photometer. The critical constants are as follows: approximately 5 mg of bone ash was weighed into necked deep crated 3/16-in. electrodes (National Carbon Co. No. 4000) and arced at 16.5 amp to completion. A glass filter, to absorb second-order interference lines, was placed before the 30-μ slit. A rotating sector allowed the transmission of 35 percent of the light. Kodak SA No. 1 film was used and D-19 developer at 3 min and 20°C. The Sr 4607 line was used as the analysis line and Ca 4579 was the monitor line.

5. Additional data on individual samples may be obtained from us.
6. K. K. Turekian and J. L. Kulp, *Geochim. et Cosmochim. Acta,* in press.
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Chemically Altered "Permanent" Behavior Patterns in Fish and Their Cure by Reserpine

In the course of enzymatic studies on the mode of action of a variety of drugs, we had occasion to use the guppy (*Lebistes reticulatus* as a test organism. It soon became apparent that this organism provided an excellent tool for the study of the effects of chemical substances on behavior, primarily because any abnormal alterations in behavior were easy to observe. We found that the guppy responded to exposure to small quantities of LSD (lysergic acid diethylamide) in a characteristic manner.

When the fish (size or sex seemed not to influence the results) were placed in a solution containing LSD (4 μg/ml at *p*H 6.5 to 7.5 and 25° to 28° C) for 1 hour and then transferred to water, they responded with a characteristic vibrating behavior. This consisted of a rapid swimming until the wall of the container was reached, at which point the fish continued to swim apparently unaware that they were not making any progress. We found that, although many behavioral changes may be observed with various substances during exposure, possibly owing to local irritation, and so on, the changes that may be observed after the fish have been returned to water are more characteristic of true behavioral change.

A good system for observing such changes consists of keeping the treated subjects in a 500-ml beaker containing 300 to 350 ml of water and held in a quiet and undisturbed environment. The action of LSD observed under these circumstances was so characteristic that it served as a method of studying the action of this substance on behavior. The effect is not so characteristic as that observed with snails, but the behavior pattern of the fish is more complex and has the advantage of being more susceptible to observable modification. Other organisms were studied: *Betta splendens* (*1*), cavefish, goldfish, and so on. Each of these responds in a somewhat different manner, but the differing behavior patterns are all distorted aspects of normal behavior. The goldfish, for example, tends to swim backward; the cave-fish does not move at all. However, the guppy appeared to be as good a tool as the other organisms, so that it was studied more intensively.

All the kinds of fish responded to other hallucinogenic drugs (such as mescaline, yohimbine), but in a manner distinctly different from that observed with LSD and frequently with less characteristic behavior. The proper choice of experimental organism might well serve to distinguish between an array of these substances. However, this use is complicated by the fact that the response to mixtures of hallucinogenic agents produces a mixture of behavior patterns that are frequently difficult to separate. We have so far been unable to devise a quantitative method for study of the behavior pattern and are therefore limited at the moment to descriptions of its nature.

We have studied a variety of substances for their effect on the behavior pattern of the guppy without finding any that produce a pattern as characteristic as that produced by LSD. One incidental finding is of interest. The antihistaminic drugs are exceedingly toxic to the guppy and cannot be used in concentrations higher than 10^{-5} or $10^{-6}M$.

Because of the antagonism between LSD and serotonin, we attempted to antagonize the LSD effect in the guppy by previous or simultaneous exposure to serotonin. This treatment had no observable effect on the LSD response. We therefore studied other indoles in attempts to antagonize LSD. We found that 1 hour's exposure to indole or tryptamine ($10^{-4}M$, $10^{-3}M$ is toxic) followed by exposure for 1 hour to LSD (4 μg/ml), far from antagonizing the effect of LSD, tended to prolong it markedly.

In a variable number of the specimens treated with indole plus LSD (ranging from 10 to 60 percent of the fish exposed) abnormal behavior usually remained for as long as a week after treatment. In some cases these abnormalities lasted for months. The aberrant behavior consisted of periods of normal behavior interspersed at intervals (perhaps every 10 to 20 minutes) with periods of LSD-type behavior. Throughout these periods the courtship pattern of the guppy was not disturbed.

So far as our present experience goes, the permanent induction of the characteristic abnormal behavior can be accomplished by pretreatment with indole or tryptamine followed by LSD under the conditions specified here but is not induced by a variety of other substances, including an array of indoles, for example, serotonin. Indole or tryptamine alone (at $10^{-4}M$) has very little effect on repeated exposure, and the LSD symptom may be induced by repeated treatments without becoming permanently established. It appeared, therefore, that, by treatment with indole and LSD, we had influenced the behavior pattern of a living creature in a "permanent" fashion and that one could, by chemical means, set up within a living creature a behavior pattern which remained long after the substances causing it had been removed from the environment. The behavior pattern consisted of an aspect of normal behavior conducted in an exaggerated and abnormal manner.

We have had many fish whose abnormalities lasted for many weeks. If such fish were treated with reserpine (20 μg/ml for 3 days) their behavior pattern returned to normal and remained normal subsequently. The cycle of chemical induction of abnormal behavior and reversion to normal with reserpine may be repeated, but we have the impression that the fish are more sensitive to a second treatment. Chlorpromazine proved to be very toxic to the fish; hence, the lack of effect in normalizing behavior may be owing to the low concentrations that it was necessary to use.

It appears, therefore, that one can cure this chemically induced abnormal behavior by a further chemical treatment. The fact that the substances employed have an action in human behavior (*2*), which may well be a counterpart of their action in the fish, would seem to be more than fortuitous and would suggest that fish might be an important tool for the study of these effects.

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References and Notes

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2. The literature on these substances is so voluminous and in so active a state that we have made no attempt to refer to any of it.

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