Our report (*1*) describing the psychological and physiological effects of the hallucinogen 2,5-dimethoxy-4-methylamphetamine (DOM or STP) has been criticized by Cabe on several counts. Cabe maintains that instructing subjects that they would receive a hallucinogen may have accounted for the hallucinogenic effects of DOM. Ethical considerations require that subjects be adequately informed before obtaining their consent in such experiments. Moreover, our report (*1*) clearly demonstrates that suggestibility could not have accounted for the hallucinogenic effects observed. All subjects received the same instructions but were given doses of DOM varying from 2.0 to 14.0 mg. If the hallucinogenic effects were "suggested" to the subjects there should have been no correlation between dose and effect. Since we found a clear-cut and well-graded relationship between dose and response, the effects obtained cannot be ascribed primarily to suggestibility. In a subsequent study (*2*), we have administered low, subhallucinogenic doses of DOM or placebo to normal control volunteers in a double blind experimental design. The mild euphoria produced by these low doses of DOM was readily distinguished from placebo.

We are fully aware of and have studied (*3*) the effect of setting and suggestibility on responses to hallucinogenic drugs. Nonetheless, in several studies of the psychological effects of hallucinogenic drugs (*4–6*) we observed that suggestibility plays a lesser role than armchair reasoning would suppose. In comparing LSD with epinephrine (*5*), we found little resemblance between the clinical effects despite similar instructions preceding each trial. In a similar blind experimental design we compared a presumed psychotomimetic (3,4-dimethoxyphenylethylamine) with mescaline and placebo and found that only mescaline produced hallucinogenic effects (*6*).

Since we did not specify exactly what psychological testing procedures were used, Cabe cannot be objecting to the particular tests we employed. In determining the effects of hallucinogenic drugs, we can ask the subject to describe his experience, direct him to perform a specified task, or observe him. All three methods were used in our study (*1*). Since a clearly graded dose-response effect was obtained in both the self-reports and the psychological tests, it is unlikely that the results we obtained by these procedures could be ascribed to "faking," as Cabe suggests.

Cabe criticizes our use of subjects with some limited experience of marijuana. In our report (*1*), we indicated that "applicants with a history of frequent use of marijuana or other mental stimulants were rejected." Unfortunately, obtaining subjects fully naive to drugs is difficult. Since experienced drug users usually excel in their ability to discriminate between the effects of different agents, one could argue that such individuals might be the best subjects for studies such as ours (*1*).

SOLOMON H. SNYDER
LOUIS FAILLACE
Departments of Pharmacology and Experimental Therapeutics and *Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, Maryland 21205*
LEO HOLLISTER
Veterans Administration Hospital, Palo Alto, California 94304

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Chromosome Damage by LSD

Loughman, Sargent, and Israelstam (*1*) have confirmed earlier reports that LSD (lysergic acid diethylamide) consumption is correlated with chromosome damage in vivo. However, the authors misconstrued their results and interpreted them as indicating no evidence of damage.

An analysis of their report must proceed on the assumption that the previous studies of LSD were validly done. Therefore, all statistical tests should ask, "What is the probability that the data accidentally confirm that LSD users have chromosome damage?" In fact, Loughman *et al.* do confirm the observation of chromosome damage among LSD users, and analysis of their data indicates very small probability that their confirmation is due to an accident of sampling. In their own analysis, Loughman *et al.* used a method that asked whether LSD users differed from their one control (a nonuser of LSD). (They did not realize how sensational it would be if they had found that LSD significantly protects against chromosome damage.) In other words, to decide whether damage occurs in users, the statistical tests should be one-tailed, not two-tailed.

Their paper mentions three distinct types of changes that are indicative of chromosome damage. (i) They found that only 12 of the 112 cells of the control (10.7 percent) did not have the normal chromosome number of 46, but that 45 of 245 cells of LSD users (18.4 percent) had other than 46 chromosomes. By Fisher's exact method, the probability that this is an accidental confirmation of damage by LSD is .044, which is statistically significant evidence that the drug causes chromosome damage. (ii) Loughman *et al.* "occasionally . . . found large cells with multiple micronuclei" in cultures from LSD users, but not in cultures from the control. From their data, it is uncertain whether the observed ratio of cells from these LSD users to those from their control was about 2:1 or 6:1. If 2:1, only eight of these highly abnormal cells would give a statistically significant confirmation of damage, but, if 6 : 1, they would have had to see 20 cells for it to be statistically significant. In either case, their observations confirm the previous observations of chromosome damage in LSD users. (iii) Chromosome aberrations were seen three times in 697 cells of LSD users, but not in any of 112 cells of the control. The exact probability for this distribution is .64, which is not small. However, this is the expected result if LSD is associated with chromosome damage.

Thus, Loughman *et al.* observed three types of abnormalities associated with chromosome damage, and each was more severe among LSD users than in the control. It is impossible to make an overall estimate of the probability that these confirmations of previous reports could be due to chance alone, but the combined probability is likely to be very low, which would make the confirmation highly significant.

