## Effects of the Psychodysleptic Drug Psilocybin on Visual Perception. Changes in Brightness Preference

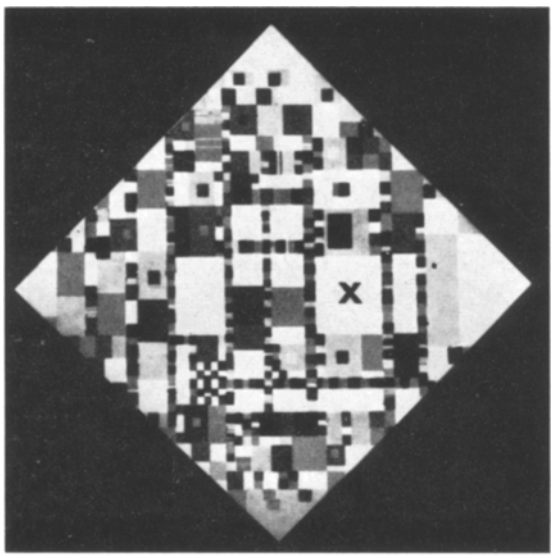
This paper reports on changes in certain perceptual and behavioral parameters which occur during the psychodysleptic or hallucinogenic drug induced state[1,2]. Specifically, changes in brightness preference elicited under the influence of moderate doses of psilocybin in 15 college age volunteers will be described. Our observations lend additional support to the apparent independence of an autonomic variable – pupillary dilation – and perceptual performance under psilocybin produced (model) psychosis[3].

Following a 30 min dark adaptation period at 4 m candle ambient illumination the subject's pupil diameters were measured. He then was positioned behind a gross field aperture through which he viewed a projection screen at 2 m distance. Three 35 mm slide reproductions of abstract paintings (Figure 1) were successively projected on the screen in the course of the testing, while ambient illumination was maintained within $\pm 1.5$ m candles. The brightness of these targets could be controlled by a 3 log unit neutral density optical wedge. The log 0 luminance values at particular (white) reference points for each target are indicated in Figure 1.

Subjects were asked, while viewing a target, to select a degree of brightness at which the artist would have wanted them to view the painting. Using this criterion most of the subjects quickly learned to give consistent settings, but practice continued before each experiment until reliability (settings within $\pm 0.1$ log density units) of performance was attained.

After completion of training and just before a subject received 160–200 μg/kg psilocybin ($T_1$), 2 types of control settings were made for each target:

(1) *Forced choice technique.* Each subject was forced to select preferential brightnesses according to the scheme in Figure 2. For each target a subject was offered 4 pairs of decisions (or 3, if the 2 luminances at the third level were equally satisfactory) and the optimum brightness was determined to the nearest 0.1 log density unit of the 3 log unit range available in each instance.

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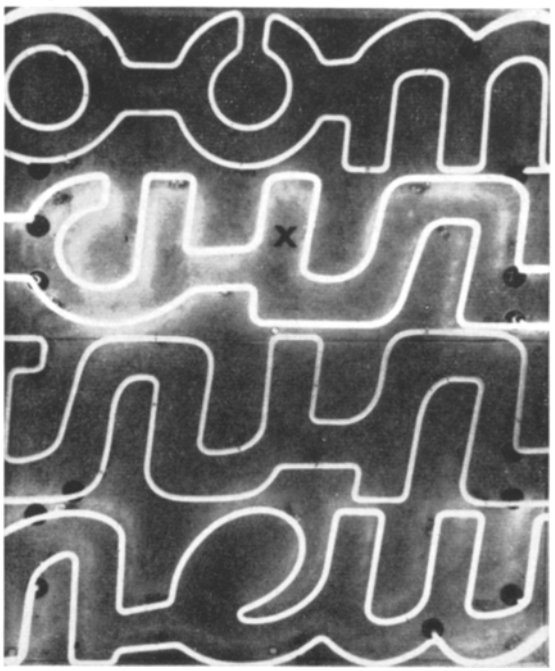


