

cies, *Sarcina lutea*, grown either aerobically or anaerobically (surface growth only) produced no detectable metabolites of DDT.

We noted that strict anaerobes may be variable with regard to DDT degradation. Of two species of *Clostridium* studied, *Cl. sporogenes* showed no detectable activity, while *Cl. pasteurianum*, an anaerobic nitrogen fixer, converted nearly 30 μ g of DDT to DDD in 14 days. Another nitrogen-fixing species, the aerobe *Azotobacter* sp., produced no discernible metabolites of DDT. The degradation pattern of *Aerobacter aerogenes* seems to indicate a secondary conversion of DDD to other unknown metabolites in view of the fact that the 20 μ g of DDD detected after an incubation of 7 days had diminished to 12 μ g after 14 days.

The pattern of degradation in some organisms (*Erwinia* sp., *E. ananas*, and *X. uredoovor*) seemed to parallel the rate of growth. On the other hand, *X. stewartii*, *Pseudomonas tabaci*, and *Bacillus subtilis*, as well as others, produced only traces of DDD after 7 days, despite heavy growth, and yet converted appreciable amounts of DDT to DDD during the final 7 days.

Recovery of DDT from the controls, which were run repeatedly, exceeded 95 percent. Of significance, however, is the fact that, where degradation occurred, we were unable to account for approximately 10 percent of the insecticide as either DDT, DDD, or DDE [1,1-dichloro-2,2-bis(*p*-chlorophenyl)ethylene] after incubation for 14 days. In these instances, gas-liquid chromatography (GLC) peaks of unknown origin, particularly with *E. chrysanthemi*, *Pseudomonas syringae*, *X. uredoovor*, and *Aerobacter aerogenes*, were regularly observed. These suggest the degradation of DDT by bacteria to a number of metabolites still unidentified. The report of Barker and Morrison (10) on the degradation of DDD by *Proteus vulgaris* seems to support this contention.

The retention times (GLC) and the R_F values (TLC) of the standards and culture extractions of DDT and DDD were identical. We were unable to detect any autodegradation in control samples or as the result of column conversion (GLC) (11). Quantitation was based on integration counts compared to standards with the disk chart integrator.

Our results indicate that a broad range of plant pathogenic and saprophytic bacteria have the capacity to

convert *p,p'* DDT to *p,p'* DDD under anaerobic conditions in vitro and that this phenomenon is more ubiquitous than had previously been reported.

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Addiction Liability of Albino Rats: Breeding for Quantitative Differences in Morphine Drinking

Abstract. Selective breeding produced two strains of rats that differ in their susceptibility to morphine addiction. Inbreeding the more susceptible rats in an unselected population produced susceptible offspring; inbreeding resistant rats produced resistant offspring. Further selection and inbreeding increased the strain difference in the F_2 and F_3 generations. The F_3 generation also differed in their susceptibility to alcohol addiction.

A procedure, based on operant conditioning techniques and the known physiological effects of opiates, has been devised which can cause a relatively lasting change in the behavior of rats toward morphine. Weeks after their last dose of morphine, rats continue to show opiate-directed behavior (1-3).

The procedure used in this study was developed from an analysis of human drug addiction. If one accepts two propositions—(i) that opiate addiction is *not* something unique, but merely the repetition of a response, and (ii) that responses are repeated because they are followed by reinforcers—then it seems reasonable to believe opiates may be reinforcers.

Opiates appear to share at least one important characteristic with many other reinforcers: they reduce drives. Drives are tensions which goad a person into activity. But an opiate makes the subject inactive: after a "fix," an addict enters a stuporous, semi-dozing state. The drives produced by pain, hunger, anxiety, and sex are all simultaneously reduced by opiates (4); this property suggests that the opiates should be powerful reinforcers.

When the effects of an opiate wear off, the initially suppressed drives re- turn. Actually, these drives rebound

with increased vigor because they are augmented by the body's counteradaptations (3-5). Their return is experienced as tensions which soon increase to the point of distress. Human addicts, faced with approaching withdrawal, energetically seek drugs; this, with other evidence, indicates that the addicts are in a high-drive state (3).

It follows from this analysis that opiates would have a greater reinforcing or behavior-changing effect if taken when the subject is in the withdrawal stage because the opiates would have greater drive-reducing potential under these conditions. This deduction has been experimentally verified (3).

The procedure used in this experiment operantly conditions the response of drinking a normally refused morphine solution. The degree of behavioral change is quantified by choice tests in which individually caged rats are offered two calibrated 100-ml drinking tubes (Kimble No. 44875), one containing tap water, and the other a morphine solution (0.5 mg morphine per milliliter of water). Inexperienced rats prefer water and drink only 1 to 2 ml of the morphine solution in 24 hours. But during the cyclical reinforcing stage of treatment, rats drink increasingly more morphine solution on interposed choice tests. This change in

their behavior persists after they have been taken off the drug. Control studies have shown that the change in morphine drinking is not due to an association of morphine with thirst (1).

