was added to an untreated cabbage mitochondrial preparation, there was an immediate evolution of oxygen, which continued for some time. This was presumably attributable to the presence of catalase. It took 76 μmole of hydrogen peroxide per flask to cause a 30 percent inhibition in rate of oxygen uptake. This 30 percent inhibition was reversed with 16 μmole of ascorbic acid plus 20 μmole of reduced glutathione. These experiments indicated that the action of ozone did not involve the intermediate formation of hydrogen peroxide, since the relatively large amounts of hydrogen peroxide required for inhibition could not have been formed from the smaller amounts of ozone that were added. The results also suggested that ozone and hydrogen peroxide might have been acting in a similar manner, since reversal could be obtained in both cases. If this were the case, then the action of these agents could have been attributable to simple oxidation, and other strong oxidizing agents (such as peroxyacids and ozonides) could perhaps produce a similar reversible inhibition.

The addition of excess cofactors—sodium ethylene-bis(dithiocarbamate), sodium bisulfide, cysteine, 2,3-dimercapto-1-propanol—to ozone-treated mitochondria did not reverse the ozone inhibition. In many cases, the addition of these compounds inhibited oxygen uptake. These experiments suggested that some type of specificity existed for the reversing agent.

The results presented here suggest that the effects of small amounts of ozone on cabbage, spinach, and liver mitochondria were reversed by ascorbic acid, reduced glutathione, and ozone-affected enzymes that were associated with the mitochondrial citric-acid-cycle activity.

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Effect of Lysergic Acid Diethylamide on Absolute Visual Threshold of the Pigeon

There have been many recent reports that human subjects receiving small doses of lysergic acid diethylamide (LSD) tend to behave in some ways like psychotic patients. These reports have stimulated efforts at careful specification of the psychological and physiological effects of LSD. Prominent among the effects found thus far have been disturbances of visual functions, including apparent changes in visual sensitivity. E. V. Evarts (*1*) recently reported that monkeys recovering from large doses of LSD were active but behaved as though they were blind. Carlson (*2*) has noted a slight rise in the absolute visual threshold of human subjects following intravenous administration of 100 μg of LSD. In a related neurophysiological study (*3*), LSD markedly reduced the postsynaptic response in the lateral geniculate nucleus to stimulation of the optic nerve of the cat.

Such findings suggest that elevation of the absolute visual threshold is characteristic of the action of LSD. The present study (*4*) uses a recently devised technique (*5*) to measure this effect in the pigeon. The method is rather complex and its restatement here will be brief. The pigeon stands in a light-tight box and views a stimulus patch fixed in the wall. It pecks one response key when the stimulus patch is visible and another key when the patch appears dark. These pecks, operating through automatic control circuits, cause the intensity of the stimulus to vary up and down across the pigeon's absolute threshold. A recorder charts the stimulus intensity, indicating the bird's threshold through time. The automatic controls provide the pigeon with periodic rewards of food for correct responses.

The subjects were three male domestic pigeons (White Carneaux). The bird to be tested first was dark-adapted for at least 1 hour in the experimental box. The stimulus patch was then illuminated by a light beam of 500-mμ wavelength from a Bausch and Lomb grating monochromator. The bird responded to this stimulus for at least 30 minutes, or until its threshold appeared to be stable. Then the experimental box was opened in darkness, and a dose of water or LSD solution (100 or 300 μg/kg) was administered either orally or by intraperitoneal

