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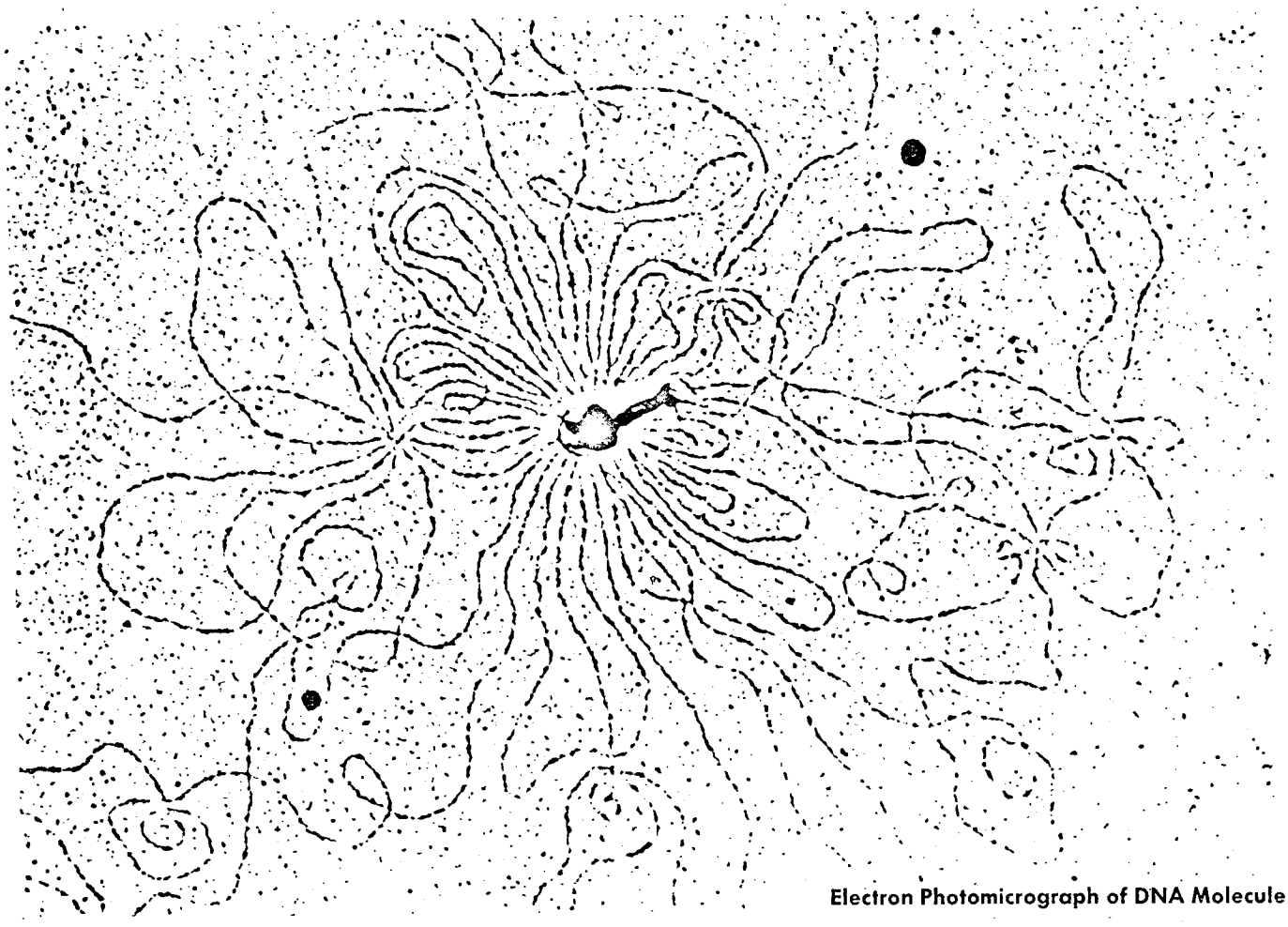

Electron Photomicrograph of DNA Molecule

LSD, CHROMOSOMES AND SENSATIONALISM

Joel Fort & Ralph Metzner

The growing literature on this explosive subject is critically examined with a view to sifting fact from sensationalism.

