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Effect of Mescaline, Lysergic Acid Diethylamide and Psilocybin on Color Perception*

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With 1 Figure in the Text

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Enhanced color perception and vividly colored visual hallucinations are frequently reported by persons treated with psychotomimetic drugs (KLÜVER 1942; LANDIS and CLAUSON, 1954; ABRAMSON et al., 1955a; ABRAMSON et al., 1955b). These findings are not explained readily by neurophysiologic or psychophysiologic studies of the action of these drugs. In this respect, the vivid and unusual experiences of color associated with lysergic acid diethylamide (LSD-25) or mescaline intoxication seem paradoxical in view of evidence of increased thresholds for axonal response beyond the thalamic synapses (EVARTS, 1955; BISHOP, 1958), and demonstrations of increased absolute and differential limens for vision (CARLSON, 1958). If anything, these data suggest that the marked visual effects associated with the action of the psychotomimetic drugs are not due to increased sensitivity to the normally adequate stimuli for color visual experience.

Some clues to this apparent paradox are provided by the facilitating effects of sensory input from other modalities on the perception of visual hallucinations, commonly referred to as synesthesia. In such cases, perceptual responses may be evoked by stimuli which ordinarily evoke a separate sensory response, for example, sounds evoking colored patterns. One might hypothesize that some psychotomimetics interfere with the normal integration of experience within specific sensory modalities. The way we chose to test this hypothesis was to study the effects of stimuli varying in degree of adequacy for evoking color experience, both before and during the administration of three psychotomimetic drugs. The stimuli employed included those directly involving color perception (discrimination of hues and reports of colors of after-images), those usually marginal in terms of color experience (gazing at an episcotister),

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those usually completely devoid of visual experience (listening to pure tones) and a combination of the latter two stimuli.

A stimulus producing Provost-Fechner-Benham subjective colors was chosen as the marginally adequate stimulus for color experience (COHEN and GORDON, 1949). While most persons report some color experience when exposed to intermittent light (flicker), the colors are not reported as saturated to any great degree, nor are they especially distinctive. Moreover, the pattern of intermittent light or the illumination of the stimulus and background influence the adequacy of the stimulus. The specific stimulus used in the present study was pre-tested and found to be marginal in evoking colors without the administration of psychotomimetic drugs.

Methods

Design

The present study systematically compared three psychotomimetic drugs. Doses of drugs were fixed as follows: Mescaline, 5 mg./K; LSD-25, 1 mcg./K; psilocybin, 150 mcg./K. Volunteer subjects were tested at weekly intervals, order of drug presentation was randomized, and the subjects were unaware of the identity of individual test drugs. All drugs were administered as capsules indistinguishable from each other.

During each drug trial, measurements were made of the subject's reaction to the adequate and inadequate stimuli before and approximately two hours after drug administration. While subjects vary in regard to the times of maximal effect of these drugs, the period from two to three hours is always marked by conspicuous clinical effects. Three forms of analysis of drugs effects were made as follows: (1) Before-after drug administration differences; (2) subjects by trial analysis of variance of the pre-drug administration measures; and (3) complex mixed analysis of variance (effects due to subjects, drugs, and the interaction) of the after-drug administration measures, but if the before-after drug administration differences in a measure were insignificant, the more complex analysis was not undertaken.

Subjects were placed into three groups of six each as follows: Group A consisted of persons considered naive in regard to drug effects and psychological concepts. Group B was comprised of graduate students in psychology and Group C consisted of persons with high levels of education (graduate students) who were not particularly familiar with the drugs or the measurement variables used in this study.

Apparatus

Pure tone generator: A low frequency audio-oscillator coupled to low impedence earphones delivered pure tones of known frequency and amplitude to the subjects.

Episcotister. This unit consisted of a Stoelting color mixing wheel bearing a 180° black and white cardboard disk, powered by a constant current source transformer and controlled by a potentiometer. The four frequencies of rotation (flicker) used in this study to induce perception of hue from temporally varying, achromatic stimuli (Provost-Fechner-Benham colors) were calibrated with a Grass photic stimulator.

Color-Comparator. This unit consisted of a light-tight box with a one inch square sand blasted glass view plate. The view plate was set beneath a double slide rule type arrangement containing two slides, one for color and the other for brightness. The color slide was comprised of 14 Wratten filters as follows: 3 — light yellow, 9 — dark yellow, 23A — orange, 34 — light magenta, 36 — dark magenta, 45A — blue, 49 — dark blue, 48 — blue green, 52 — light green, 53 — medium green, 54 — dark green, C-05 — light violet, 29 — red, and 72B — brownish orange. The brightness slide contained squares of neutral density filters which ranged from .2 to .8.

