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EFFECT OF LSD ON VISUALLY EVOKED RESPONSES TO COLOR IN VISUALIZER AND NON-VISUALIZER SUBJECTS

BARBARA B. BROWN, PH.D.

Experiential Physiology, Veterans Administration Hospital, Sepulveda, Calif. 91343, and Department of Psychiatry and Human Behavior, U.C.I. College of Medicine, Orange, Calif. (U.S.A.)

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INTRODUCTION

The visually evoked cortical response (VER) in man is reported to differ markedly from subject to subject (Ebe *et al.* 1962; Rietveld 1963; Rietveld and Tordoir 1965) but to remain relatively constant in the same individual over long periods of time (Dustman and Beck 1963; Rietveld 1963). Certain components of the VER reflect visually conducted information as influenced by other neuronal activity related to awareness, attention, perception, and even cognitive ability (Chalke and Ertl 1965; Spehlmann 1965; Callaway 1966; Sutton *et al.* 1967) and may also reflect characteristics of color perception (Monnier *et al.* 1964; Shipley *et al.* 1965). In an earlier study, we related red specific EEG responses to flickering light to degree of visual imagery ability (Brown 1966). The present study was made to determine whether a similar relationship held for VERs to color, and whether LSD-induced enhancement of visual perception could be detected in the VERs to color.

METHOD AND MATERIAL

The data were obtained during experiments from which EEG results have been reported (Brown 1968a). Two groups of subjects were employed. One group of seven was classified as possessing vivid visual imagery ability (claimed "projected" images; *i.e.*, occupied real visual space). A second group of seven was classified as non-visualizers (claimed total absence of visual imagery ability). For other details including those of experimental procedure see the previous papers (Brown 1968a,b).

Fifty flashes were given during the control period for each color condition: white, white while counting the flashes serially, red, blue and green, and were repeated at 40, 80 and 160 min intervals following LSD. Order of the colors was randomized.

Results obtained during the 160 min interval after LSD (0.75–1 μg/kg orally) showed optimal changes and only these are reported.

For analysis the 50 responses for each color condition were summed (CAT 400), using an analysis time of 250 msec. Latencies and peak-to-peak voltages were measured from the responses written out by means of an X–Y plotter.

To analyze these VERs further, all successive, readily identifiable peaks and inflection points were initially measured and grouped. Although a number of trends of cumulative effect were noted, inter-trial variation eliminated all but a few peaks from further consideration. After further analysis of pre- and post-drug VERs, 4 negative peaks were selected. These were peaks which could be identified in both the control and post-LSD responses in all subjects. The criteria required for each of these were: (a) peaks which could be readily identified as dominant peaks in the majority of color VERs and in the majority of subjects both before and after drug; (b) for this majority, a continuing voltage development after change in direction of at least 25% of the largest peak (measured in mm from X–Y plots of the summed responses) occurring in any of the subject's VERs to the 5 color conditions; (c) occurrence within a pre-selected time range, es-

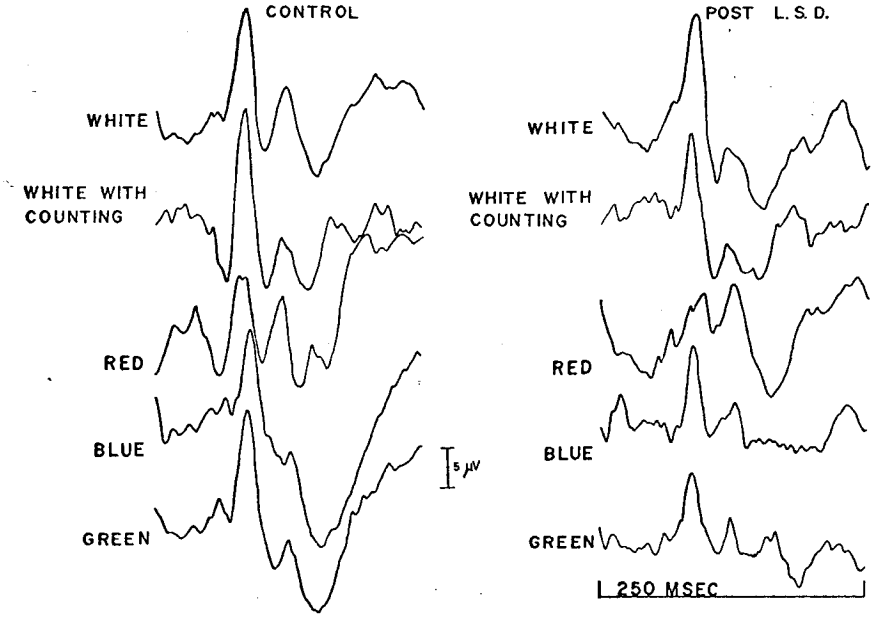

Fig. 1
Examples of VERs to color recorded from right occipital bipolar electrodes in a non-visualizer subject. Each trace is the average of 50 responses (CAT 400).

tablished from the values of times to the highest peaks across all subjects; and (d) by the number of major peaks of similar character which preceded it.

