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The Effects of Psilocybin on a Test of After-Image Perception*

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The ingestion of Psilocybin frequently results in the hallucination of color and geometric design, altered perception of shape and proportion, and changes in after-image perception. Because stroboscopic and entoptic stimulation produce some of these effects, such sensations are thought to at least partially depend on changes in retinal function (KLUVER 1942). Several studies have demonstrated specific objective effects of hallucinogenic drugs on the visual system. Lysergic Acid Diethylamide (LSD) decreases both the photopic and scotopic thresholds to light in humans (CARLSON 1958). KRILL et al. (1960) have indicated that LSD decreases the scotopic threshold and changes the scotopic electroretinogram but does not effect the photopic threshold in humans. The findings pertinent to the scotopic state indicate a depression in the activity of rod based retinal and/or central mechanisms that mediate the perception of light and crude form. The findings of CARLSON would indicate that similar changes occur in the cone-based systems that mediate perception of color and detail. It has been demonstrated (HOLLISTER and HARTMAN 1962) that LSD and Psilocybin increase the ability to discern color in a stimulus of low color saturation and decrease the ability to accurately discriminate between stimuli of adjacent hues in humans. Some inferences that may be derived from this study will be considered below.

A study concerning the effects of Psilocybin on after-image perception was undertaken in the hope of demonstrating additional photopic effects that might help elucidate the neurophysiological basis for the subjective visual syndrome. An attempt was made to determine the nature and extent of simultaneous subjective visual changes so that correlation between changes in afterimage perception and visual sensation could be demonstrated.

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Method

Ten young adults participated as subjects; these individuals were employed in various capacities at the Center where the experiment was performed. They were known by the investigator to be free from gross psychiatric disturbance, to adjust acceptably to study or work and to conduct themselves in accordance with conventional social mores. Subjects were not paid so as to avoid overcoming any resistance to take the drug; none had to lose salary to participate. The subjects were told that Psilocybin evoked an unusual and often interesting reaction. Most anticipated an insightful experience; those who expected to hallucinate anticipated seeing people, objects, scenes, etc., rather than distortion, design and color. Several agreements concerning activities on the experimental day after leaving the laboratory communicated that the investigator considered taking Psilocybin to be a serious matter. Subjects agreed not to drive an automobile, not to be alone in a house or apartment, not to attend social gatherings and if unmarried, not to "date".

The test instruments pertinent to the experience to be reported included a device that measures after-image relations and a check-list of visual effects.

Direct measures of after-image strength and duration are unreliable but a technique exists in which the induced negative after-image of a stimulus may suppress perception of the stimulus itself. The subject reports which of two colors is seen. A repetitive cycle of colored stimulus (.017 seconds), white stimulus (.1 seconds) and relative absence of stimulus (.083 seconds) is presented; these stimuli follow each other without interval. For certain luminance values of the colored stimulus (red, for example) there are luminance values of the white stimulus below which only red and above which only green is perceived. Although termed green, the color is more accurately termed cyan, or blue-green, the complement of red. The colored stimulus is a piece of opal glass transilluinated from the rear so as, for this experiment, to be of red (625 mμ) hue and 25 millilamberts luminance. This red stimulus is seen through an aperture in a white screen which receives the same illumination as does an episcoster rotating five times per second between the observer's eye and the screen. The episcoster presents a 30° slot, a 180° white and 150° "black" segment in that order five times per second. A diffuse white (2860°K) light source is situated above and to the front of the episcoster; a variable diaphragm between this light and the episcoster permits control of the illumination of the episcoster and screen. The 180° white segment presents a white stimulus for .1 seconds; the 150° black segment presents relative absence of stimulus for .083 seconds. (As the luminance of the white stimulus is varied between 5 and 140 millilamberts the luminance of the black stimulus varies between .1 and 3 millilamberts.) The 30°