Much attention has been focused by the mass media on the alleged damaging effects of LSD on chromosomes. The initial "scientific" report by Cohen et al. (4), which appeared in Science in March, 1967, was followed within 24 hours of its publication by press statements which translated the inconclusive and ambiguous findings into flat assertions that abnormal offspring would be produced by LSD use. Evoking memories of the 1963 Thalidomide disaster, in which a widely-used "tranquilizer" was found to produce malformed babies, such statements injected a strong current of fear into the chaos of contradictory opinions and passions already surrounding the topic of LSD. In such a charged atmosphere few people are willing or able to examine impartially the actual scientific evidence.

Typical of the often shameless disregard for objectivity manifested by the media is

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The Saturday Evening Post's cover story on "The Hidden Evils of LSD"(7). Replete with uncaptioned, unidentified photographs of persons apparently in states of fear or confusion, the article features also a photographically distorted picture of a baby (again uncaptioned), with the obvious implication: if you take LSD your baby will look like this. The (true) statement at the beginning of the article, that "the scientific evidence linking LSD with the baby's deformities, the broken chromosomes, the leukemia-like chromosomal abnormality and the convulsions is still circumstantial" is forgotten as the rest of the article goes on as if that statement had not been made. Page-headings such as "If you take LSD, your children may be born malformed or retarded" are known to logicians as vacuous. Since the second half of the proposition is true, anything can be said in the first half; e.g. "if you drink Coca Cola beiore breakfast, your children may be...etc." Of course logic has never been of prime concern to the mass media or politicians. The studies in the scientific literature finding no chromosomal abnormalities from LSD fail to receive any attention from the popular press.

REVIEW OF FINDINGS

Trenchant methodological criticisms of the Cohen study were made by Prince (12) who pointed out that only three examinations were done—white blood cells (from two "normals") exposed in test tubes to high concentrations of LSD and white blood cells from one schizophrenic who had received LSD therapy; that no germ cells or embryos were involved; that the dose-response curve was highly irregular, suggesting a high degree of random experimental variability; that a single control figure was used rather than simultaneous normal controls; and that the general culture technique and cytogenetic methodology left much to be desired. The most damaging criticism of their study is the authors' own published statement that the purpose of their study was to prove the harmfulness of LSD, a goal at odds with the commonly accepted canons of scientific impartiality.

Irwin and Egozcue (9) found a significant difference in chromosome breaks in the white blood cells of six out of eight LSD users as compared to control subjects who had not used LSD. The breakage rate seemed to be correlated with the doses taken. Two subjects had chromosomes similar to those seen in leukemia. One control also had breakage attributed to X-ray therapy. In a magazine interview one of the authors enumerated various possible consequences of chromosomal abnormalities, which had in fact no relation to the actual findings presented in their scientific paper.

In contrast to these results are two studies with human subjects finding no chromosomal abnormalities. One, by Loughman et al., (10) examined the lymphocytes of eight persons with recent exposure to large doses of LSD (up to 4000 micrograms), and found no significant damage. The authors suggest that other tissues of the body must also be examined. These findings are confirmed by those of Petrakis (11), who found no difference in chromosome breakage between five normal controls and five LSD users. Bender and Sankar (3) have recently reported that the children of their study, some of whom received weekly doses of LSD for over a year, showed no chromosomal abnormalities. This is the only one of these studies in which the LSD ingested is of known purity. The possibility that earlier results are attributable to impure black market substances should be investigated.

A second report by Cohen and his collaborators (5), published in the New England Journal of Medicine along with a dark editorial on the "radiomimetic" properties of LSD, deserves close scrutiny for its rather cavalier handling of data. A group of 22 LSD users is reported to have a mean of 13.2% chromosomal breakage, compared to a mean of 3.8% in a group of 12 non-users. However, we note that of the 22 "LSD-users" not one had used only LSD; all except 3 had used amphetamines, most had used heroin and many phenothiazines (tranquilizers used to treat mental illness and to counteract LSD). We also find that the original control group contained 14 persons, two of them being eliminated from the data because they had viral infections shortly after the blood sample was taken. These two individuals had a very high rate of chromosomal breakage

and if they are included in the calculations, the mean for the control group jumps to 18.4%, which is higher than the "LSD group." Cohen et al. also give data on a group of 6 persons who had used drugs other than LSD (amphetamines, opiates, phenothiazines), whose man breakage rate (not shown by the authors) was 12.6%. One must conclude that by their own data, LSD users do not have a higher rate of chromosomal breaks than anyone who uses common tranquillizers or stimulants, or who has had viral infections.