RESULTS

Examples of VERs to color before and after LSD are shown in Fig. 1 for a non-visualizer subject. This is included to indicate the types of differences found among the 5 dimensions of the experiment and the necessity for analyzing the data in terms of patterns.

Average times for the occurrence of each of the selected negative peaks for the two groups of subjects are summarized in Table I. Owing to inter-subject variation, *average* times for individual peaks fell within similar ranges and indicated relatively little change with either change of color or effect of LSD for the majority of responses.

Because of these intra-subject differences as well as the inter-subject differences in pattern, information about the average times for each peak as a function of color did not prove to be a satisfactory index. Further, it was not so much the absolute time of the peak that was important, but (1) the relative times of the same peaks for different colors in an individual subject, and (2) the effect of LSD on these relative times as a function of color.

The difficulties inherent in comparing complex patterns in relation to a variety of variables made it desirable to reduce the quantitative peak times (in msec) to qualitative "ranks" to facilitate these comparisons. The peak patterns were compared along the 5 dimensions of the experiment, namely: (1) visualizers *vs.* non-visualizers; (2) individual subjects within each of these groups; (3) control *vs.* LSD responses; (4) the 5 different colors; and (5) the 4 peaks in the evoked response selected for analysis.

To simplify the comparisons we started with the individual peaks in the evoked response for a single individual. We then scaled the latency times to these peaks in relation to the 5 color situations in the following fashion: for a given peak, for example the second negative peak in a subject's VER, we assigned the number 1 to the *shortest* time for that peak which occurred among

TABLE I

Average times in msec to major VER negative peaks*

Subject group	Color	Control				Post-LSD			
		1	2	3	4	1	2	3	4
Visualizers (7)	White	19	67	103	171	27	52	101	140
	White, counting	25	60	116	165	32	51	100	142
	Red	22	54	109	152	24	59	101	149
	Blue	22	63	107	147	23	59	101	136
	Green	25	63	102	150	27	46	85	129
Non-visualizers (7)	White	35†	67	108	143	32	65	101	140
	White, counting	34	51	96	180	0	57	97	146
	Red	30	57	102	186	35	66	95	163
	Blue	33	62	102	166	32	57	97	156
	Green	31	58	102	173	34	58	97	144

* Standard errors ranged between 9 and 19% of the means for peak 1, between 4 and 14% for peak 2, and 7–10% for peaks 3 and 4.
† All initial negative peaks significantly different between the two subject groups at the 0.02 level (Chi Square Median Test).

the 5 color responses (*e.g.*, this might be for the color red). For the *same* subject and the *same* peak number, the next shortest time was then assigned the number 2 (*e.g.*, the peak in response to white). Times which did not differ by at least 25% were counted as "equal". Thus, if the next shortest time was *not* different by 25%, it also received the rank number 2. Hence for a given subject, if the latencies for each of the 5 color situations differed successively by exactly 25%[1], the resulting "ranks" among the 5 color latencies of a particular peak would be 1, 2, 3, 4, 5.

If some differences for the same peak among the 5 colors were less than 25%, the pattern of "ranks" might be of the following type:

Red	White	White with counting	Blue	Green
1	2	2	2	3

[1] This lower bound of 25% change, required of successive peak times before they were given different "ranks", was assigned on the basis of the standard errors for the averaged peaks given at the bottom of Table I. As an example, if the standard error is 10% of the mean value, and 3 times the standard error is used as the criterion for significance of the differences, then the range of values for any individual peak could contain at least 3 intervals of 25% differences between minimal and maximal values. If, however, the values for the same peak are averaged across *all* colors, the variation is increased, the standard error becomes somewhat larger and 4 intervals of 25% differences are possible.

For some other individual, the pattern of "ranks" for this same peak might be:

Red	White	White with counting	Blue	Green
1	2	1	2	2

After the ranks were assigned in this way for each subject and for each of the 4 peaks, the ranks for a given peak were averaged *across subjects* within the visualizer group. Similar averages were obtained across subjects within the non-visualizer group. These averages were calculated both for the control and for the post-drug conditions.