slot presents the screen (this has the same brightness as does the white stimulus) and the colored stimulus (625 mμ at 25 millilamberts at all times). The system is viewed through an eyepiece with an artificial pupil 2 mm in diameter to prevent any changes in subjects pupillary diameter from altering retinal illumination. The observer, looking through the eyepiece sees a $1^1/_2°$ central colored spot on a white surround. This surround limited to 10° by the design of the eyepiece, is of the same luminance as the white stimulus when either the white stimulus or the screen surrounding the colored stimulus is presented and of the luminance of the "black" stimulus for the rest of the cycle. Its average brightness is thus slightly greater than that of the white stimulus. A five cycle per second flicker is visible in this surround. A determination of after-image threshold is made by increasing the luminance of the white stimulus from a low value till green rather than red is seen; this is repeated three times, and by decreasing the luminance of the white stimulus from a high value till red rather than green is seen; this is repeated three times. The average of these six values is taken as the after-image threshold. The apparatus is described in more detail elsewhere (KEELER 1962).

The visual check list includes 32 items of visual sensation. Seventeen of these (listed as "major" in the appendix) had been reported in previous experiments by at least two subjects during the height of a Psilocybin reaction (between 45 and 120 min after the drug was given) but neither before nor after the height of the Psilocybin reaction nor during a Placebo nor a Ephedrine reaction. The other 15 items, listed a "minor" in the appendix, had been reported not only during the height of the Psilocybin reaction but during at least one of the other conditions noted.

The subjects were instructed to eat a light breakfast even though this introduces the problem of irregular absorption of Psilocybin. This eliminates any effects of fasting which might influence the findings. Either .2 mgm per kilogram of body weight of Psilocybin or a placebo of identical appearance was administered orally at 9:00 a.m. in double-blind conditions. Those receiving the drug received placebo at 11:00 a.m. and vice versa. The subjects knew only that they would receive Psilocybin on at least one of the two occasions. Subjects and investigators at the Center have invariably been certain und correct as to whether placebo or Psilocybin was given on any one day. They are less certain and occasionally in error as to which drug is given when Psilocybin and placebo are given two hours apart. When placebo is given after Psilocybin any change in the period after placebo may reflect the diminution of Psilocybin effect as well as the onset of placebo effect. This may increase the apparent effectivness of Psilocybin as compared to placebo but cannot produce a drug effect if none is present.

The after-image test was administered as described at 9:00 a.m., 11:00 a.m. and 1:00 p.m. Each subject was given this test at the same times on another day within two days of the experimental day; for five subjects this preceded and for five it followed the experimental day. The visual check list was self-accomplished hourly from 9:00 a.m. through 2:00 p.m. of the experimental day. The experimental protocol also included the Minnesota Multiphasic Personality Inventory.

An assistant who did not know the purpose of the experiment administered the after-image test; the principal investigator was present neither when the afterimage test was administered nor when the check list was filled out. Subjects were left to themselves or could have the company of the investigator or assistant when the protocol permitted.

Results

Table 1 indicates the luminance values of the white stimulus at which reversal of color perception occurred during the control and experimental days. For reasons of clarity only the 9:00 a.m. (the baseline) readings on both days, the 11:00 a.m. readings on the experimental day and the changes in between 9:00 and 11:00 a.m. and 11:00 a.m. and 1:00 p.m. of both days are indicated. Astericks indicate changes in the two hour

Table 1. *Effects of Psilocybin on a test of after-image relations*

Subject	Experimental Day Values #				Control Day Values #		
	9 a.m.	11 a.m.	Change 9—11 a.m.	Change 11—1 p.m.	9 a.m.	Change 9—11 a.m.	Change 11—1 p.m.
a	77	113	+36*	−19	52	+14	4
b	36	99	+63*	−69	36	+ 6	+ 2
c	28	109	+81*	−37	28	+24	+ 5
d	48	139	+91*	−59	58	+ 7	+ 5
e	40	139	+99*	−16	50	− 2	+ 4
f	30	44	+14	+30*	27	+ 4	+22
g	69	97	+28	+30*	44	− 2	+ 4
h	69	70	+ 1	+67*	52	+ 4	+20
i	40	84	+44	+51*	60	+ 9	+16
j	52	63	+11	+70*	50	+ 8	−16

Luminance of white stimulus (Millilamberts) at reversal of color perception.
* Change in two hour period after Psilocybin.

