In 1967, LSD was briefly labeled a breaker of chromosomes

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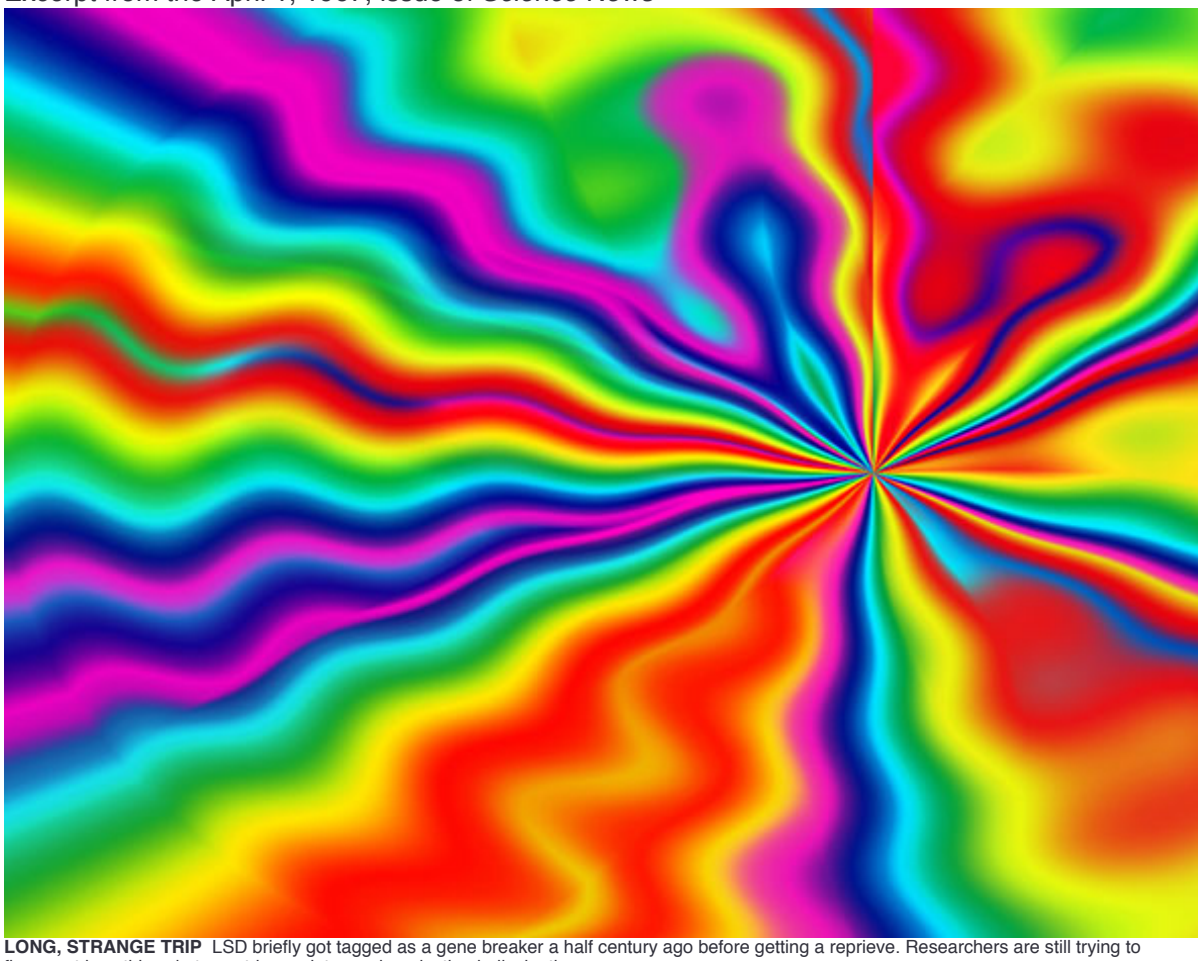

LONG, STRANGE TRIP LSD briefly got tagged as a gene breaker a half century ago before getting a reprieve. Researchers are still trying to figure out how this substance triggers intense, long-lasting hallucinations.
ZORAN RAS/SHUTTERSTOCK