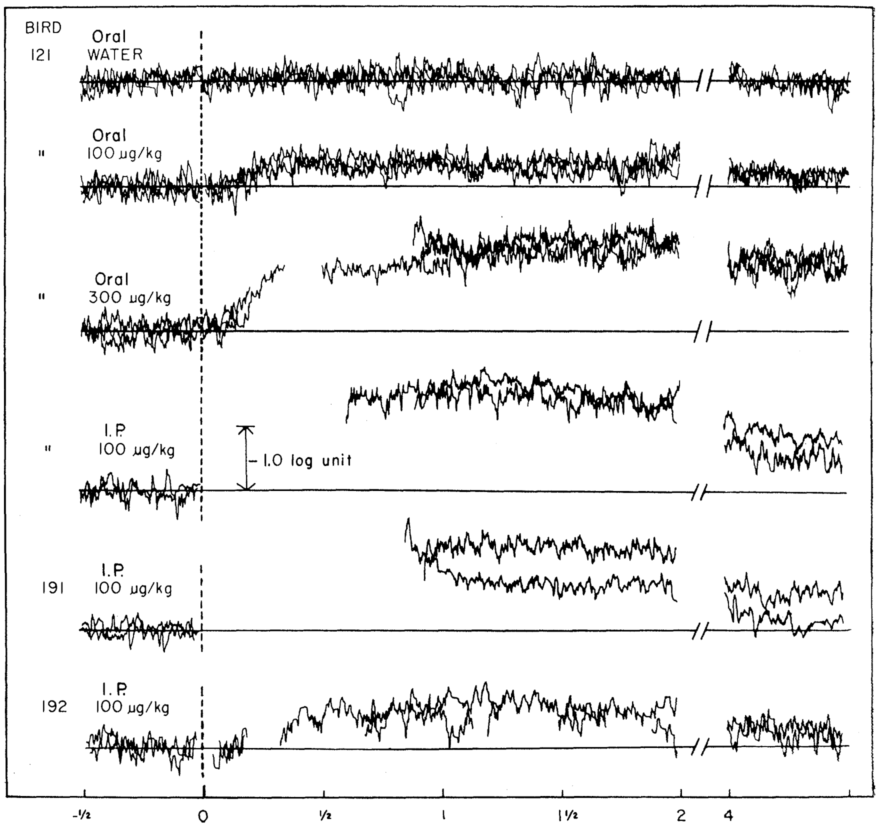

Fig. 1. Effect of LSD on the pigeon's absolute visual threshold. Vertical shifts in the curves represent changes in the brightness of a "just visible" stimulus patch. A single oral dose amounted to about 4 ml of solution (10 ml/kg). A single intraperitoneal dose amounted to about 0.4 ml of solution (1 ml/kg).

injection. Following administration, the bird's threshold was recorded for 2 hours. The bird then rested in the dark until a 30-minute test was made during the fifth hour after administration of the dose. In several instances, a final test was made about 22 hours after administration of LSD. The birds were allowed from 3 days to 2 weeks for recovery between doses of LSD.

Some of the original data are reproduced in Fig. 1. The curves represent the brightness of the stimulus patch as a function of time before and after dosage. The base line for each curve extends through the midpoint of the threshold recorded before a dose was given. Three curves from single sessions are superimposed in the case of data obtained after administration of oral doses, while two curves make up each function in the case of data obtained after intraperitoneal administration. The uppermost function in Fig. 1 illustrates typical control data. Gaps appear in the records when the bird failed to respond. This often happened for a time after administration of the larger doses of LSD.

It is apparent that LSD caused a striking rise in absolute threshold. Bird 121 was affected the most. It showed a swift and substantial rise in threshold with both doses and with both routes of administration. Intraperitoneal doses of 100 μg/kg given to this bird produced the largest threshold rise that was observed. The rise amounts to approximately 1.8 log units, a linear increase of roughly 60-fold.

Samples of the data from the other two pigeons are plotted as the lowest two functions in Fig. 1. The threshold changes observed in these birds were similar to those found with pigeon 121, though of somewhat smaller magnitude.

In most cases, the effect of LSD had diminished considerably by the fifth hour after administration. This was especially true in the case of intraperitoneal dosage. In no case was a threshold elevation still evident in the tests made after 22 hours.

It might be argued that the rise in threshold is only apparent and that the findings actually represent a failure by the birds to perform correctly in the discrimination situation. However, in a previous study, LSD at these dose levels improved the pigeon's performance on a visual discrimination task, rather than producing a decrement (*6*). Furthermore, spurious departures from a stable threshold have been marked in past studies by increased variability, rather than by the stable shift in level evidenced here.

Small doses of LSD thus appear to affect the visual threshold of the pigeon without grossly disturbing motor or discriminative functions. This fact may be a valuable clue in understanding the physiological action of the drug. It also suggests the use of visual threshold measurement as an assay technique in the study of LSD and related substances.