Test Procedures Associated with Color Experiences

Color Discrimination. The Farnsworth-Munsell hue dicrimination test consists of 85 colored buttons arranged in four banks of graded hues: Red through yellow-green, yellow-green through blue-green, blue-green through purple-blue, purple-blue through red. Buttons from each bank were thoroughly mixed, and subjects were then asked to re-array them in the sequence of graded hues. The test was administered and scored in the standard fashion.

Afterimage series (AI). Subject was asked to fixate for five seconds on a 100-watt incandescent bulb located five feet ahead. He then closed his eyes and named colors as they appeared to him. After reporting that the AI had faded, he was requested to match each of the colors named during the trial. Records of colors matched and duration of the AI were kept.

Test Procedures Marginal for Color Experiences (Subjective Colors)

Color Perception Induced by Achromatic Stimuli (Flicker Frequency). Subject fixated on the episcotister located five feet ahead. The disk was illuminated by north daylight to approximately 3.2 ft. can. as measured three inches from the white sector of the disk. Four frequencies of rotation were used: 46 cps, 34 cps, 16 cps, and 8 cps. Orders of presentation were randomized, each subject receiving four trials on each occasion. Whenever the subject perceived color on or some place between himself and the disk, he was asked to match it as best he could with the color comparator.

Combined Flicker Frequency and Tone. Each subject viewed the episcotister for two randomized series of the four frequency settings

listed above. At each frequency setting, pure tones of 500 cps, 1000 cps, 2000 cps, and 4000 cps at 45 db, 40 db, 35 db, and 30 db respectively were presented. The tone was presented for approximately three seconds, and the subject was asked to pause five seconds before reporting and comparing any color or visual imagery which was induced by the combined flicker and tone.

Test Procedure Devoid of Color Experiences

Pure Tone. Each subject was instructed to close his eyes and listen for the sound. If he reported visual imagery or color, he then opened his eyes and matched the perceived color on the color comparator scales. Sixteen tones were presented, divided evenly among the four frequency settings. Order of presentation was randomized for each subject and each trial. Throughout all these tests, excepting that for color discrimination, subjects wore a light-tight face mask with a 4 mm. artificial pupil cut for the right eye. Thus all measures were for monocular viewing.

Results

Effects of the Trials (Pre-drug administration measures)

The criteria measures which showed a significant pre-drug effect due to the sequence of trials were the color discrimination test (F 7.68, df 2 and 34, p .05), and color evoked by flicker (F 4.12, df 2 and 32, p .01). (Table 1.) Further analysis (t-tests) demonstrated that in each

Table 1. *Summary of trend analyses of the effects of trials with pre-drug administration measures*

Measure	Mean square Effect of trials	Mean square Subjects × trials residual	df	F [1]
Color discrimination	3130.89	407.87	2 and 34	7.68
After-image: Colors matched	0.30	0.83	2 and 32	—
After-image: Duration . . .	220.85	288.55	2 and 32	—
Flicker	30.26	7.34	2 and 32	4.12
Combined Flicker and Tone .	2.90	216.53	2 and 32	—
Pure tone.	No analysis attempted			

[1] 2 and 32 degrees of freedom = 3.30 is significant at the .05 level
5.34 is significant at the .01 level
2 and 34 degrees of freedom = 3.28 is significant at the .05 level
5.29 is significant at the .01 level

case the differences due to the trials was a function of the comparisons of the first and second pre-drug trials. Thus the trials effects were due more to the practice the subjects received on the first trial rather than a cumulative drug effect over the entire series of trials. As each drug

was administered equally often in each position in the sequences, there should be no reason to believe that any systematic bias was introduced. For the remaining criteria measures, changes in performance due to the trials was not significant.

Stimuli Associated with Color Experience

Color Discrimination test. Before-after drug administration comparisons (t-tests of correlated means) showed that total error scores were increased by all drugs, but only by psilocybin to a significant degree ($t = 2.51$, $df = 17$, $p < .02$). (Tables 2 and 3.) Analysis of between-drug differences, however, failed to demonstrate that the three drugs differed from one another. Interaction between the groups and drug treatment effects was significant at better than the .05 level, ($F = 3.55$, $df = 4$ and 30). (Table 4.) Further analysis showed that this interaction was due to the naive group's decreased hue discrimination when LSD-25 and mescaline were administered.