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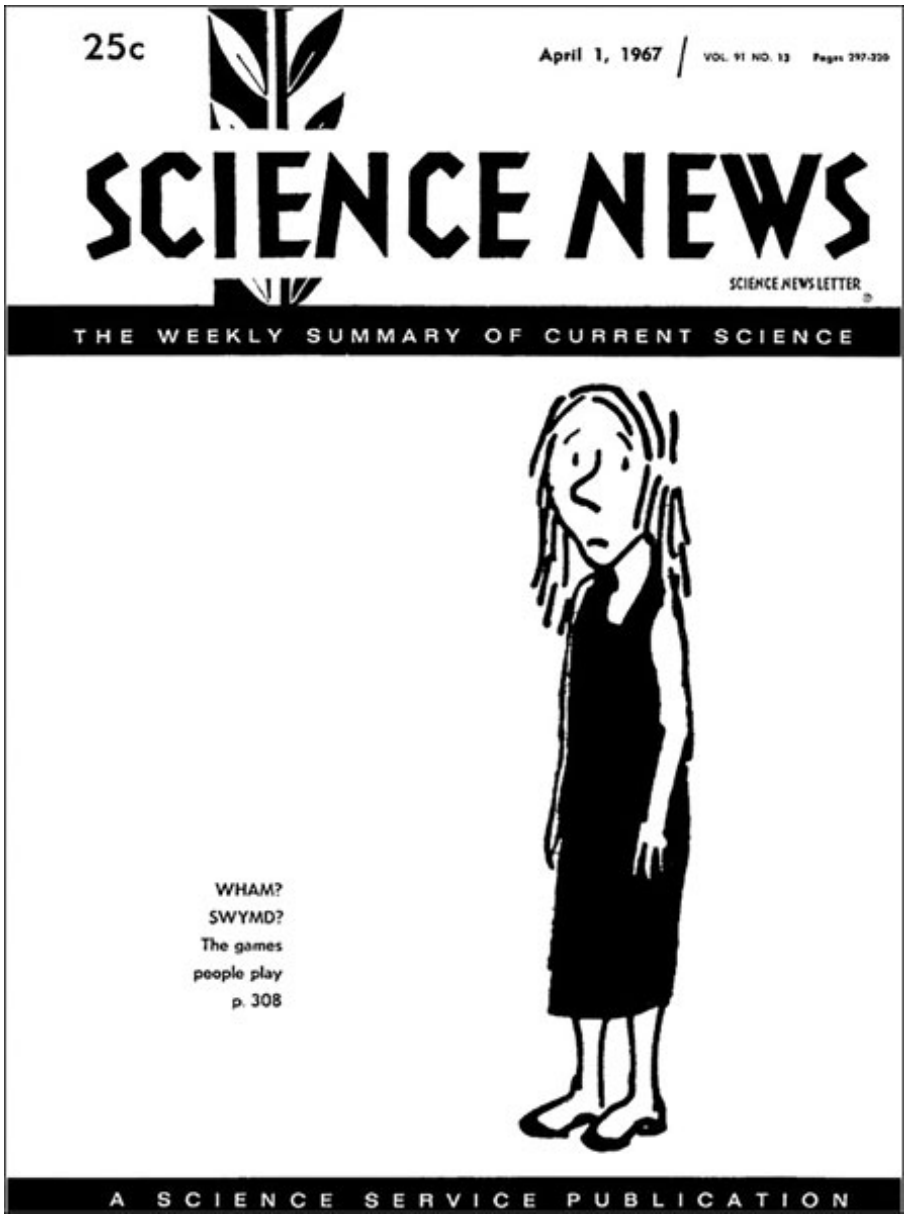

LSD may damage chromosomes

Two New York researchers have found the hallucinogenic drug will markedly increase the rate of abnormal change in chromosomes. [Scientists] tested LSD on cell cultures from the blood of two healthy individuals … [and] also found similar abnormal changes in the blood of a schizophrenic patient who had been treated with [LSD]. The cell cultures showed a two-fold increase in chromosomal breaks over the normal rate. — *Science News*, April 1, 1967

Update

Psychedelic-era reports that LSD damages chromosomes got lots of press but fell apart within a few years. A review in *Science* in 1971 concluded that ingesting moderate doses of LSD caused no detectable genetic damage. Researchers are still trying to figure out the molecular workings of the drug. Recent evidence suggests that the substance gets trapped in a pocket of the receptor for serotonin, a key chemical messenger in the brain. Its prolonged stay may explain why LSD trips can last up to a day or more (*SN: 3/4/17, p. 16*).