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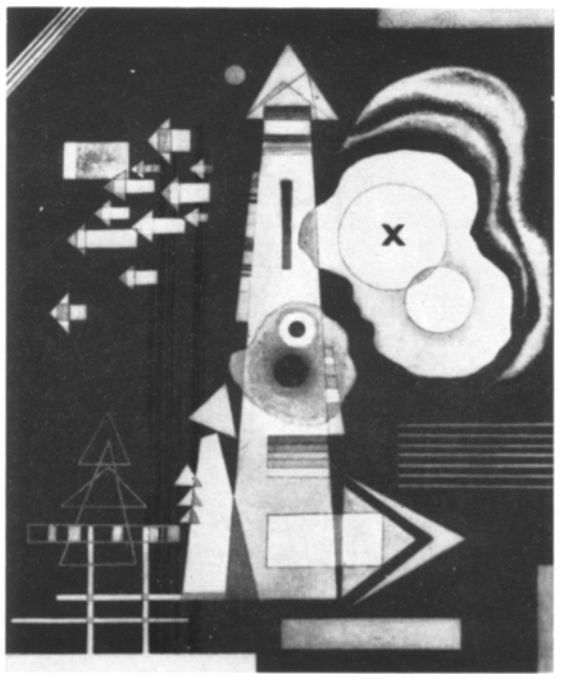


III

Fig. 1. The 3 targets viewed by the subjects with their luminance reference points and values. Slide I is of Mondrian's 'Broadway Boogie Woogie', slide II is Chryssa's 'Americanoom, 1963', and slide III is Kandinsky's 'Arrows'. X, luminance reference points of the projected slides. I, 40.8 m-candles; II, 20.5 m-candles; III, 51.1 m-candles.

[1] R. Fischer, P. A. Marks, R. M. Hill and M. A. Rockey, Nature *218*, 296 (1968); R. Fischer and D. Warshay, *Pharmakopsychiatrie Neuro-Psychopharmakologie* (Thieme, Stuttgart 1968), in press.

[2] R. M. Hill, R. Fischer and D. Warshay, Experientia *25*, (1969).

[3] R. Fischer, P. A. Marks and M. A. Rockey, Arzneimittel-Forsch., in press (1968).

(2) *Free response technique.* The subject was allowed to control the wedge when selecting his preferential brightness. To prevent gross interference with his adaptation state the subject was asked to start at the lower luminances.

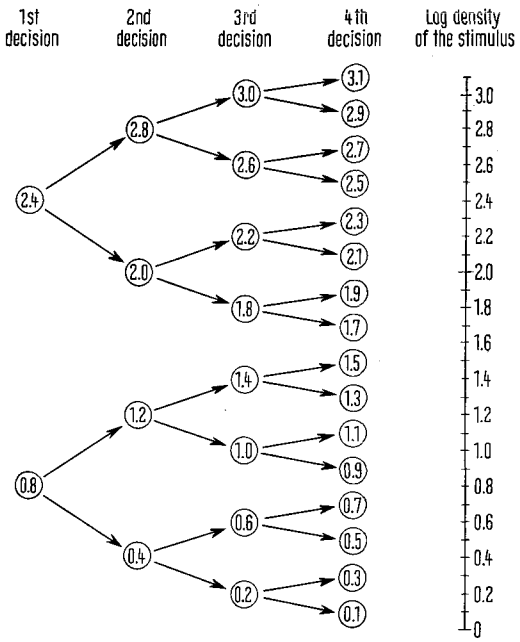


Fig. 2. Forced choice scheme for brightness preference.

These 2 procedures were applied to each of the subjects when viewing the 3 targets 55, 110 and 270 min following the oral administration of the drug, i.e. at $T_2$, $T_3$ and $T_4$ respectively.

Pupillary diameters were measured just before each test while the subject viewed the blank screen (4 m candle illumination) from a distance of 2 m.

There are significant, positive correlations between the ranked brightness values obtained under free response and forced choice techniques, for the 15 subjects, for each target at pre-drug and drug peak (Table I, below).

Twelve of the fifteen subjects preferred less brightness at drug-peak than they did at pre-drug, and 3 subjects preferred more brightness. Changes in preferential brightness in a representative subject from each of these groups, i.e. the 'reducers' and the 'augmenters', are illustrated in Figures 3 and 4 respectively. The 3 'augmenters' also

Table I. Spearman rank order correlations between free response and forced choice techniques for slides I, II, III

| Pre-drug | | | Drug-peak | | |
|---|---|---|---|---|---|
| Slide I | Slide II | Slide III | Slide I | Slide II | Slide III |
| 0.78 | 0.79 | 0.71 | 0.73 | 0.80 | 0.65 |

$p < 0.01$, 1-tailed test.

