EFFECT OF LYSERGIC ACID DIETHYLAMIDE (LSD-25) ON THE ABSOLUTE VISUAL THRESHOLD

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The importance of lysergic acid diethylamide (LSD) lies largely in the temporary psychotomimetic effects it produces without at the same time debilitating *S* or causing serious side reactions. Distortions in visual perception and hallucinogenic effects have figured prominently in the psychiatric literature on LSD, and certain electrophysiological findings are available. The present study is concerned with determining whether LSD raises the absolute visual threshold in man, and, if so, whether this effect seems to be due to the interference of LSD-induced hallucinatory activity or to a more direct depression of neurophysiological function.

Apter and Pfeiffer (1) have concluded that LSD-induced hallucinogenic activity depends upon spontaneous action potentials produced intraocularly and elaborated through further facilitatory effects on synaptic transmission in the afferent visual pathways. Under these circumstances one would expect the psychophysical visual threshold to be raised, because *S* would have to discriminate the test stimulus from the additional perceptual phenomena arising within the visual system itself. These interfering effects should in addition increase the variability of the threshold, since the subjective manifestations presumably shift and vary from moment to moment (9). LSD also has certain inhibitory effects, however, on cortical synaptic processes, so that depression of perceptual sensitivity independent of any supposed hallucinogenic activity is possible.

METHOD

Subjects

Seven male and two female normal volunteers, approximately 20 years of age, served as *S*s for this study. All had had previous experience with LSD, from which it was determined whether 50 μg. or 100 μg. would produce a strong subjective effect in *S* without making him unduly sick. Three *S*s could tolerate only 50 μg. about as well as the other six could tolerate 100 μg., and these were the dosages used. A tenth *S* became sick with 50 μg. and could not complete the experiment. All *S*s reported a strong general subjective effect from each administration of the drug.

Apparatus and Procedure

A modified Hecht-Shlaer adaptometer was used, providing a large light-adaptation field of 12 log μμL., a small red fixation point, a 2° circular test stimulus, and a shutter-controlled stimulus exposure of 1/5-sec. Operation of the shutter recorded the time of occurrence of each exposure, and *S* pressed a switch recording on the same chart paper whether or not he perceived the stimulus. The right eye only was used in all the determinations.

The *S* was thoroughly practiced beforehand in the task of threshold measurement, including practice under the influence of LSD, and then tested under a control condition and a drug condition each week for four weeks. The LSD was administered intravenously approximately 1 hr. before testing was begun. At each session a 10-min. foveal dark-adaptation curve was obtained (central fixation), as was a 30-min. curve with the fixation point shifted 8° to the right of the stimulus spot (side fixation). Two minutes of light adaptation was followed by randomly alternated ascending and descending series of test-stimulus luminances with an ascending series terminated by a positive response from *S* and a descending series terminated by a negative response. The central and side-fixation conditions each occurred first in half the sessions with a 5-min. rest period between them. In each 30-min. curve a 1-min. rest period was provided at the eleventh minute and 2-min. rest periods at Minutes 16, 21, and 26. All the rest periods occurred in darkness, and at these times *E* asked *S* to describe his subjective impressions.

Since LSD dilates the pupil, a 2-mm. artificial pupil was used with the first four *S*s (two male and two female) in the main part of the experiment. For two *S*s pupil size was equalized for control and drug conditions by topical administration of homatropine. The natural pupil and a special procedure were used with the last three *S*s. The reasons for these additional conditions will be presented later.