Cohen et al. (5) also report broken chromosomes in 2 children of mothers who had taken LSD in the first third of pregnancy, although no breaks if the LSD was taken later in pregnancy. There were no physical abnormalities in the children themselves. Brecher (3) states that several unreported studies of babies born to LSD-using mothers find essentially the same results.

Several animal studies of the effects of LSD injected during pregnancy have been reported. Alexander et al. (1) have reported finding arrested or stunted growth in four out of five litters of rats given LSD. Auerbach and Rugowski (2), in an undergraduate study, found that 57% of mice embryos had brain malformations when the females received LSD injections seven days after mating (said to be equivalent to days 16-22 in human pregnancies); control litters had 10% abnormalities. LSD injections in later stages of pregnancy had no significant effect on embryos. Geber (8) finds mescaline and LSD producing fetal malformations in hamsters injected on the 8th day of pregnancy. This period is stated to be "effective ... for the evaluation of the ability of a variety of compounds to cause teratogenesis." Warkany and Takacs (14) on the other hand report failing to find foetal damage in rats following LSD.

These animal studies essentially confirm common medical knowledge that during the period of gestation almost any drug or treatment can interfere with normal embryonic growth.

The most serious finding here is the one by Zellweger (13) who describes a baby with a deformed leg born to a woman who had taken LSD on the 25th and the 45th days after her last menstrual period, plus two more times later. Although no definitive causal statement can be made on the basis of one case, the suggestion of a link is strong because the 7th week (days 42-47) is the critical period for leg deformities, according to studies carried out with Thalidomide users.

Contrary to this finding is the personal knowledge of one of the authors of at least two women who took LSD several times during pregnancy, including the first three months, and produced perfectly healthy children.

GENERAL COMMENTS

Quite apart from the factual question of whether chromosomal breakages are produced by LSD in vitro or in vivo, which is by no means decided, there is the further question of the significance of such changes. It is not at all clear what, if any, is the relationship between chromosomal changes in white blood cells and genetic changes in mother or offspring. Germ cells are very different from blood cells in characteristics and life-cycle and no studies have shown chromosomal changes in germ cells, which are the transmitters of the genetic blueprint. The studies in animals or men showing abnormalities of embryonic growth after drug injections in the early months of pregnancy have essentially no relevance to the chromosome question (6), since these are most likely direct effects of the drug on the fetus.

In interpreting journalistic accounts about possible relationships between the use of LSD by pregnant females and birth defects, bear in mind the National Foundation estimates that 250,000 American children are born each year with such defects, few of which can be attributed to any specific external causes.

Many drugs, conditions, forms of radiation etc. are known to produce chromosomal breaks or even genetic changes. This includes measles or measles vaccine, other viruses, amphetamines, chlorpromazine, caffeine, X-ray therapy—all of which are

much more prevalent than LSD. Nuclear radiation has certainly demonstrated its capacity to produce harmful effects on genes and newborn infants. Yet few scientists or newspapers seem concerned, or support jail sentences for those who use or disseminate these clear dangers against the wishes of the recipients. The situation is very different for LSD or other drug-medications, where after all, no one has to be exposed who does not wish to be.

The concept of "damage" being used in public discourse has a social rather than a scientific definition, as one can readily see by noting that there exists proof, not conjecture, of the lethal effects of drugs such as alcohol or tobacco, yet these facts are not viewed with nearly as much alarm as the inconclusive evidence for possible chromosomal damage from LSD. There is also ample evidence that indiscriminate use of unknown doses of impure LSD can lead to psychological and social damage so that one does not have to resort to false or hysterical arguments to demonstrate this.