Loughman *et al.* stated, "We conclude from our work that LSD . . . has not been shown to damage the chromosomes of human peripheral blood lymphocytes in vivo." On the contrary,

previous reports had already indicated such damage, and their own work provides statistically significant evidence in favor of the hypothesis that LSD users sustain chromosome damage.

HERMAN M. SLATIS
Department of Zoology, Michigan State University, East Lansing 48823

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Slatis has raised a single valid point. The chromosome-per-cell distributions displayed in our Table 3 (*1*) are different in a statistical sense. Lumping nonmodal cells and testing them against modal cells, with a 2 by 2 contingency chi-square test ("Fisher's exact method"?), does give $P = .044$, indicating the difference is significant. A heterogeneity chi-square test, to determine which values if any raise the chi-square disproportionately, shows that the 42-chromosome class accounts for over one-fourth of total chi-square. This class contains less than 2 percent of the observations, and is 11 percent of the total classes. We believe that the large random errors in the eight (subject) subgroups, when the data were combined, produced one of the nine-chromosome number classes with errors adding mostly in the same direction. This is acceptable as a chance event. Ignoring that class, or weighting all classes with estimated variances, brings the probability associated with total chi-square to a value above .05, indicating no significant difference in the distributions, which was our conclusion. We do understand that the data as given could support some contention about LSD-induced cellular damage, but we believe the evidence is far from convincing. The data cannot support an argument that the chromosomes themselves were damaged.

When the chromosome aberration data were examined, Slatis compared the ratios 3/697 and 0/112. Our *t*-test for the significance of the difference between the two proportions gives $t = .696$, $P =$ somewhat higher than .5. The difference can thus be attributed to chance variation, as Slatis has indicated with his value of .64. It is evident that conclusions with regard to the cause and effect of chromosome aberration, based on this value, are not reliable.

Slatis has analyzed our "micronucleated cell" observations with closeness. However, we stated that we could not put numbers on our observations. We do recognize the implications of such damage in our experimental cell populations, if the observations were significantly elevated above control values. We cannot say that they were, or that they were not.

We feel that Slatis' attempt to show chromosome damage by pointing to differences which are the result of random sampling error is not a matter of a one-tailed or a two-tailed test.

We agree that the pertinent statistical tests, at least for data in our Table 2, should be one-tailed. In fact, our conclusions were based on one-tailed *t*-tests, the full results of which were not tabulated. The confidence limits given with our data were for the convenience of readers who wished to inform themselves of the magnitude of random sampling errors associated with the percentages in the table. They were not, in themselves, part of any statistical test.

WILLIAM D. LOUGHMAN
THORNTON W. SARGENT
Donner Laboratory and Donner Pavilion, University of California, Berkeley

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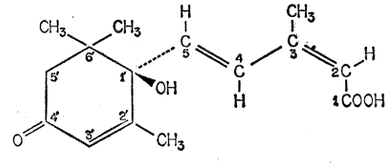
Abscisic Acid: A New Name for Abscisin II (Dormin)

Abscisin II was the name given to the second of two abscission-accelerating substances isolated (*1*) from cotton fruit. The same substance was subsequently isolated (*2*) from sycamore leaves as the result of a search for a "dormin" [an endogenous substance inducing dormancy (*3*)]. Since then, the substance has been identified in a large number of higher plants. The structure of abscisin II has been determined and confirmed by synthesis (*4*); structure and correct absolute configuration (*5*) are shown by the insert.



(*S*)-ABSCISIC ACID

Some confusion has developed from the use of the two names, abscisin II and dormin, derived from the abscission and dormancy effects of the compound. The more recent discovery of several other physiological effects has emphasized the need for an agreed terminology.

We now propose the term abscisic acid as a reasonable and useful compromise which gives an indication of the compound's chemical nature, facilitates naming derivatives, and is close enough to the original name to avoid confusion arising from the change.

We suggest that authors specify racemic abscisic acid when they use it in experiments by calling it (*RS*)-abscisic acid, and that the naturally occurring enantiomorph be called (*S*)-abscisic acid when it is necessary to draw attention to the stereochemistry. As an abbreviation for abscisic acid, we propose ABA. For specifying positions within the molecule, the numbering system shown in the figure (which conforms to the systematic name for the substance) is recommended. We propose that the question of renaming abscisin I be deferred until its structure is known.

The foregoing proposals were agreed at the Sixth International Conference on Plant Growth Substances (Ottawa, 1967) and are published in the proceedings of that conference.

F. T. ADDICOTT, J. L. LYON
K. OHKUMA, W. E. THIESSEN
University of California, Davis
H. R. CARNS
U.S. Agricultural Research Service, Beltsville, Maryland
O. E. SMITH
University of California, Riverside
J. W. CORNFORTH
B. V. MILBORROW, G. RYBACK
Shell Research, Limited, Milstead Laboratory, Sittingbourne, United Kingdom
P. F. WAREING
University College of Wales, Aberystwyth, United Kingdom

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