"Ranks", obtained and averaged in this fashion, are presented in Table II. In this Table, comparisons are meaningful down any column, but not along the rows. Each column should be inspected for its pattern of ranks, and then this *pattern* (not the individual numbers) should be compared between control and post-drug conditions, between visualizers and non-visualizers, and between successive peaks. This makes more apparent the rationale for assigning the ranks. Results in Table II show that an average rank of 3 or more occurred only in 4 instances out of the total of 80 peaks ranked (an incidence of 5%). For a given column within an experimental "block" in this table, the 5 average ranks were inspected for values that deviated significantly

TABLE II

Averaged ordering of VER latencies*

Subject group	Color	Control				Post-LSD			
		1	2	3	4	1	2	3	4
Visualizers (7)	White	2.0	*1.6*	1.5	1.2	2.0	2.0	1.8	1.2
	White, counting	*3.2*	2.4	1.0	1.0	*1.0**	1.6*	2.2*	1.2
	Red	2.2	*1.4*	1.3	1.5	*1.3**	2.0	1.7	*2.4**
	Blue	2.4	2.4	1.4	1.5	2.0	2.6	2.0	1.2
	Green	2.5	2.4	1.6	1.6	2.2	3.0	1.3	1.0*
Non-visualizers (7)	White	1.8	2.2	1.2	1.6	1.8	2.0	2.2*	1.8
	White, counting	1.8	1.8	1.5	1.6	1.7	1.5	1.7	2.0
	Red	*1.0*	1.6	1.8	*2.4*	*2.6**	*3.0**	1.7	*2.5*
	Blue	1.6	1.8	1.5	2.0	*3.0**	1.7	1.8	1.7
	Green	1.7	2.2	1.6	*1.2*	*2.6**	*2.6*	1.7	*1.0*

* Significant differences (by Student's *t*) are indicated as follows: (a) values in italics are significantly different from those for other color conditions for the same peak number (comparisons down columns); (b) values with asterisks are significantly different from comparable control values.

from the others in that column. Such deviant values are italicized. In each control group (left half of Table II), only 3 rank averages of 20 were significantly different (in italics). Following LSD, the incidence of significant differences increased to six of twenty for visualizers and five of twenty for non-visualizers.

Discussion of the following results was based upon the two criteria[1]: (1) a tendency was assumed when the significance of the difference between any *individual* comparable peaks was at the 1% probability level (Student's *t*), and (2) a real difference between experimental and control data was assumed when at least *two* peaks for any individual VER in one block were significantly different (to the 1% level) from values for comparable peaks in the corresponding VER in the other "block".

A comparison of *column* patterns isolated differences between visualizer and non-visualizer subjects during both experimental conditions.

[1] Since averages of ranks were used to determine significance of differences and since each number represented a 25% difference, the probabilities of extracting significant differences had been reduced. Significance of the results was increased further by requiring that at least 2 peaks of a VER in the experimental "block" (tabulated data for each of the 4 possible combinations of experimental group and conditions) be significantly different from comparable peaks in the corresponding VER in the control block. Such significant differences are marked by asterisks in Table II.

In *visualizers*, averages for ordering of latencies (Table II) revealed no outstanding differences among the color responses except for a tendency for a longer latency for peak 1 for the white while counting reponse and tendencies for shorter latencies for peak 2 in the responses to white and red. A comparison of row patterns within the control block for visualizers indicated that wave form configurations for white and red differed from those for blue and green. After LSD only the VERs to white while counting and to red were significantly changed. The response to white while counting was markedly changed in configuration as indicated by acceleration of peaks 1 and 2 and a slowing of peak 3. The VER to red showed acceleration of peak 1 and slowing of peak 4. A comparison of row patterns indicated that the VERs to white, blue, and green were little changed by LSD in the visualizers.

In *non-visualizers*, differences in VERs for the 5 color conditions in the control block were quite small for peaks 1 and 2 (lower rank averages) as compared to those for the visualizers. The marked differences of peaks 1 and 4 of the VER to red indicate the considerable differences of wave form configuration as compared to that for the other colors. Except for this difference (to red), times for individual peaks were similar for all responses (row patterns) within this block. Following LSD, the latencies for peak 1 showed significant slowing in the VERs to all 3 colors

TABLE III

Average ordering of the largest VER amplitudes

Subject group	Condition	White	White, counting	Red	Blue	Green
Visualizers (7)	Control	2.7	1.6*	2.7	2.0	2.3
	LSD	2.1**	1.6	2.1**	2.4	2.4
Non-visualizers (7)	Control	2.3	1.1	2.2	2.2	1.8
	LSD	1.6	3.0***	2.0	2.1	1.6

* Increase over white and red significant at 1% level (Student's t).
** Increase over control significant at 1% level (Student's t).
*** Decrease from control significant at 1% level (Student's t). Largest of the 4 peaks among the 5 colors was given a value of 1. Values of 2, 3, 4 and 5 were assigned to those peak amplitudes of corresponding latency smaller by successive 25% increments.

but not in the VERs to white or white during counting (comparison of *column* patterns). Comparisons between data blocks for the experimental conditions revealed marked slowing of peaks 1 and 2 in the post-LSD response to red indicating change in wave form configuration. Ranks of latencies of the VER to white while counting were virtually unchanged by LSD.

