5 times at 1 min intervals. After this, they were submitted to a time production task which consisted in estimating a 60 sec interval, 10 times in succession. The first 5 estimates (Estimates T1) were without feedback. Immediately after each of the last 5 (Estimates T2), the experimenter gave the subject feedback about his performance by saying either "Correct," "Too short," or "Too long." The first tonal preference session was then conducted. Five min after the end of the session, subjects ingested the drug and pulse rate was measured several times at 20 min intervals. The second tonal preference session was conducted 60 min after drug ingestion. Following this the time estimation task was repeated. Estimates T3 were without feedback and estimates T4, with feedback. The experimenter interviewed the subjects 60, 80, and 120 min after drug ingestion, asking questions about their subjective feelings and sensations. The psychological effects of drug action were graded from 0 to 4, according with a scale of subjective symptoms previously described [4, 9, 10]. The average time spent in the predrug phase was 45 min, and from drug ingestion to the end of the experiment, two hr.

Tonal Preference Test

A slight modified version of the procedure used by Vitz [17] was employed here. Eight pure tones of 60, 110, 210, 400, 750, 1410, 2660 and 5000 Hz were presented to the subjects in a paired comparison task. Each tone was paired with each other, once in the sequence a–b and once in the sequence b–a. There were, as a result, 14 presentations of each tone, and 56 pairs per session. The modification with relation to Vitz' procedure consisted in the use of an intensity correction for equal loudness, which was based on the values of the equal loudness contour for 80 phones determined by Fletcher and Munson [6].

The tones were generated by two audio oscillators (Hewlett-Packard 200 AB), and were presented binaurally through earphones (Grason-Stadler TDH 39-300 Z). Two attenuators (Hewlett-Packard 350 D) were used for intensity control. A Bruel & Kaer impulse precision sound level meter (Type 2204) was used in conjunction with a Bruel & Kaer artificial ear (Type 4152) and a Bruel & Kaer high stability precision condenser microphone (Type 4144) for measuring the acoustic pressure produced by the phones. With an input voltage of 1.0 V the phones were found to yield 109 dB re: 0.0002 dynes/cm^2 $\pm$ 0.5 dB at 1000 Hz, and no more than 2 dB variation within the range of frequencies used in this study. These calibrations were performed by the Instituto de Electrotécnica of the University of São Paulo.

The interval between the two tones in each pair and their duration was controlled by electronic timers (Lafayette 100 B). These durations were held fixed throughout the experiment at the value of 1 sec for tone duration and 1 sec for intertone interval.

Each subject was submitted to two sessions, one before, and the second 60 min after, drug ingestion. A signal light controlled by the experimenter indicated the beginning of each trial. When it was turned on, the subject received instructions to press a button that triggered presentation of a pair of tones. After listening to each pair the subject indicated which of the two he preferred by pressing one of two keys, labelled, respectively, first and second.

RESULTS

Results showing the effect of Δ^8-THC upon pulse rate, time estimation and subjective effects will not be given here in detailed form, since they have replicated those obtained in a previous study [9]. Table 1 summarizes the results obtained here. With relation to pulse rate, percentage increase in pulse rate was calculated by comparing postdrug values with the average of the 5 predrug measures taken as 100%. The effect on time estimation was expressed in terms of the deviation ($\pm$ SE) in seconds from 60 seconds, in the estimates without feedback (T3) and with feedback (T4). The subjective effects reported were represented by the median of the grades obtained with each of the treatments.

It can be seen from Table 1 that the effect of Δ^8-THC in increasing pulse rate was dose dependent, and at the lowest dosages it did not differ statistically in its effects from placebo. It can also be observed that the drug significantly affected the capacity of estimating time. This effect was greater in T3 and in T4, as with previous results [4, 9, 10]. Average deviation from 60 sec was significantly different from placebo for time estimates in T3 after ingestion of 20 and 40 mg of Δ^8-THC. These were also the dosages of the drug necessary to produce subjective effects that differed from placebo in their rating.