RESULTS

Threshold Difference and Variability

The average drug threshold values are clearly higher than the control thresholds throughout the course of the curves (Fig. 1). This is also true for each *S* individually except one, who showed some overlap between drug and control points through the middle of the peripheral curve. This individual's foveal curve, however, is almost identical with the averaged one in Figure 1. Each *S*'s average difference for the photopic thresholds was

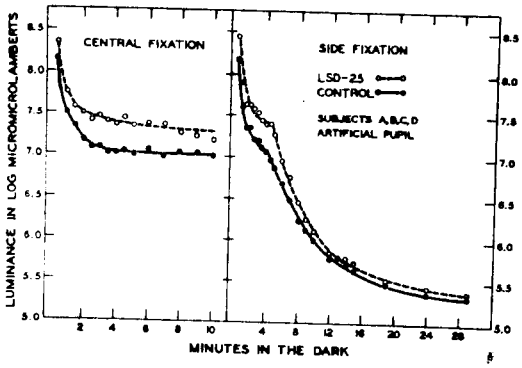

FIG. 1. Averaged foveal and 8°-parafoveal dark-adaptation curves using 2-mm. artificial pupil.

compared with that for the scotopic thresholds by means of a t test. The drug had a significantly greater effect on the photopic threshold for each of the four *S*s ($p < .005$). The variances for the LSD points were compared with those for the control points by means of a sign test, and the drug variances were quite randomly larger or smaller than the corresponding control variances along each curve.

With LSD the *S*s generally reported greater difficulty in maintaining steady fixation because the fixation point seemed to "jump around." If fixation were not as constant, the drug threshold values might be artificially raised at the beginning of the foveal curve and lowered toward the end due to inadvertent shifting of the test stimulus from cones to rods. The last three points in the LSD foveal curve of Figure 1 do in fact tend downward, although there is no comparable tendency toward relatively greater threshold elevation in the early part of the curve. The LSD scotopic values may perhaps be slightly too high due to occasional inadvertent shifting of fixation from the fixation point toward the location of the test stimulus. The apparently greater elevation in photopic as compared with scotopic threshold would seem, therefore, not to be explainable in terms of less constant fixation. With an artificial pupil, however, a moderately large eye movement could shift the stimulus spot out of view altogether, leading to a bias in the direction of a higher threshold throughout the data. To check this possibility, pupil size was equalized for drug and control conditions with two *S*s by the instillation of homatropine in the eye rather than by use of an artificial pupil (Fig. 2). Here, effective pupil size is greater, shifting both control and drug curves down somewhat, but the difference in threshold values is comparable to that in Figure 1. One of these two *S*s failed to show a significantly greater drug effect on the photopic threshold and also had a statistically significant preponderance of larger LSD variances ($p < .05$). This *S*, particularly, complained of being distracted by (minimal) outside noises, but, in general, *S*s reported the feeling of an inability to maintain directed concentration and attention with LSD as well as they could normally.

Greater inattention in this experimental situation, whether related to stability of visual fixation or not, might well lead to increased variability and perhaps to a bias in favor of a higher threshold as well. Consequently, a procedure was used with three *S*s designed to maximize possible effects of inattention if they were present. Instead of using the shutter, *E* presented the test stimulus continuously, always starting a trial well below threshold and increasing the luminance of the stimulus slowly until *S* reported that he perceived it. Presumably, if *S*'s attention wandered at times, the light would become brighter than necessary for detection before he would notice it, leading to a higher average threshold and greater variability. Data were also collected using the same procedure as with the other six *S*s (with shutter), but since the essential issue here was a comparison between the two methods of stimulus presentation only, the

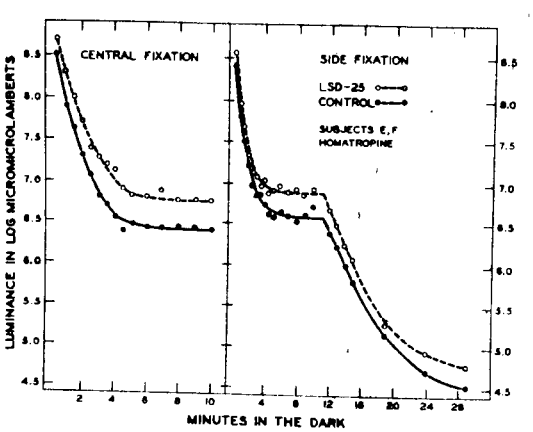

FIG. 2. Averaged foveal and 8°-parafoveal dark-adaptation curves with natural pupil dilated by homatropine.

natural pupil was used. The results were practically identical for the two procedures, and none of the *S*s showed greater variability for the LSD values in either method of stimulus presentation.