Table 2. *Summary of effects of psychotomimetic drugs on hue discrimination (before-after comparisons)*

Drug	Discrimination error within hues	df	Sum of differences	Standard error of differences	t[1]
LSD-25	Total	20	−203	121.5	−1.67
Mescaline	Total	20	−103	124.6	−0.83
Psilocybin	Total	19	−208	83.0	−2.51
LSD-25	Area R—Y	19	− 73	25.5	−2.86[2]
	Area Y-O	19	− 83	32.3	−2.57
	Area G—B	19	+ 36	67.5	0.53
	Area B—P	19	− 14	30.3	−0.46
	Area Violet				
Mescaline	Area R—Y	19	− 86	43.9	−1.96
	Area Y—O	19	− 42	38.5	−1.09
	Area G—B	19	−124	62.6	−1.98
	Area B—P	19	− 46	28.8	−1.60
	Area Violet	19	− 28	43.8	−0.64
Psilocybin	Area R—Y	19	− 41	22.2	−1.85
	Area Y—O	19	− 36	23.2	−1.55
	Area G—B	19	− 24	38.3	−0.63
	Area B—P	19	− 38	26.1	−1.64
	Area Violet	19	− 50	24.2	−2.07

[1] For 19 degrees of freedom $t = 2.09$ is significant at .05 level

[2] $t = 2.86$ is significant at .01 level

The effects of the drugs on color discrimination differed for various hues. LSD-25 increased errors significantly in the red-yellow and yellow-orange areas ($t = 2.86$ and 2.57 respectively, $p = .01 < .02$), with little other effect (Table 2). Mescaline increased errors throughout a wider

range of hues, approaching significance in red-yellow and green-blue areas. Psilocybin increased errors in all areas, approaching significance in the violet area, but curiously sparing the green-blue area.

Table 3. *Summary of mean scores of stimuli before (B) and after (A) drugs*

Mean scores of stimuli	LSD		Drugs mescaline		Psilocybin	
	B	A	B	A	B	A
Total errors in hue discrimination	45.2	52.0	45.7	49.6	31.6	43.2[1]
Duration of after-images (seconds)	100.1	102.3	97.7	104.3	87.7	97.7[1]
Number of after-image colors matched	4.4	5.7[1]	4.3	5.4[1]	4.1	4.9[1]
Colors evoked by flicker	4.4	13.7[1]	4.8	16.2[1]	4.7	8.8[1]
Colors evoked by flicker and tone simultaneously (increase over flicker alone)	2.2	4.7[1]	3.2	2.2	3.3	1.3
Colors or other visual effects from pure tone	0.3	3.0[1]	0.2	2.7[1]	0.3	1.1

[1] p-value of .05 or less, t-test of correlated means.

Table 4. *Summary of the mixed analyses of variance of the effects of the drugs, the groups, and the interaction of these effects*

Measure	Effects		
	Groups F	Drugs F	Interaction F
Errors in hue discrimination	2.73	1.89	3.55[1]
Duration of after-image	<1.0	<1.0	1.10
Colors of after-images	3.58	2.33	<1.0
Colors evoked by flicker	1.27	7.95[2]	<1.0
Colors evoked by combination of tone and flicker	8.08[2]	2.14	1.95
Colors evoked by tone	<1.0	2.57	1.80

[1] $p<.05$. [2] $p<.001$.

Afterimage (AI) measures. Tests of differences *within* each drug treatment indicated that only psilocybin significantly increased duration of AI ($t=2.44$, $df=17$, $p<.02$); the other drugs tended to increase duration slightly (Table 3). All three drugs significiantly increased the number of AI colors reported and matched at better than the .05 but less than the .01 level. Analysis of *between* groups and drug treatment effects failed to show significant differences either in duration of AI or number of AI colors (Table 4).

Stimuli Marginal for Color Experience

Flicker. All three psychotomimetic drugs significantly increased perception of subjective colors evoked by flicker (episcotister presentation), a normally marginal stimulus. These differences were significant at better than the .001 level (Table 3).

Mixed analysis of variance of *between* drug effects showed a highly significant effect ($F = 7.95$, $df = 2$ and 30, $p < .001$) (Table 4). Further analysis (t-tests) indicated that the large difference was due to the comparisons of LSD-25 and mescaline with psilocybin. LSD-25 and mescaline were both associated with significantly more color responses from this stimulus than was the case for psilocybin (Table 5). The colors reported from various flicker presentations were similar from LSD-25 and mescaline; colors reported from psilocybin covered more of the spectrum though less frequently evoked.