A position ranking technique was also used to evaluate changes in amplitude of the VERs found for the different conditions of the study. The *largest* of the 4 peaks occurring among the 5 VERs for each subject was assigned a value of 1, and values of 2, 3, 4 and 5 to those peak amplitudes of corresponding latency which were smaller by successive 25% decrements. The remaining 3 selected peaks were not analyzed. The ranks thus obtained for each color VER were then averaged for the subjects of each group and for each experimental condition (Table III). *Visualizers.* Ordering of the amplitudes for the visualizer group showed that the largest amplitudes occurred in the VER to white while counting, and that the corresponding peaks in the VERs to white and red were the smallest. After LSD, amplitudes of the VERs to white and red were reduced in amplitude whereas amplitudes of the other color conditions were relatively unchanged. *Non-visualizers.* As in visualizers, maximal amplitudes also occurred in the VERs to white while counting in spite of the differences in ranks of *latencies* between the two groups. For the non-visualizers, however, no consistent differences among amplitudes of the color VERs were found. Moreover, LSD did not affect amplitudes of any of the color responses. Amplitude of the VER to white was slightly enhanced but the response to white while counting was markedly decreased.

EEG and subjective changes. During both control and post-LSD recording periods, 60% of all subjects retained an alert EEG pattern throughout presentation of the light stimuli. Alpha activity occurred irregularly in the other subjects, but occurred less frequently in the non-visualizers. Following LSD the activation pattern became more intense in the visualizer subjects and less intense in the non-visualizers. Analysis of level of EEG activation for these subjects has been reported (Brown 1968a).

All visualizer subjects reported that the colored light stimuli seemed more intense after LSD and volunteered information as to their beauty, patterns, and interest. In contrast, the non-visualizers expressed little interest in the colors either before or after LSD.

DISCUSSION

The differences in VERs to different color conditions found between visualizer and non-visualizer subjects demonstrate differences in central data processing between the two subject groups. The VERs of visualizer subjects evidenced a tendency for color specificity indicated by differences in both latency and amplitude values when responses to white and to red were compared to those to blue and to green. The VERs in non-visualizer subjects were remarkably like each

other except for the VER to red. Ranking of latency and amplitude values revealed that the response configurations for all VERs differed between the two groups. The color responses of the two groups were, moreover, affected differently by LSD.

The differences in VERs to color and their differing changes after LSD between the two subject groups are similar to those reported using colored flickering light and EEG photic following responses (Brown 1968a).

The different configurations found for the VER to red is similar to the result obtained by Monnier *et al.* (1964) and by Shipley *et al.* (1965), both of whom found the VER to red different from that to blue. Monnier *et al.* (1964) also reported VER wave forms to red to be independent of events at the retina. The present report supplies additional information about the peculiarities of the VER to red by the finding that among color VERs, that to red was the most susceptible to effect of LSD and was different for the two subject groups.

The tendency for visualizer subjects to exhibit different wave form characteristics for different sets of colors (red, white *vs.* blue, green) may be a correlate of visual imagery ability. The VER wave forms for blue and green were not significantly changed by LSD and, with the exception of red, relationships among the color responses (both row and column patterns) were not changed. As contrasted to the changes seen for the non-visualizer group, this evidence could suggest the visualizers discriminated and perceived the colors similarly both before and after LSD. The failure of non-visualizer subjects to show significant central color discrimination, except to red, *before* LSD and to show only suggestive evidence of a change in latency but not amplitude of the color VERs *after* LSD parallels the subjective reports that non-visualizers not only lack visual imagery ability, but experienced no conscious change in visual perception after LSD. Employing a somewhat similar technique of analysis, Begleiter *et al.* (1967) found that change in affective meaning of the stimulus significantly altered configuration of the VER. This suggests that colored stimuli may contain greater affective significance for visualizers than for non-visualizers, and indirectly relates such differences in visual perception to the differences in visual imagery ability of the two groups.