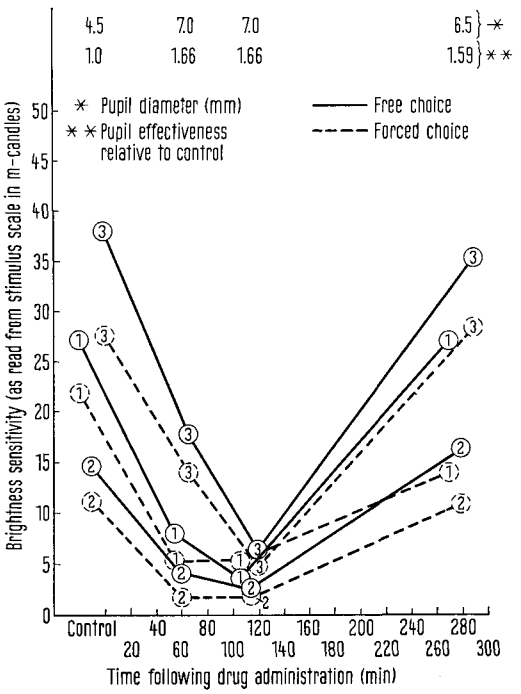


Fig. 3. Free response and forced choice preferences of a 'reducer' for each target at $T_1$, $T_2$, $T_3$ and $T_4$ showing decreased brightness preference during the midcourse of the drug. The entrance pupil diameters and effectiveness of the pupil at each time relative to that of $T_1$ are given. Using conversion curves taken from SCHOBER and FRY[5], the relative pupil area was corrected for the Stiles-Crawford effect of the first kind. The circled numbers on each curve indicate which target was used.

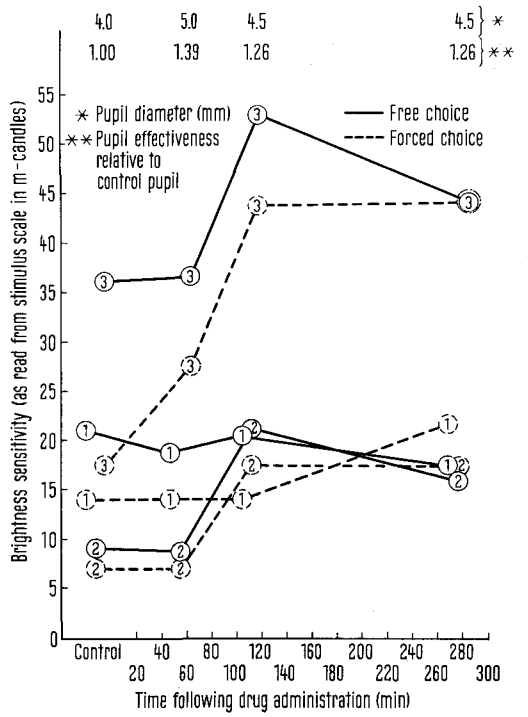


Fig. 4. Free response and forced choice preferences of an 'augmenter' for each target at $T_1$, $T_2$, $T_3$ and $T_4$ showing increased brightness preference during the midcourse of the drug. The entrance pupil diameters and effectiveness of the pupil at each time relative to that of $T_1$ are given. The circled numbers on each curve indicate which target was used.

constitute the lowest group of Minnesota Multiphasic Personality Inventory (MMPI) drug-reactors[4]; all have actual MMPI drug-reactivity scores of less than 300 and occupy the lowest 10% in the range of scores for the entire group of volunteers (Figure 5). The rankings for each of the 15 subjects on (1) preferential brightness for both free responses and forced choices, for each target, at pre-drug and drug-peak, (2) the psilocybin-induced change in brightness sensitivity from $T_1$ to $T_2$ and (3) MMPI drug reactivity are given in Table II.

