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Comparison of a Placebo, N-dimethyltryptamine, and 6-hydroxy-N-dimethyltryptamine in Man

By

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With 1 Figure in the Text

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Recently it has been suggested (SZARA and HEARST) that the effects of N-dialkyltryptamines may be due to the activity of their 6-hydroxylated metabolites.

The present study was designed to compare the effects of a placebo and equal doses of N-dimethyltryptamine (DMT) and 6-hydroxy-N-dimethyltryptamine (6-HDMT) in man.

Method

Five former opiate addicts who were serving sentences for violation of United States narcotic laws volunteered for this experiment. Each subject was male, age 25—35, and exhibited no major signs of physical illness or psychosis.

A "single-blind" (subjects did not know the drugs they were receiving), cross-over design was employed. Each subject received intramuscularly at weekly intervals a placebo, DMT, and 6-HDMT in randomized order. Four subjects received 1 mg/kg of either drug; the fifth subject received 0.75 mg/kg (all doses refer to free-base weight).

Rectal temperature, respiratory rate, pulse rate, blood pressure, kneejerk threshold, and subjective response (questionnaire and clinical grade) were determined by the methods and controlled conditions previously employed with other psychotomimetic agents (ISBELL et al., 1956). Pupillary size was photographically recorded under constant lighting conditions.

One or two pre-drug determinations were made within one hour before drug administration. The post-drug subjective response (questionnaire) was determined at 30, 90, 150 and 210 minutes. Pulse rate, blood pressure, respiratory rate, pupillary size and kneejerk threshold were measured at 15—25, 60, 120, 180, and 240 minutes. Rectal temperature was determined at hourly intervals.

For each parameter the pre-drug value was subtracted from the post-drug response at each interval, and the mean difference for the 5 subjects at each interval was calculated. From this data time-action curves were

constructed. In addition, the differences obtained with each drug at various intervals were compared to their respective placebo response by the *t*-test for paired observations.

Results

Fig. 1 illustrates the mean time-action courses for the subjective response (questionnaire) obtained with a placebo and equal doses of DMT and 6-HDMT (1 mg/kg, 4 subjects; 0.75 mg/kg, 1 subject).

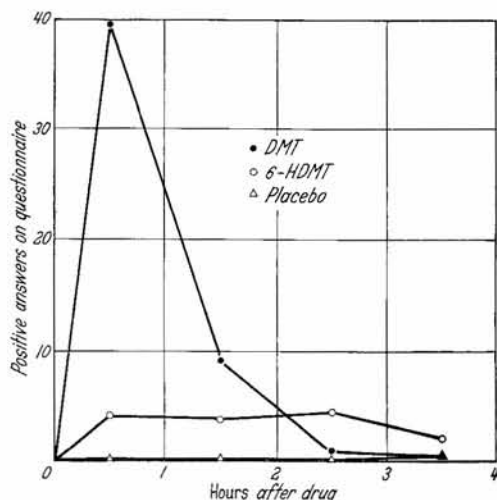


Fig. 1. Time course of the subjective response after a placebo and equal doses of DMT and 6-HDMT

pre- and post-drug response at 15–30 minutes obtained from 5 subjects receiving a placebo and equal doses of DMT and 6-HDMT (1 mg/kg, 4 subjects; 0.75 mg/kg, 1 subject) at weekly intervals. The statistical comparison for each drug with its respective placebo value is indicated.

This data indicates a significant ($P < 0.05$) increase in systolic and diastolic blood pressure, pupillary size, subjective response, and a significant decrease in the kneejerk threshold at 15–30 minutes following the administration of DMT. By similar analyses, not listed in the table, a significant increase remained for pupillary size at 60 and 120 minutes. In no instance was a significant difference obtained between 6-HDMT and the corresponding placebo values.

In several respects the response with DMT qualitatively resembled the subjective and autonomic effects of LSD in former opiate addicts reported previously (ISBELL et al., 1956). The mental effects consisted of anxiety, hallucinations (usually visual) and perceptual distortions.

quite apparent that DMT provoked a marked subjective response, while a similar dose of 6-HDMT produced only minimal effects (in 2 of the 5 subjects).

Similar time-action curves were obtained for DMT with regard to pupillary dilatation, systolic and diastolic blood pressure elevation, and decreased kneejerk threshold. However, 6-HDMT had no apparent effect for these parameters.

The table lists the mean difference for each parameter between the

Table. *Comparison of effects with a placebo and equal doses of N-dimethyltryptamine (DMT) and 6-hydroxy-N-dimethyltryptamine (6-HDMT) in man*

Measure ¹	Placebo	DMT	6-HDMT
Temperature	+0.09 ± 0.11	- 0.03 ± 0.10	+0.10 ± 0.06
Pulse rate	+4.40 ± 1.33	+ 9.60 ± 4.03	+5.00 ± 7.42
Systolic blood pressure . .	+5.60 ± 2.25	+33.00 ± 5.14 ³	+9.40 ± 4.36
Diastolic blood pressure . .	0.00 ± 2.74	+22.80 ± 3.92 ²	+4.80 ± 5.38
Respiratory rate	+2.50 ± 1.06	+ 4.20 ± 1.47	+2.80 ± 1.39
Kneejerk threshold	+0.25 ± 2.84	- 7.55 ± 4.68 ⁴	+1.15 ± 0.87
Pupil size	-0.55 ± 0.25	+20.45 ± 4.22 ³	-0.16 ± 0.35
Positive answers on question- naire	0.00 ± 0.00	+39.60 ± 3.26 ²	+4.00 ± 2.85
Clinical grade	0.00 ± 0.00	+ 3.10 ± 0.10 ²	+0.70 ± 0.44

Each figure represents the mean difference ± standard error of the mean difference between pre- and post-drug response at 15–30 minutes (except 60 min. with regard to temperature) obtained from 5 subjects receiving a placebo and equal doses of DMT and 6-HDMT (1 mg/kg, 4 subjects; 0.75 mg/kg, 1 subject). The signs indicate an increase (+) or decrease (—) from pre-drug control values.

¹ All values are expressed in conventional units except kneejerk threshold—minimal degree arc through which a mounted reflex hammer must fall in order to elicit the patellar reflex; pupil size—area in mm²; and clinical grade—0 (no change to 4 (hallucinations with loss of insight).

² Indicates significance ($P < 0.01$) compared with placebo.

³ Indicates significance ($P < 0.02$) compared with placebo.

⁴ Indicates significance ($P < 0.05$) compared with placebo only when the data obtained with the low dose of DMT (1 subject, 0.75 mg/kg) is excluded.

In contrast to LSD, however, diastolic hypertension was present and tachycardia was absent. In addition, the effects of DMT appeared and subsided more quickly.

Comment

The results of this study suggest that 6-hydroxy-N-dimethyltryptamine is not the active metabolite responsible for the psychotomimetic and autonomic effects produced in man by N-dimethyltryptamine. However, factors such as comparative degradation rates and brain permeability with either drug in man must also be considered.

Summary

1. Five human subjects received intramuscularly at weekly intervals a placebo and equal doses of 6-hydroxy-N-dimethyltryptamine (6-HDMT) and N-dimethyltryptamine (DMT) (1 mg/kg, 4 subjects; 0.75 mg/kg, 1 subject).

2. DMT produced markedly significant mental effects including anxiety, hallucinations, and perceptual distortions and autonomic changes consisting of pupillary dilatation, increase in systolic and dia-

stolic blood pressure, and a decrease in the kneejerk threshold. These effects appeared within 15—30 minutes and subsided within 1—2 hours.

3. The effects of 6-HDMT were not significantly different from those produced by a placebo.

References

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