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17 May 1957

Age of the Sandia Culture

The introduction of radiocarbon dating has proved that the figures found in America by geologic and archeological dating are obsolete. Therefore, in his lecture on "Early man in North America," given on 17 July 1951 at the University of Erlangen, Germany, F. C. Hibben (*1*) used explicitly and exclusively figures found out by C^{14} measurement and communicated the dates of 9000 B.C. (maybe an estimate based on Libby's Two Creeks C^{14} dates published on 2 Feb. 1951?) (*2*) for the Folsom layer and 17,000 B.C. for the Sandia layer in Sandia Cave, N.M.

In a paper (*3*) published some months later, I quoted from this lecture an *age* (that is, years before present time) of 11,000 and 19,000 years, respectively, for the Folsom and Sandia layers in Sandia Cave; this dating of mine is, of course, identical with Hibben's. Consequently, I am not in error in my dates, but Hibben is in error when he maintains that his dates were derived by stratigraphy from Bryan's geologic work. K. Bryan (*4*), in his appendix to Hibben's excellent monograph on Sandia Cave (*5*), placed the Sandia layer just before 25,000 years before the present and the Folsom level just after this date on geologic grounds. I cannot understand how it is possible to derive from this geologic dating the figures 9000 and 17,000 B.C. The date 17,000 B.C. (omitting the appended "-plus") is approximately the mean of Hibben's (*6*) alleged C^{14} dates (17,000-plus and 20,000-plus years ago). Consequently, I have not confused geologic and C^{14} dating.

H. R. Crane (*7*) found, by C^{14} measurement of two ivory samples from the Sandia level, "that there appears to be no significant difference in counting rate between the Sandia samples and the control samples of dead CO_2, when the statistical limits and the degree of consistency between runs are considered." According to his measurement (*7*, Fig. 1, p. 689) the ivory samples are older than 35,000 years. I, therefore, do not understand why, later on, Crane (*8*) dated the two Sandia samples as older than 20,000 years only.

The Pleistocene stratigraphy of Sandia Cave has been stated by Hibben (*5*, pp. 11–18), and Bryan (*4*, p. 48) as follows: layer 1, upper cave breccia, 1 to 4 ft thick (Folsom layer); layer 2, yellow ochre, 2 in. to 2 ft thick (sterile); layer 3, lower cave breccia, 0 to 3 ft thick (Sandia layer); layer 4, basal clay, 0 to 2 ft thick (sterile).

According to R. Lais (*9*), the sequence of the Pleistocene stratigraphy displayed by cave fill depends on considerable climatic fluctuations. The degree of chemical weathering of limestone debris in caves is a function of temperature, moisture, and time. Layers 2 and 4 of the afore-mentioned sequence are the residues of dissolved limestone and are thus the products of very long, warm (at least temperate), and moist intervals. In Central European caves, the basal clay was deposited during the last Interglacial period, as evidenced often by paleontological and archeological findings.

Layer 2 of Sandia Cave certainly correlates with the European *Höhlenlehm* (cave loam), mostly about 0.20 m thick, intercalated between the lower breccia (formed by frost action) containing Mousterian artifacts and the upper breccia containing Upper Paleolithic levels. In Europe the *Höhlenlehm* corresponds to the Göttweig loam known from cross sections of loess; both were formed during a long temperate interstadial (formerly called Würm I/II), the Göttweig Interstadial (*10*), preliminarily dated by C^{14} at Groningen as about 42,000 to 28,000 before the present. The North American equivalent of the Göttweig Interstadial has been recently discovered by R. F. Flint and M. Rubin (*11*) in Ohio and estimated to have been about 16,000 years in length; this interstadial separates the Early Wisconsin and the Main Wisconsin stadials corresponding to the Altwürm and Hauptwürm stadials in Europe.

So long as this correlation has not been refuted by incontestable evidence, we dare ascribe the Sandia level of Sandia Cave to the Early Wisconsin stadial (in agreement with Crane's first C^{14} dating), for in the meantime some archeological sites in North America have been dated by C^{14} as older than 37,000 years—namely, Lewisville (*12*), Tex., and Santa Rosa Island (*13*) off