It should be pointed out that chemicals very closely related to LSD, namely lysergic acid amide as contained in certain types of morning-glory seeds, as well as other indole psychedelics such as the psilocybe mushrooms, have been in use in certain parts of Mexico from before the time of the Spanish conquest, that is for at least 18-20 generations. If significant deleterious genetic changes were occurring the users of these plants might well have died out, or we would have seen congenital abnormalities in the descendants of these people. Observers of the psychedelic cults in Mexico have never noticed such abnormalities. LSD-25 has itself been used since 1943 by probably more than a million people without foetal abnormalities being noted!

Finally, we must consider the question of whether all genetic changes, assuming they do occur, must necessarily be harmful or whether they might be irrelevant, or even beneficial. It is commonly assumed that since the present human species has been selected out over many millenia of evolution, any mutation must necessarily be "bad" in the sense of mal-adaptive. This assumption is, however, based on the idea that the physical environment in which we presently find ourselves does not change. On the other hand, considering the fact that our world is subject to both slow-gradual and sudden changes, resulting from natural causes as well as man's increasing tampering with the planet's ecology, the possibility of beneficial (or irrelevant) mutations must not be overlooked.

CONCLUSIONS AND RECOMMENDATIONS

1. At the present time, the question of whether human chromosomal breaks (or genetic changes) occur as a result of LSD ingestion is undecided scientifically.

2. Malformed embryos have been shown to result in lower animals (and possibly in one human case) where the females received LSD by injection early in pregnancy. This may be due to direct physiological effect of the drug, rather than chromosomal or genetic changes.

3. Women in the first trimester of pregnancy would be wise to avoid the use of all drugs, particularly those which affect the brain and mind including alcohol, caffeine, and nicotine.

4. The mass media, politician-bureaucrats, and drug police tend to sensationalize certain drugs in a self-serving manner with a callous disregard for truth or logic. Readers should look with a critical eye at statements or articles appearing in the popular press (and the training, experience, and biases of those being quoted) on the subject of chromosomal or other effects of LSD (and other drugs).

5. If scientific evidence should later indicate that LSD does produce genetic damage, research should be directed towards finding chemicals which are capable of producing the same psychological results without affecting genes; and LSD be made available only to the elderly or others who have definitely decided not to, or are unable to, produce further offspring.

6. Drug usage can only be decreased through educational and preventive pro-

grams. Continued sensationalism and criminalization of users will only increase usage and problems.

Additional Note: Very recently, Fitzgerald and Dobson, in a letter published in The Lancet (16), raised several of the same points made in this article. They point out that "many agents ...cause both chromosome breakage and give mutation, but it is by no means certain that all chromosome-breaking agents are mutagenic." They also indicate that the level of irradiation commonly used in diagnosis "cause both increased chromosome breakage and increased gene mutation."

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POSTSCRIPT

Since this article went to press, reports of apparently contradictory results continue to multiply in the scientific literature. Skakkebaek et al. (a) reported breakage in the meiotic (germ cell) chromosomes of LSD-treated mice; the dosage used was 1 mg per kg. of body weight. In the average 70 kg man this would be equivalent to a dose of 70,000 mcg — somewhat higher than the standard dose of 300-500 mcg. Browning (b) reports mutagenic effects of LSD in Drosophila males; but again the dose here was several thousand times the highest human dose, so high in fact that only 15 of the 75 animals so treated survived. Even so, another study of Drosophila germ cell chromosomes, by Grace et al. (c), also using enormously high doses, failed to find mutations or chromosome breaks. Court Brown (d) has questioned the report by Zellweger (15), cited in the article, of chromosomal abnormalities in the mother of a deformed child: "the findings in the mother may not differ significantly from what has been found in women, aged 15-24 years, in a randomly selected sample from the ordinary population." Jarvik and Kato (e) have similarly questioned the validity of inferring that LSD is teratogenic from its effects on leucocytes: many substances, including aspirin and caffeine, produce chromosome breaks when added to cultures of human leucocytes. "Let us not forget however, that leucocytes are expendable, as any infection will demonstrate. The human organism is capable of eliminating damaged cells, be they somatic or gametic." Sparkes et al. (f), of UCLA Medical School, found no significant chromosomal damage in a group of 8 LSD users.

Clearly a great deal more research needs to be done before any definite conclusions are warranted, and the case for genetic damage of LSD must be regarded as so far unproven.

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