An additional indication of difference in perceptual activity was that latter components of the VER to red in visualizers after LSD and in non-visualizers both before and after LSD were significantly different than for the other color conditions. Latter components of the VER as indicators of perceptual activity has been demonstrated by Sutton *et al.* (1967) and John *et al.* (1967).

It has been reported (Eason 1964; García-Austt *et al.* 1964; Donchin and Lindsley 1966) that VERs are enhanced during attentional states accompanied by activated EEGs. In the present study EEG activation levels were higher in non-visualizers during the control periods but were lower than those of the visualizers following LSD; however, these changes were not paralleled by absolute changes in VER amplitudes. Recent studies have shown, however, that selective attention, rather than non-specific attention or vigilance, yields VERs of enhanced amplitude (Haider *et al.* 1964; Spong *et al* .1965). The VER to white while the subject counted the flashes was used as a rough index of effect of increased level of attention. The two subject groups differed significantly in their VERs to this condition both before and after LSD. In the visualizer group this response resembled more closely the VERs to blue and green in both latencies and amplitude, and after LSD not only continued to be maximal in amplitude but also showed accelerated early peak times. Such evidence of an enhanced response may relate to the reported increase in visual interest of the visualizers.

In sharp contrast, in the non-visualizer group the VER to white while counting the flashes was virtually identical to the other VERs (except red) in latencies and these were completely unaffected by LSD. The amplitude of this response was markedly suppressed after LSD and may relate to the lack of change in visual perception reported by this group, and in fact, suggests a loss of externally or perceptually directed attention.

SUMMARY

1. The visually evoked responses (VERs) to color of visualizer subjects evidenced a signifi-

cant degree of color specific characteristics and selective alteration in color specificity after LSD. The changes were somewhat more pronounced in the amplitude domain. Configuration of the VER to white and red were consistently different from those to blue or green. Visualizers also reported enhanced visual perception after LSD.

2. In non-visualizer subjects the VERs to all color conditions except to red were virtually identical. Following LSD, early components of all 3 color VERs, most noticeably for red and green, were changed in configuration, all changes being in the latency domain.

3. Maximal amplitudes occurred in the VERs to white while counting the flashes in both subject groups. After LSD this was unchanged in visualizers but was markedly attenuated in responses of the non-visualizers.

4. A technique for ranking components of a complexly organized set of responses was used which permitted extraction of critical data from a complex of intercurrent intra- and inter-subject variation. The technique isolated patterns of response by which changes over time could be conveniently compared within and between subject groups, and as these were affected by the experimental condition. This proved useful in isolating significant differences in a multidimensional system in which the external stimuli, light and LSD, were both contained within reasonable physiologic and pharmacologic limits.

RÉSUMÉ

EFFET DU LSD SUR LES RÉPONSES ÉVOQUÉES À LA COULEUR CHEZ DES SUJETS AVEC ET SANS IMAGERIE MENTALE

1. Les réponses évoquées visuelles à la couleur chez les sujets avec imagerie mentale montrent un degré significatif de caractéristiques spécifiques à la couleur et une altération sélective dans la spécificité des couleurs après LSD. Ces changements concernent surtout l'amplitude. La configuration de la réponse évoquée visuelle au blanc et au rouge est nettement différente de celle au bleu et au vert. Les sujets avec imagerie mentale rapportent également un accroissement de la perception visuelle après LSD.

2. Chez les sujets sans imagerie mentale, les réponses évoquées visuelles à toutes les conditions de couleur, excepté le rouge, sont virtuellement identiques. Après LSD, des composantes précoces des réponses évoquées visuelles aux trois couleurs, et plus particulièrement au rouge et au vert, sont changées dans leur configuration, ces changements affectant les latences.

3. Les amplitudes maximales s'observent pour des réponses évoquées visuelles au blanc lorsque les sujets des deux groupes comptent les éclairs. Après LSD ceci est inchangé chez les sujets avec imagerie mentale, mais est nettement atténué pour les réponses des sujets sans imagerie mentale.

4. Une technique de rangement des composantes d'un jeu de réponses à organisation complexe est utilisée pour permettre l'extraction des données saillantes d'un ensemble de variations intercurrentes intra- et inter-individuelles. Cette technique isole des patterns de réponses au moyen desquels des changements dans le temps peuvent être convenablement comparés à l'intérieur des groupes et entre les groupes, et leur sensibilité à la condition expérimentale mesurée. Cette technique s'est révélée utile pour isoler des différences significatives dans un système multidimensionnel dans lequel les stimuli externes, la lumière et le LSD, étaient contenus à l'intérieur de limites à la fois physiologiques et pharmacologiques raisonnables.

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