Increase with Psilocybin exceeds that with Placebo at $p < .01$ (Wilcoxon Matched-Pair Signed-Rank Test).

Increase with Psilocybin exceeds that at same time in control day at $p < .01$ (Wilcoxon Matched-Pair Signed-Rank Test).

Subjects a, b, c, d, e received Psilocybin and subjects f, g, h, i, j received Placebo at 9:00 a.m. on the experimental day. Those receiving Psilocybin at 9:00 a.m. received Placebo at 11:00 a.m. on the experimental day. No medication was given on the control day.

period after Psilocybin. The increases in the two hour period after drug exceede those in the two hour period after placebo at $p < .01$ as tested by the Wilcoxon matched-pair signed-rank test. The increases after drug exceede those that occurred during the same interval of the day when neither drug nor placebo was given at $p < .01$ as tested by the Wilcoxon matched-pair signed-rank test.

Table 2. *Correlation of changes in after-image threshold and reports of unusual visual experience 120 minutes after receiving Psilocybin*

Subject	Visual Changes Reported			Changes in After-Image Value *	
	Major	Minor	Rank	Millilamberts	Rank
a	1	6	1	+36	3
f	1	9	2	+30	1.5
g	2	9	3	+30	1.5
h	2	12	4	+67	6
i	4	2	5	+51	4
b	4	4	6	+63	5
c	5	9	7	+81	8
d	5	10	8	+91	9
j	6	7	9	+70	7
e	7	9	10	+99	10

* Reading 120 min after receiving Psilocybin less reading immediately after receiving Psilocybin.

r_3 (Visual Experience and After-Image Changes) = .88 (Spearman Correlation Coefficient); $p < .001$.

r_3 (Rank order in major visual changes only vs rank order in minor visual changes only) $< .1$.

r_3 (Rank order in visual changes in table and changes in after-image value corrected for changes in after-image on control day) = .88.

The rank orders in "major" and "minor" visual changes and the values and rank order of changes in the after-image threshold corrected for changes in the control day can be obtained by calculation from Tables 1 and 2.

At 11:00 a.m. on the experimental day the lowest value for those who had received drug at 9:00 a.m. exceeded the highest value for those who had received placebo at 9:00 a.m.; this is significant at $p < .01$ as tested by the Fischer exact probability test. At 11:00 a.m. of the experimental day subject "a" who had received drug at 9:00 a.m. thought he had received placebo and subjects "f" and "h" who had received placebo at 9:00 a.m. thought they had received drug. This indicates that the double-blind condition introduced uncertainty as to when Psilocybin was given.

Table 2 compares the rank-order of subjects in terms of the results of the visual questionnaire and changes in the after-image threshold two hours after receiving Psilocybin. The questionnaire data is ranked

in terms of the number of "major" changes; "minor" changes are used only to break ties, a system decided on in advance. The correlation coefficients to be reported would not be changed if ties in rank as determined by number of "major responses" were not so broken.

When rank order in terms of visual change reported is compared to rank order in terms of increases in the after-image threshold the correlation is significant at $p < .01$ as tested by the Spearman rank correlation coefficient. The correlation is similarly significant if the changes in the after-image threshold after Psilocybin are corrected for the changes that occurred during the same time interval of the control day.

The fact that there is no correlation between the number of major and minor items checked (The Spearman correlation coefficient is less than .1) indicates that something more than a drug induced willingness to admit to unusual experience is involved in responses to the questionnaire. No subject reported major changes two hours after initially given placebo; three subjects reported major changes two hours after placebo when placebo was given after Psilocybin (thus four hours after Psilocybin).

Discussion

The data indicate that Psilocybin produces a significant change in an after-image phenomenon and that this change is powerfully correlated with reports of unusual visual experience. This effect is objective and occurred in double-blind conditions. The sensitivity and variability of the measure as indicated by some of the changes that occurred in non-drug conditions does not impugn this finding because of the considerably greater magnitude of the changes that occurred with Psilocybin. Determinations such as reported herein and in the work of others cited do not establish the locus of Psilocybin action on visual sensation. Interpretation of the after-image finding is further confounded by the fact that the precise mechanisms involved in the suppression of a stimulus by its induced negative after-image have not been worked out.