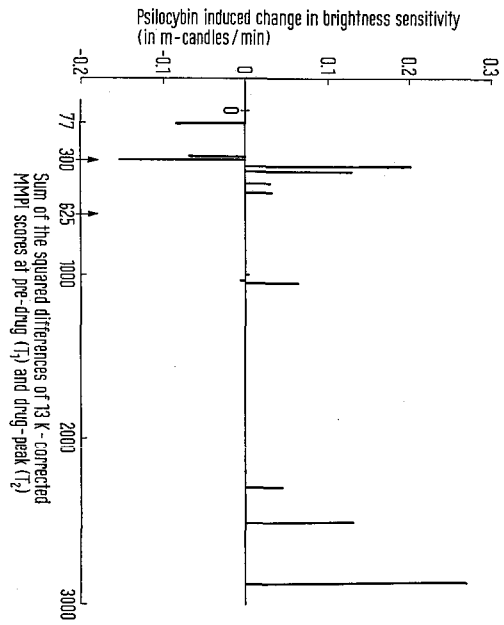


Fig. 5. The relation of psilocybin-induced change in brightness sensitivity to MMPI drug reactivity (N = 13). The behavioral characteristics of all 15 subjects reported here have been described in greater detail[1,3]. 2 subjects with excessive dispersion values (S.D.) have been omitted from this Figure.

One of the interesting incidental findings is the relatively small influence of drug-induced corrected pupillary area increase upon brightness preference. Indeed, there is in 'augmenters' an inverse relationship between preferential brightness and corrected pupillary area ($p = 0.05$; FISHER exact probability test).

There is a simple relationship between (1) the re-test variability of subjects on a perceptual task – such as, taste threshold and visual distortion threshold[1] – without any drug ($T_1$), (2) their drug-induced and MMPI measured behavioral reactivity at $T_2$ and (3) their preferential brightness. The 3 'augmenters', i.e. subjects who prefer more light at $T_2$, display the smallest re-test variance on perceptual tasks to begin with, i.e. at $T_1$[1], and are, then, also behaviorally stable at $T_2$, whereas the converse is true for the 12 'reducers'. The observations on the influence of psilocybin on subjectively tested visual sensitivity by DELAY et al.[6] in a sample comparable to ours report hyperesthesia in 8 of his cases, and hypoesthesia in one instance. This ratio is quite comparable to our ratio of 'reducers' to 'augmenters' and implies a relationship between perception and behavior. This is illustrated in Figure 5, in which 'reducers' can be sub-

[4] Low MMPI drug reactivity, i.e. a stable personality profile, means that there is little change and lack of psychopathology under the influence of the drug. Drug-MMPI reactivity is calculated using the sum of the squared differences for each of 13 K-corrected MMPI T-scores at pre-drug and drug-peak. A 'reducer' is a subject who reduces the light input at drug-peak ($T_2$). The minority of subjects, the 'augmenters', show a converse relation.

[5] H. A. W. SCHOBER and G. A. FRY, Vision Res. *8*, 1107 (1968).

[6] J. DELAY et al., in *Les Champignons Hallucinogènes du Mexique* (Ed. R. HEIM and R. GORDON WASSON; Archives du Musée National d'Histoire Naturelle, Paris 1958), p. 273.

Table II. Ranking of 15 subjects according to (1) preferential brightness on slides I, II, III under pre-drug ($T_1$) and drug-peak ($T_2$) conditions; (2) psilocybin-induced change in brightness sensitivity from $T_1$ to $T_2$, and (3) MMPI drug reactivity