The procedure itself consists of three major parts: the stage before injection, the cyclical-reinforcing stage, and the abstinence stage. The stage before injection, which prepares the subjects for the cyclical reinforcing stage, is both preceded and followed by choice tests. These choice tests provide a base line of morphine-drinking before training. After the initial choice test, daily intraperitoneal injections of morphine HCl are started at 10 mg of morphine per kilogram of body weight per day. Tap water and food are provided without limit during this stage. The morphine dosage is increased by 5 mg until 20 mg per kilogram of body weight per day is being injected; this amount is kept constant for 17 successive days after which no additional injections are given. The postinjection choice test is precautionary only and measures any direct effect of the morphine injections on morphine-drinking. (None has been found so far.)

The cyclical-reinforcing stage consists of ten 3-day training cycles in which morphine is offered each time after an abstinence period. In each cycle the rats first are deprived of water for 24 hours. Then, during the next 24 hours, they are given only an aqueous solution of morphine HCl (0.5 mg morphine per milliliter of water) in a 100-ml drinking tube. At the end of this period, the morphine solution is removed and a similar tube containing tap water is given for 24 hours. This 3-day treatment schedule of no liquids, morphine solution, and water completes one training cycle. After five cycles, a third choice test is administered; after the tenth and last training cycle, a fourth choice test is given.

The abstinence stage of the treatment is a 2-week period of complete abstinence from morphine. Afterward a fifth and final choice test is given (1).

The abstinence choice test measures the persistence of the morphine-drinking habit. During abstinence, physiological disturbances (withdrawal symptoms) increase to a peak in about 3 days, but subside after 7 to 12 days to a point where near normal physiological functioning is reestablished (3-6). During the same interval, physical dependence on the drug becomes quite low (7). A choice test administered on the 14th day of abstinence,

therefore, measures the selection of morphine when physiological functioning is near normal and physical dependence on the drug is minimal. Although their physical need for opiates (that is, their physical dependence) is quite low, rats nevertheless continue to drink substantial amounts of morphine solution on the abstinence choice test. But some animals drink more than others (1).

The present experiment, a study of differences in susceptibility, began with 223 Sprague-Dawley rats (8). These rats (182 females and 41 males) were given the treatment described above, and their scores on the 14-day abstinence test were ordered by rank. Rats with scores in the highest quartile (that is, the more susceptible animals) were inbred randomly to produce the F_1 generation group S_1 ($n = 148$). Similarly, animals in the lowest quartile (that is, more resistant) produced the F_1 generation group R_1 ($n = 148$). Thus, there were two strains in the F_1 generation, an "addiction-prone" or susceptible group, S_1 , and an "addiction-resistant" group, R_1 .

Subjects in the F_1 and succeeding generations were selected for breeding in a manner similar to that used in the parental, or F_0 , generation. The highest quartile of group S_1 was inbred to produce group S_2 ($n = 151$). The lowest quartile of group R_1 produced group R_2 ($n = 138$). Similarly, groups S_2 and R_2 produced groups S_3 ($n = 90$) and R_3 ($n = 95$), respectively.

Drinking scores on choice tests were transformed to show the relative preference of the rats for the morphine solution in terms of their total liquid intake (in milliliters):

$$\frac{\text{morphine} - \text{water}}{\text{morphine} + \text{water}}$$

This score is a measure of opiate-directed behavior (ODB). A change from a negative ODB score toward zero or to positive shows an increasing relative preference for the morphine solution, that is, an increasing degree of ODB (9).

Figure 1 shows the mean ODB scores of the several groups. Note that the differences on the tests given before the animals were trained are small; they are also statistically nonsignificant. This lack of an initial difference makes it seem unlikely that the strains differ in preference for novel stimuli, in their preference for morphine when they are inexperienced, or in their ability to taste the morphine solution (0.5

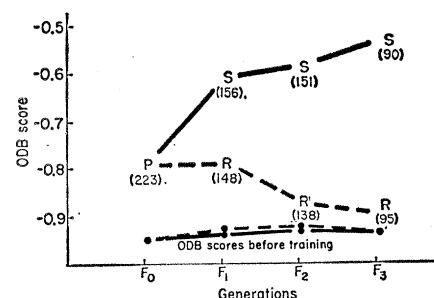


Fig. 1. The curves show the effect of selective breeding on morphine drinking by rats. From an unselected population (P), an addiction-susceptible strain (S, solid line) and an addiction-resistant strain (R, broken line) were bred. The number of subjects in each group is given in parentheses. The ODB score is a measure of opiate-directed behavior.

mg of morphine per milliliter of water).

The strains do differ in susceptibility in the F_1 , F_2 , and F_3 generations ($P < .005$ in all cases). Also, this difference between the strains became significantly greater from the F_1 to the F_2 , and from the F_2 to the F_3 generations ($P < .005$). These data confirm those of a previous study (10).