Tonal preference results, shown in Fig. 1, indicate that before drug ingestion, the average number of preferences is highest around 210, 400 and 750 Hz, and steadily declines towards lower and higher tone frequencies. Examples of the 3 types of curve that were obtained after drug ingestion are

TABLE 1

INCREASE IN PULSE RATE, DEVIATION IN TIME ESTIMATION AND SUBJECTIVE EFFECTS PRODUCED BY INGESTION OF Δ^8-THC AND PLACEBO

Drug	Dosage (mg)	Average increase in pulse rate ± SE	Deviation in time estimation (average sec ± SE)* T3	T4	Median of subjective effects
Placebo	1 ml	0.2 ± 0.5	7.1 ± 7.3	4.9 ± 4.9	0
Δ^8-THC	5	2.9 ± 3.9	7.5 ± 4.9	5.8 ± 4.5	0
Δ^8-THC	10	6.7 ± 5.3†	7.5 ± 3.1	5.6 ± 1.9	0
Δ^8-THC	20	10.3 ± 8.2†	14.5 ± 9.8†	8.8 ± 6.1	1‡
Δ^8-THC	40	18.7 ± 9.7†	13.5 ± 4.1†	7.1 ± 3.9	2‡

*The values below represent the average of 25 estimates performed under each drug treatment (5 estimates per each of the 5 subjects).

†Comparison made with placebo group (Student t test; $p \leq 0.05$).

‡Comparison made with placebo group (Mann-Whitney U Test; $p \leq 0.05$).

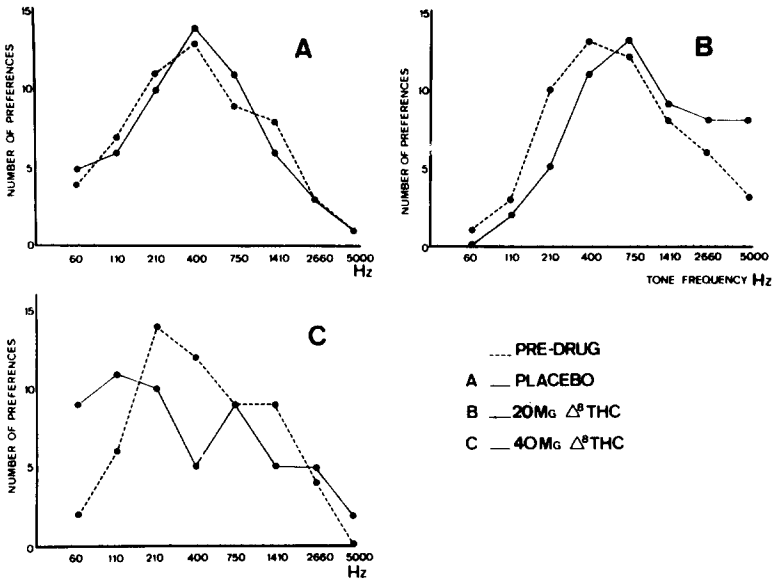

FIG. 1. Tonal preference as a function of sound frequency for 3 different subjects, before (dotted lines) and after (filled lines) the ingestion of placebo (A), 20 mg of Δ^8-THC (B) and 40 mg of Δ^8-THC (C).

plotted in Fig. 1 for 3 different subjects, together with the curves obtained before drug for each of these subjects. In one type of result, labelled A in Fig. 1, the postdrug curve practically superimposed the predrug one. The second type of result, labelled B, showed a peak shift in the distribution of preferences and an increase in the number of choices of the highest pitched tones, especially 5000 Hz, for the post-drug curve. The curve labelled C shows the third type of result, that is, a disruption of preference after drug ingestion, expressed in random responding. The number of subjects from each group exhibiting each of the 3 types of curve described above is shown in Table 2. A tendency to present Type A result was predominant with placebo and 5 mg of Δ^8-THC, whereas the number of subjects yielding Type B curves increased with the higher doses of the drug. Only 3 subjects produced Type C curves.