| Subject | Pre-drug | | | | | | Drug peak | | | | | | Signed change pre- to drug peak slope analysis Free response | MMPI-drug reactivity |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Free response Slide | | | Forced choice Slide | | | Free response Slide | | | Forced choice Slide | | | | |
| | I | II | III | I | II | III | I | II | III | I | II | III | | |
| 1. WR[a] | 9.0 | 14.0 | 10.0 | 11.0 | 7.5 | 11.0 | 7.0 | 5.0 | 7.0 | 4.0 | 6.0 | 5.5 | 1.0 | 1 |
| 2. DD[a] | 2.0 | 10.0 | 3.0 | 3.0 | 7.5 | 3.5 | 4.0 | 5.0 | 12.0 | 11.5 | 3.5 | 11.0 | 4.0 | 2 |
| 3. RM[b] | 1.0 | 2.0 | 1.0 | 1.0 | 3.5 | 3.5 | 1.0 | 1.0 | 1.0 | 1.0 | 1.5 | 1.5 | 7.0 | 3 |
| 4. BN[b] | 14.0 | 14.0 | 12.5 | 11.0 | 12.5 | 15.0 | 8.0 | 10.0 | 6.0 | 7.0 | 11.5 | 3.5 | 2.0 | 4 |
| 5. VM[b] | 14.0 | 9.0 | 14.5 | 11.0 | 12.5 | 11.0 | 10.0 | 7.0 | 12.0 | 11.5 | 11.5 | 11.0 | 6.0 | 5 |
| 6. DS[b] | 11.0 | 14.0 | 12.5 | 11.0 | 12.5 | 11.0 | 13.5 | 13.5 | 12.0 | 11.5 | 11.5 | 11.0 | 11.0 | 6 |
| 7. HM[a] | 3.0 | 4.0 | 8.0 | 3.0 | 3.5 | 1.0 | 3.0 | 8.0 | 4.0 | 4.0 | 6.0 | 3.5 | 10.0 | 7 |
| 8. SH[a] | 11.0 | 11.5 | 9.0 | 11.0 | 12.5 | 11.0 | 13.5 | 13.5 | 12.0 | 11.5 | 11.5 | 11.0 | 12.0 | 8 |
| 9. SS[b] | 14.0 | 6.5 | 2.0 | 11.0 | 7.5 | 3.5 | 13.5 | 11.0 | 5.0 | 11.5 | 11.5 | 11.0 | 8.0 | 9 |
| 10. SA[b] | 11.0 | 11.5 | 11.0 | 5.5 | 12.5 | 11.0 | 13.5 | 13.5 | 12.0 | 11.5 | 11.5 | 5.5 | 9.0 | 10 |
| 11. AM[a] | 7.5 | 6.5 | 4.0 | 11.0 | 12.5 | 11.0 | 5.0 | 5.0 | 3.0 | 11.5 | 11.5 | 11.0 | 5.0 | 11 |
| 12. SJ[a] | 5.0 | 8.0 | 7.0 | 5.5 | 7.5 | 6.5 | 2.0 | 3.0 | 2.0 | 2.0 | 1.5 | 1.5 | 3.0 | 12 |
| 13. BT[a] | 6.0 | 1.0 | 14.5 | 11.0 | 1.0 | 11.0 | 11.0 | 2.0 | 12.0 | 11.5 | 3.5 | 11.0 | 15.0 | 13 |
| 14. KT[a] | 7.5 | 3.0 | 5.0 | 11.0 | 3.5 | 6.5 | 9.0 | 9.0 | 8.0 | 6.0 | 6.0 | 11.0 | 13.0 | 14 |
| 15. HS[a] | 4.0 | 5.0 | 6.0 | 3.0 | 3.5 | 3.5 | 6.0 | 13.5 | 12.0 | 4.0 | 11.5 | 11.0 | 14.0 | 15 |

[a] Male, [b] female. Highest ranks are assigned always to the highest positive value.

divided according to their perceptual-personality characteristics. Those with scores over 2000 on the MMPI drug reactivity (abscissa in Figure 5) display the highest amount of psychopathology at the peak of a psilocybin induced experience and are the most variable subjects on perceptual tasks without any drug. PETRIE's data[7] also suggest that certain perceptual-personality characteristics are related to the control of perceptual intake and processing[8].

*Zusammenfassung.* Die in gesunden, jungen Volontären durch Psilocybin hervorgerufene, reversible Veränderung der bevorzugten Helligkeit kann mit der Stabilität der Wahrnehmungspersönlichkeitsstruktur, nicht aber mit der mydriatischen Wirkung der Droge in Beziehung gebracht werden.

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[7] A. PETRIE, *Individuality in Pain and Suffering* (The University of Chicago Press, Chicago 1967).