Table 5. *Summary of within drug and between drug comparisons (before-after drug administration) differences in colors perceived as a result of flicker frequency*

Within drug	df	Sum of difference	Standard error Sum of difference	t[1]
Within drug				
LSD-25	18	183.0	33.6	5.45[2]
Mescaline	17	209.0	33.7	6.19[2]
Psilocybin	18	101.0	26.2	3.85[2]
Between drugs				
LSD-25 and mescaline . .	17	−44.0	30.5	1.44
LSD-25 and Psilocybin . .	17	88.0	33.8	2.60[1]
Mescaline and psilocybin .	17	130.0	45.4	2.86[1]

[1] For 17 degrees of freedom, t's = 2.11 and 2.90 are significant at .05 and .01 levels respectively.

It became apparent that some subjective colors were more often reported after flicker than others (Fig. 1). Further, the frequency of reports of color seemed to be correlated with degree of error in hue discrimination in the same spectral areas. Ranking both sets of measures from high to low across areas of red-yellow, yellow-green, green-blue, blupurple and purple-red-purple, correlations were —.60, —.90 and —.90 for LSD, mescaline and psilocybin respectively. Thus, decreased color sensitivity to relatively monochromatic light was related to lower appreciation of sujective colors evoked by intermittent light in the same spectral areas. No such correlations could be demonstrated for before-drug measurements, but in this instance subjective colors were infrequently reported and with less reliability than following flicker.

Combined flicker and tones. Before-after drug differences in subjective colors beyond those evoked by flicker alone were significantly increased

for LSD-25 ($t = 2.43$, $df = 18$, $p < .05$), but not for mescaline or psilocybin. Moreover, there was a highly significant groups effect ($F = 8.08$, $df = 2$ and 15, $p < .001$), but effects attributable to the drugs and the groups by drugs interaction were not significant (Table 4). The significant groups effects was further analyzed and the difference was found to be

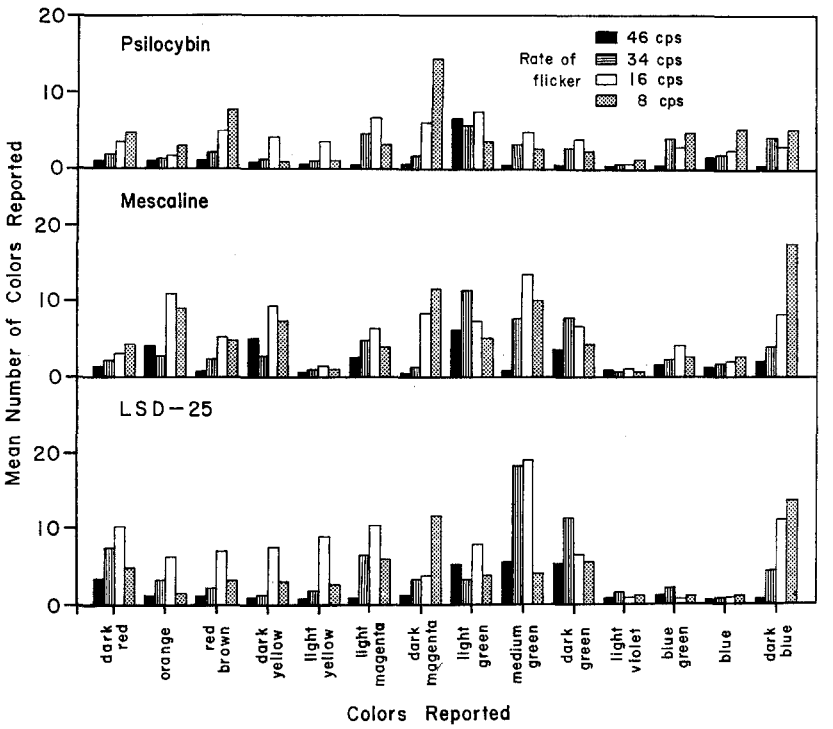

Fig. 1. Spectrum of colors reported from the three drugs at varying rates of flicker

attributable to the sophisticated subjects-Group C. Unfortunately this group was tested by a different experimentor on this particular measure, and the most parsimonious explanation is that directions given this group were somewhat different.

When the subjects were intoxicated with LSD-25, combined flicker and tone stimulation led to responses beyond those elicited by flicker or tone alone, indicating some degree of facilitation of color experience due to stimulation by the ordinarily inadequate stimulus in conjuction with stimuli which is marginal for evoking color experience.