LSD and Genetic Damage

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Abstract

Of nine studies in vitro, six have indicated some degree of induced chromosomal breakage after exposure to LSD; three failed to confirm these results. The damage, when found, was generally of the chromatid type, arising during or after DNA synthesis. This damage, with one exception, was the result of concentrations of drug and durations of exposure which could not be achieved in humans with reasonable dosages. There did not appear to be a dose-response relation. The magnitude of damage, when found, was in the range encompassing the effects of many commonly used substances. The absence in vitro of excretory and detoxifying systems present in vivo, as well as several negative reports, cast doubt on the relevance of in vitro results.

In 21 chromosomal studies in vivo, 310 subjects were examined. Of these, 126 were treated with pure LSD; the other 184 were exposed to illicit, "alleged" LSD. A maximum of only 18 of 126 (14.29 percent) of the subjects in the group exposed to pure LSD showed higher frequency of chromosome aberration than the controls. In contrast, a maximum of 90 of 184 (48.91 percent) of the subjects taking illicit LSD showed an increase in frequency of aberrations. Of all the subjects reported to have chromosome damage, only 18 of the 108 (16.67 percent) were exposed to pure LSD. The frequency of individuals with chromosomal damage reported among illicit drug users was more than triple that associated with the use of pharmacologically pure LSD. We conclude that chromosome damage, when found, was related to the effects of drug abuse in general and not, as initially reported, to LSD alone. We believe that pure LSD ingested in moderate dosages does not produce chromosome damage detectable by available methods.

No significant work on carcinogenic potential of LSD has been reported so far. No cause-and-effect relation and no increase in the incidence of neoplasia among LSD users have been demonstrated. Case reports (three in 4.0 years) of leukemia and other neoplasia in this population are rare.

The results of early chromosome studies suggested that true genetic damage might be a consequence of LSD exposure. The comprehensive evidence from

studies on drosophila indicates no mutagenic effect from 0.28 to 500 μg of LSD per milliliter and a definite mutagenic effect from 2,000 to 10,000 μg/ml; this is consistent with a threshold response or a sigmoid dose-effect relation. We believe that LSD is, in fact, a weak mutagen, effective only in extremely high doses; it is unlikely to be mutagenic in any concentration used by human subjects.

Circular dichroism experiments suggested that the specific mechanism of action of LSD on DNA may be a direct interaction resulting in conformational changes in the DNA helix. These changes are unlikely to result in a decrease of internal stability sufficient to cause breakage of chromosomes, but they may be the physical basis of the weak mutagenicity.

Early chromosomal studies implicated LSD as a potential cause of congenital malformations, fetal wastage, and germinal chromosome damage. First reports of a teratogenic effect in hamsters and rats have not been confirmed. A review of 15 rodent studies indicated a wide range of individual, strain, and species susceptibility to the effects of LSD. The applicability of such investigations to man is doubtful. In a study of human pregnancies, those exposed to illicit LSD had an elevated rate of spontaneous abortions. There is no reported instance of a malformed child born to a woman who ingested pure LSD; there are six cases of malformation associated with exposure to illicit LSD, four of which have similar limb defects. Given, however, the high frequency of unexplained "spontaneous" birth defects, the rare occurrence of malformed infants born to women who used illicit LSD may be coincidental. While there is no evidence that pure LSD is teratogenic in man, the use of any drug during pregnancy requires that its potential benefits significantly outweigh its potential hazards.

From our own work and from a review of the literature, we believe that pure LSD ingested in moderate doses does not damage chromosomes in vivo, does not cause detectable genetic damage, and is not a teratogen or a carcinogen in man. Within these bounds, therefore, we suggest that, other than during pregnancy, there is no present contraindication to the continued controlled experimental use of pure LSD.

Note added in proof: A brief review has been brought to our attention. Although based on a sample of only 15 studies the author reached conclusions similar to our own (*92*).