Post-drug preferences for the several frequencies used can be seen in Table 3, in which median frequencies for each treatment are presented. Preference for 5000 Hz was significantly greater than placebo after 10, 20 or 40 mg of

TABLE 2

DISTRIBUTION OF SUBJECTS ACCORDING TO TYPE OF CURVE OF TOTAL PREFERENCES AFTER PLACEBO AND Δ^8-THC TREATMENTS

Drug	Dosage (mg)	Number of subjects according to type of curve of tonal preference A	B	C
Placebo	1 ml	4	1	0
Δ^8-THC	5	3	1	1
Δ^8-THC	10	2	2	1
Δ^8-THC	20	2	3	0
Δ^8-THC	40	1	3	1

TABLE 3

TONAL PREFERENCES (MEDIAN FREQUENCY) AFTER Δ^8-THC AND PLACEBO FOR THE TONE FREQUENCIES USED

Drug	Dosage (mg)	Median frequency for preference for 60	110	210	400	750	1410	2660	5000 Hz
Placebo	1 ml	4	6	10	12	10	7	6	0
Δ^8-THC	5	2	5	9	12	11	8	5	0
Δ^8-THC	10	3	4	8	9	9	6	7	5*
Δ^8-THC	20	3	6	10	11	11	7	4	3*
Δ^8-THC	40	4	6	9	11	10	7	7*	2*

*$p \leq 0.05$; comparison made with placebo group (Mann-Whitney U Test)

Δ^8-THC. This happened with 2660 Hz only after the greatest dosage of the drug.

The tendency to prefer 5000 Hz was also apparent when the comparison was made between the preferences before and after drug for each subject. At the two highest doses, 20 and 40 mg of Δ^8-THC, 4 subjects increased their preference for 5000 Hz; this number decreased to 3 with 10 mg, to 2 with 5 mg, and was only 1 for the placebo group. These results are coincident with the spontaneous report from some of the subjects that they had the impression that after the treatments they "liked higher pitched tones better."

DISCUSSION

The results obtained with the measurements of time estimation, pulse rate increase, and subjective effects agree with those previously described for Δ^8-THC [8,9].

Tonal preferences before drug ingestion and for placebo subjects, with the exception of one, confirm the results reported by Vitz [17].

Data on tonal preferences after drug ingestion showed that Δ^8-THC was capable of producing a reliable change in this perceptual task. This result is particularly interesting in relation to the fact that another auditory function along the same physical continuum, that is, frequency discrimination, is not affected [3,5].

The most consistent change in tonal preference was the increase in preference for 5000 Hz. Three subjects, even, spontaneously reported their liking high frequencies more after drug ingestion.

The attempts at explaining these results should consider a comparison between the task used in the present experiment and that of frequency discrimination, where negative results were found [3]. At least two aspects differentiate them. On the one hand, judgements on tonal preference imply a more complex task, and possibly, as a consequence,

different neural integrating mechanisms. This might explain that the drug used affects one type of function, leaving the other unaltered. A second aspect that differentiates the two situations is the fact that preference judgements involved hedonic value of stimuli, that is, their position along an irritating-relaxing scale [7,17]. In this respect, it is of relevance to recall results obtained by Berlyne *et al.* [1] on EEG recording during presentation of one second tones of 200, 400, 800, and 1600 Hz. Their data showed that duration of desynchronization was least for the two middle frequencies, and greatest for both extremes. They found a U-shaped curve similar to the one found by Vitz [17] and confirmed in the predrug and placebo results of the present experiment. According to these results, then, tones that are most pleasant are the ones that interfere the least with EEG synchrony, which is characteristic of the relaxed state. Along this line, one might suppose that the action of Δ^8-THC in this task is not due to its greater complexity, but rather to variables such as motivation, reinforcement and attention, which are relevant to hedonic value judgements [17]. A first test of this hypothesis would be a replication of the experiment of Berlyne *et al.* [1] to determine whether a comparable shift on the distribution of EEG desynchronization effects would appear under Δ^8-THC.

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