Stimulus Devoid of Color Experience

Pure Tones. Less than fifty percent of the subjects perceived colors after stimulation with pure tone, but other visual effects were more

frequently reported. These effects were described as brightening of the visual field, shattering of patterns, or patterning of form within the visual field. To provide some basis for statistical evaluation, frequency of color responses was combined with the frequency of the reports of other forms of visual imagery; for example, patterns movement and brightening of the visual field. Before-after drug administration differences in visual effects associated with sound were highly significant ($p < .001$) for LSD-25 and mescaline; however, analysis of treatment effects *between* the three drugs failed to demonstrate significant differences (Table 4).

The low incidence of color experience evoked by tones compared with other stimuli indicated that reports and comparisons of colors were not indiscriminately made. In short, the criteria measures did not appear to be indiscriminant or due to suggestion but were valid experiences of the subjects when treated with the drugs and subjected to the stimulus conditions described in this research.

Discussion

All three psychotomimetic drugs increased color experiences elicited from a variety of stimuli. This was true regardless of whether the stimulus was one which might frequently elicit some color experience (colors in after-images), one which marginally produces subjective colors (flicker) or one which never produces colors or other visual effects (pure tones). It is curious that a test which does not call for introspective reports, such as hue discrimination, showed some deterioration under the drugs, specific drugs tending to affect certain spectral areas. Thus, given some basis for the initiation of color experience, introspective reports of color were increased under the drugs. The effects of a stimulus completely devoid of color experience ordinarily (pure tone) were of much smaller magnitude. Yet clinical evidence suggests that such synesthesia is real, indicating that possibly the doses of drugs in this study or the experimental setting may have tended to mask this effect.

Two other findings also raise questions for further study. First, subjects showing some degree of "blindness" for certain spectral elements, as measured by errors in hue discrimination, also failed to perceive these colors when responding to inadequate stimuli during drug treatment. Second, frequency of flicker, within certain limits, correlated inversely with the number of colors evoked from the inadequate stimulus. These limits must be more clearly defined, and the effects of frequency of flicker on specific visual areas (especially the lateral geniculate) of animals might well be studied both with and without the influence of psychotomimetic drugs.

A number of interesting differences between the drugs emerged. Psilocybin impaired hue discrimination over a wider spectral range than the other two drugs. On the other hand, both LSD-25 and mescaline caused more colors to be evoked by flicker, but LSD-25 alone increased color experiences when flicker and tones were combined. Both LSD-25 and mescaline were more likely to evoke the phenomenon of synesthesia in contrast with psilocybin. These results tend to confirm clinical impressions that hues are neither as vivid nor as varied in the imagery produced by psilocybin as with the other two drugs.

While we believe our data indicate that the three drugs tested act similarly in enhancing visual responses to various stimuli, obviously much more is involved in producing a visual hallucination. Clinically, such hallucinations have content as well as form and color and along with other mental states (introspection and "déjà vu" phenomena) resemble the effects of some stimulations of the temporal lobe in conscious subjects (PENFIELD, 1959; HOLLISTER, 1961). Seizure-like discharges in temporal cortex and associated limbic system structures of the cat has been recorded during the action of cyclohexamines, a somewhat different class of psychotomimetic drug (ADEY and DUNLOP, 1960). Other evidence indicates that surgical ablations in these areas affect visual discrimination (PRIBRAM and MISHKIN, 1956). It is possible that the temporal lobe as well as the central visual pathways are involved in distortions of color perception.

Summary

Twenty subjects were given three psychotomimetic drugs (mescaline, LSD-25 and psilocybin) in fixed doses, 18 receiving all three. Color experience was tested by applying stimuli involving color perception, stimuli eliciting subjective colors, and stimuli usually devoid of visual experience.

Almost all measures of color perception were affected. Hue discrimination was decreased significantly by psilocybin, to a slightly lesser extent by the other two drugs. Color reports in after-images were significantly increased by all three drugs, but duration of after-image was increased significantly only by psilocybin. Elicitation of subjective colors from flicker was increased by all three drugs, significantly more by mescaline and LSD-25 than by psilocybin. The combination of flicker and pure tones evoked more color reports than flicker alone. The increase was significant only after LSD-25, no significant differences being demonstrated between the effects of the three drugs. Visual effects, both colors and patterns, elicited by pure tones were significantly increased by LSD and mescaline, though these effects were not great at the

doses used in this study. Spectral patterns of evoked colors varied slightly between the three drugs.

These results are interpreted as indicating that stimuli which evoke subjective color phenomena, or even those not usually associated with visual phenomena, are enhanced by psychotomimetics. On the other hand, the usual perception of color, as judged by hue discrimination, may actually be slightly decreased.

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