To test the question as to whether the susceptibility of each of these two strains to morphine addiction was unique or whether it was a specific expression of a more general trait of susceptibility, a second experiment was run to measure the susceptibility of these two strains to alcohol addiction. Experimentally inexperienced females of the F_3 generation, ranging in age from 300 to 400 days, showed no initial difference in alcohol preference. These animals had never received morphine in any form. When given a choice between a 10-percent alcohol solution and plain water, 16 susceptible and 17 resistant rats drank the same mean amount of the alcohol solution (1.7 ml). Their ADB (alcohol-dependent behavior) scores were not statistically different (a mean of -0.768 for the resistant rats and -0.821 for the susceptible rats). The susceptible rats drank slightly more water (35.5 versus 27.8 ml) but this difference too was not significant.

Because the physiological "rebound" is much shorter for alcohol than for morphine (unpleasant symptoms may occur after a few hours of sleep), the experimental design was changed. The alcohol solution, the only liquid offered the rats, was made available 24 hours per day during the treatment stage of the experiment. It was expected that the biological rhythms of

eating and sleeping would provide a cyclical reinforcing action somewhat analogous to that of the 3-day morphine cycles. Seven choice tests were given during the experiment; five were given at approximately 2-week intervals during the reinforcing stage (68 days of alcohol drinking). Then, alcohol was removed and all rats returned to plain tap water for 2 weeks, after which they were given a final choice test.

Three rats (two resistant and one susceptible) died during the treatment. One more rat in each group died during the 2-week abstinence period. One death was due to a tumor. The remaining deaths appear to have been due to the age of the animals and the physiological stress of the treatment. The drinking records of these rats were like those of other rats in their respective groups. There are no indications that the overall results would have been different had they lived.

The susceptible rats drank significantly more alcohol on about half the training trials (35 out of 68). Most significant differences occurred early; the first 14 trials were all significantly different, but the last 14 trials were all statistically nonsignificant. In contrast, the rats did not differ significantly in ADB on the first five choice tests. The difference in their ADB scores (-0.092 versus -0.475) on the sixth choice test, which terminated training, was barely significant ($P < .05$). The susceptible rats drank more alcohol (means: 19.0 versus 11.9 ml).

But the relapse scores were quite different. After a 2-week interval of no alcohol, the susceptible rats drank twice as much alcohol as the resistant rats (means: 24.0 versus 12.0 ml). The mean final ADB score of the susceptible rats was -0.024 versus -0.473 for the resistant rats ($P < .005$).

These strains, bred for a differential relapse to morphine drinking, show a similar differential relapse to alcohol drinking. This is the effect of an addicting drug; quinine, equated in initial aversiveness and given in a similar drinking regimen, causes little or no change in the behavior of either strain. We have not yet isolated the factors responsible for this difference in addiction liability, but one factor seems to be passed on from generation to generation.

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Stereopsis Based on Vernier Acuity Cues Alone

Abstract. *Random-line stereograms were generated in which the only monocular cues were minute breaks occurring at random in thin vertical (or horizontal) line grids. The breaks were binocularly correlated. The stereograms yielded global stereopsis (of a square standing out in front of a surface) even with monocular breaks of as little as 16 seconds of arc, which is below the threshold for resolving two lines. This technique led to the clarification of relations between local and global stereopsis.*

Our visual system is remarkable in that it enables us to detect tiny breaks in lines even when the breaks are much smaller than the separation between the cones in our foveas. The limit of this super-resolution is called *vernier acuity* when the lines break in a plane and is called *stereoscopic acuity* when the break occurs in depth. Ordinary *visual acuity* is the limit of resolution for two dots (or seeing the spaces between lines in a grid, or detecting a gap in a ring). Optimal visual acuity for line gratings is reported to be 28 seconds of arc (1) (actually acuity is defined as the logarithm of the reciprocal of this value), and optimal vernier and stereoscopic thresholds are about 2 seconds of arc, depending on the type of test targets used (2). These values are obtained under optimal laboratory conditions and with selected subjects; in practice, values are much worse [for instance, stereoscopic threshold was measured in one terrain situation to be 24 seconds of arc, which for that situation corresponded to a distance of 580 m (3)].

The limits of visual acuity seem to be completely accounted for by the coarseness of the retinal mosaic, that is, by the distance between the cones. However, since vernier and stereoscopic acuity are much better than the intercone separation, they must be obtained by central nervous system processing. Additional evidence supporting this

view is the fact that the longer a line (up to a limit), the smaller the break that can be detected (4). The present study provides information as to whether this superresolution process precedes or follows binocular combination.

The technique of random-dot stereograms devised by one of us (5) enables the researcher to determine whether certain perceptual cues are processed at the retinal or the cortical level. In earlier studies regular square arrays of 100×100 cells were used, with individual cells painted black or white randomly. The left and right eyes' images were such arrays, identical except for a center square which was shifted horizontally in one image by an integral number of cells as if it were a solid sheet. When these images are viewed monocularly, they give the impression of a uniformly random texture without any gap or boundary. When viewed stereoscopically the center square is seen in depth in front of the unshifted surround.

The present studies used, in place of square black and white cells, short line segments. These line segments will be referred to as picture elements. Arrays of the elements were drawn by a computer-controlled display device. The smallest unit that can be portrayed is a single dot or a vector (line segment) having one-dot width. The picture elements of Fig. 1 are composed of vertical line segments one dot wide