[8] Acknowledgments: These studies are part of a plan for the investigation of psilocybin by R.F. approved by the Food and Drug Administration IDN 3530 and were assisted by Grant No. 66-341 of the Foundations' Funds for Research in Psychiatry, U.S. Public Health Service, National Institute of Health, General Research Support Grants, administered by The Ohio State University, College of Medicine and Comly Coleman Fund. Our thanks are due to Sandoz Pharmaceuticals, Hanover, New Jersey, who through the F.D.A.-P.H.S. Psychotomimetic Agents Advisory Committee provided us with psilocybin. The authors are indebted to J. R. SANDBERG for his omnipresent interest and assistance.

## The Pharmacological Action of Gastrin Pentapeptide

Since the isolation and synthesis[1-3] of gastrin and gastrin pentapeptide it has become possible to study the pharmacology of gastrin action on the oxyntic cell. It has also become possible to study the puzzling relationships between gastrin, histamine and cholinergic stimuli.

Our experiments were carried out on 5 mongrel dogs with Heidenhain gastric pouches, weighing 14–16 kg. The animals were fasted for 18 h before each experiment.

Throughout the experiments gastric secretion was stimulated either by feeding or by the continuous i.v. administration of 2 μg of gastrin pentapeptide (GP5) or 10 μg of histamine/minute. When a control plateau of secretion had been reached atropine sulphate or ganglionic blocking agents (pentolinium tartrate, hexamethonium bromide or chlorisondamine chloride) were injected s.c. in various doses arranged randomly.

Collections were for 10-min periods. At least 3 were taken at each dose level and the last 2 at each dose were used for calculations. Acid was titrated to pH 7.

In Figure 1 it will be seen that pentolinium alone was without effect upon basal gastric acid secretion, but in Figure 2 it greatly enhanced the response to i.v. GP5. The same result exactly was obtained with the other 2 blocking agents. Atropine on the other hand profoundly depressed GP5 and pentolinium enhanced secretion (Figure 1). The acid response to histamine in contrast was significantly depressed by ganglionic blockade (Figure 2). This finding indicates that the mechanism by which histamine stimulates the oxyntic cell is different from that by which GP5 does. That endogenous gastrin acts in the same manner as GP5 cannot be estab-

[1] R. A. GREGORY and H. J. TRACY, J. Physiol. *169*, 18p (1963).
[2] R. A. GREGORY and H. J. TRACY, Gut *5*, 103 (1964).
[3] J. C. ANDERSON, M. A. BARTON, R. A. GREGORY, P. M. HARDY, G. W. KENNER, J. K. MACLEOD, J. PRESTON and R. C. SHEPPARD, Nature *204*, 933 (1964).

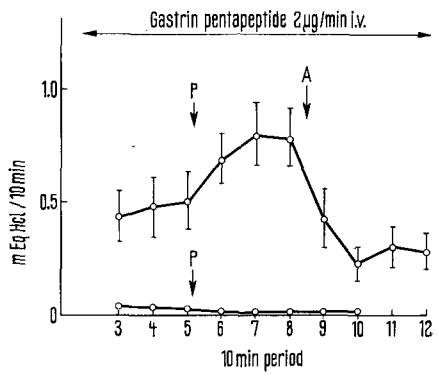


Fig. 1. The effect and standard errors of pentolinium tartrate 1 mg/kg s.c. at P on the acid secretion from unstimulated (lower curve) and GP5 stimulated Heidenhain pouches (upper curve). Atropine sulphate 1 mg s.c. was given at A. Each curve mean of 5 dogs.

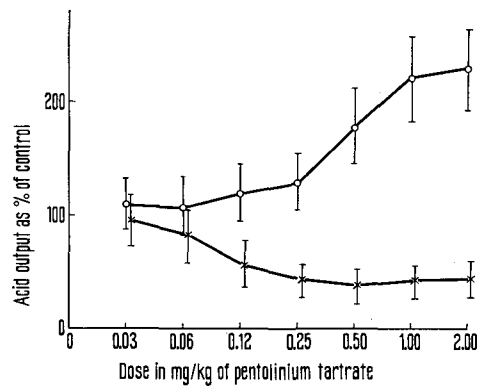


Fig. 2. The effect and standard errors of a ganglionic blocking agent on the secretion of gastric acid in response to GP5 (2 μg/min) upper curve and on histamine (10 μg/min) lower curve. Each curve mean of 5 dogs.