Finally, a few dark-adapted threshold values were obtained with the last three *S*s using an artificial pupil. Following the light adaptation, *S* merely waited in the dark for 10 min. and for 30 min. The results were comparable to those for the first four *S*s with respect to photopic and scotopic threshold differences, but under this condition all three *S*s showed significantly *less* variability in the LSD values ($p < .01$).

Subjective Reports

The subjective effects of apparent movement of the fixation point and inability to concentrate as well with LSD have already been mentioned. Other effects common in the literature on LSD were also reported by the *S*s, principally distortion in the time sense, magnification of apparent distance, increased tension, restlessness, and feelings of unreality. Of particular interest here, however, were comments related to the difficulty of seeing the test stimulus. With LSD, some *S*s said that the test light was "harder" to see because it seemed "dimmer." Some said it was "easier" to see because it appeared "brighter." No *S* at any time gave any indication, however, that he experienced interfering hallucinatory effects. All *S*s seemed willing to talk about their subjective impressions and feelings and described a variety of both specific and vague effects. It does not seem reasonable, therefore, that they were experiencing any significant hallucinatory activity without reporting it.

Other Variables

The data were additionally analyzed in the following respects with essentially negative findings. There was no demonstrably significant effect of LSD on rate of dark adaptation. No consistent pattern of individual differences appeared in relation to threshold difference, variability, and subjective reports; and no trend occurred due to practice over the four weeks of testing. Other conditions and/or a larger number of *S*s might, of course, establish hypotheses in these respects.

DISCUSSION

We must conclude that LSD raises the absolute visual threshold a small but definite amount and that this elevation is not due to interfering visual hallucinatory effects, inattention, or impaired ability to concentrate. This conclusion and the finding that the photopic threshold is raised more than the scotopic threshold are consistent with the occurrence of inhibitory effects on cortical synaptic activity (5, 7). Purpura (7) interprets the electrophysiological data as indicating a differential inhibition of axodendritic activity in nonspecific corticipetal and corticocortical synapses. It is not known that such an effect would necessarily depress the psychophysical threshold response to light stimuli; but brightness vision in man depends largely or wholly on the visual cortex, and cone vision probably depends more on the complete integrity of cortical functioning than does rod vision (8). The drug LSD causes no change in over-all cerebral oxygen and glucose metabolism (10), so that effects as great as those produced by anoxia would be unlikely. Blough (2) has demonstrated that at doses relatively much higher than those used in man, LSD raises the absolute visual threshold in the pigeon, but this effect was probably mediated subcortically. In the cat, Evarts et al. (3) have found that high doses of LSD decrease synaptic transmission at the lateral geniculate nucleus and, to a much lesser extent, at the retina, while Purpura (6) reports that doses more comparable to those used in man facilitate the primary cortical response to photic stimulation of the eye.

Whether hallucinatory activity would be reflected in greater threshold elevation has not been determined, since *S*s apparently did not experience hallucinatory effects. This result raises a question of the generality of the presumed hallucinogenic potency of LSD in normal *S*s. At the same time, it is relevant to note that psychotic and neurotic patients have shown an elevated absolute visual threshold (4), indicating another possible point of similarity between the effects of LSD in normal *S*s and the behavioral manifestations of more naturally occurring psychological disorder.

SUMMARY

Dark-adaptation curves were obtained on nine normal *Ss* after administration of LSD. The drug raised the absolute visual threshold throughout the course of the curves, and there was a relatively greater effect on the photopic threshold than on the scotopic threshold. Variability in the threshold values was not increased, and additional evidence was obtained to indicate that the elevation in threshold was not due to inattention, inability to concentrate, or interfering hallucinatory manifestations. The results are interpreted in terms of presently available electrophysiological findings with LSD.

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Received August 26, 1957.