One plausible but unproven explanation of after-image predominance is that perception of the colored (red, for example) stimulus depends on excitatory response to red. Perception of the induced negative after-image depends on post-excitatory inhibition of the red wave lengths emanating from the white stimulus (leaving green). When the total excitatory reaction to red is less than the total inhibitory reaction to red wave lengths in the white stimulus and the red image and the green induced negative after-image are alternated sufficiently rapidly for color fusion to occur the net result will be green. An increase in luminance of the white stimulus needed for reversal of color perception would indicate a relative decrease in inhibitory as compared to excitatory reactivity in systems

mediating color response. This could occur in the retina, as hypothesized by KLUVER (1942) or more centrally.

This line of reasoning permits the generation of a working hypothesis as to a mechanism that could produce hallucinations of color and design. A relative decrease in inhibitory as compared to excitatory reactivity in cone-based processes that mediate perception of color and detail would favor such imagery. The increased ability to discern color in a stimulus of low saturation and decreased ability to discriminate between color of adjacent hue (HOLLISTER and HARTMAN 1962) can also be explained on this basis. A decrease in inhibitory as compared to excitatory response in systems that perceive color would increase the ability to discern color in a stimulus of low color saturation. The ability to distinguish the color of a stimulus from one of the adjacent hue depends on the ability to limit visual response to those wave lengths actually emanating from the stimulus, an inhibitory function.

The report (CARLSON 1958) that LSD increased the photopic threshold does not fit with the hypothesis presented. He noted, however, that his subjects were not hallucinating when the thresholds were determined. Another study (KRILL et al. 1960) reports that photopic threshold determinations made while subjects were actively hallucinating were not elevated. In any event, it must be taken into account that any of the psychophysical measures described (threshold, after-image predominance, recognition of color in a stimulus of low saturation and color discriminations) may reflect different interactions of several visual mechanisms.

The hypothesis offered is useful in that it suggests further experimentation. It is similarly possible that the effects of Psilocybin are mediated at other levels of visual integration.

Summary

It is demonstrated in double-blind conditions that Psilocybin significantly changes an objective measure of after-image perception and that the occurrence of these changes is highly correlated with reports of altered visual experience. A hypothesis of how this effect and the findings of others can be explained on the basis of decreased inhibitory function in visual mechanisms involved in the perception of color and detail is presented with the caution that other explanations are possible. This study, and others, indicate the importance of knowing the nature of any subjective visual disturbance at the time that objective visual functions are performed to facilitate understanding of the mechanisms involved in hallucinogenic effect.

Appendix

Items of Major Visual Response:

1. Does there seem to be a wavering motion of solid objects?
2. Do the walls appear not to meet at right angles any more?
3. Do things seem to be moving around you?
4. Do people seem smaller?
5. Do people seem larger?
6. Do things seem to change in shape or proportion?
7. Do things appear to be closer than usual?
8. Do things appear to be farther away than usual?
9. Do textures seem to have a new richness?
10. Do details of objects change their relation to each other?
11. Do certain details seem to raise up and move away from other details?
12. Do objects or people appear to have colored lights or auras around them?
13. Do colors seem to change as you look at them?
14. Does the air appear to take on color and texture?
15. Do you see colors or designs on the wall or in the air?
16. With your eyes open, do you seem to see objects or animals or people?
17. With your eyes open, do you seem to see scenes or pictures?

Items of Minor Visual Response:

1. Does your vision seem blurred?
2. Does your vision seem more acute?
3. Do colors seem brighter?
4. Do certain details of things you look at seem to stand out?
5. Do certain objects seem to stand out?
6. Do you have trouble focusing your eyes?
7. Are after-images brighter?
8. Do after-images last longer?
9. Do the lights or lighting seem brighter?
10. Do the lights or lighting seem to change gradually?
11. When you close your eyes, can you see lights or colors or designs?
12. When you close your eyes, can you see objects or animals or people?
13. When you close your eyes, can you see geometric patterns or mosaics?
14. When you close your eyes, can you see landscapes or architecture?
15. When you close your eyes, can you see beautiful or fantastic scenes?

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