Pharmacology Biochemistry & Behavior, Vol. 32, pp. 355–356. © Pergamon Press plc, 1989. Printed in the U.S.A. 0091-3057/89 $3.00 + .00

RAPID COMMUNICATION

The Hedonic Effects of Amphetamine and Pentobarbital in Goldfish

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Received 14 November 1988

LETT, B. T. AND V. L. GRANT. *The hedonic effects of amphetamine and pentobarbital in goldfish.* PHARMACOL BIOCHEM BEHAV 32(1) 355–356, 1989.—Goldfish were confined in a distinctive chamber while drugged with amphetamine in Experiment A or pentobarbital in Experiment P. During a later test, the goldfish in Experiment A showed a preference for the chamber associated with amphetamine, whereas those in Experiment P showed an aversion to the chamber associated with pentobarbital. Thus, amphetamine produced a rewarding effect while pentobarbital was aversive. The mechanism of pentobarbital's aversive effect is unknown. However, there is convincing evidence that amphetamine produces a rewarding effect in rats, monkeys and humans by increasing the synaptic concentration of dopamine in the central reward system. Since the goldfish brain has cells containing dopamine, the same mechanism is likely to be responsible for amphetamine's rewarding effect in goldfish. This similarity suggests that the central reward systems of such diverse species as goldfish, rats, monkeys, and humans have a common evolutionary origin.

Amphetamine Conditioned place aversion Conditioned place preference
Evolutionary origin of central reward mechanism Goldfish Pentobarbital

IN common with other, more complex vertebrates, goldfish seek pleasure and avoid pain. That is, goldfish repeat actions that lead to a rewarding consequence and learn to avoid or escape aversive stimuli. For example, goldfish learn to go where food is to be found (1). They also learn to swim away from a place to avoid or escape electric shock (5). In most experiments with goldfish, the hedonic effect was produced by external stimuli. However, rewarding and aversive states can also be evoked by electrical stimulation of certain sites in the telencephalon (2). The present experiments extend these findings to hedonic effects induced by the injection of a drug, amphetamine in Experiment A and pentobarbital in Experiment P.

It is well-established that amphetamine produces a rewarding effect in humans and animals such as monkeys and rats (4,12). The aim of Experiment A was to show that amphetamine also produces a rewarding effect in goldfish. In contrast to amphetamine, the hedonic effects of pentobarbital have not been so extensively studied. Under the conditions of Experiment P, however, a subanesthetic dose of pentobarbital was expected to produce an aversive effect in goldfish.

The method of place conditioning was used to assess the hedonic effects of both drugs. To produce place conditioning, confinement in a distinctive chamber was associated with the hedonic state produced by the injection of the drug on a number of occasions. During a later test, each fish, while in an undrugged state, was allowed to swim freely between the drug-associated chamber and an adjoining, neutral chamber. If the drug associated with the distinctive chamber was rewarding, the fish should spend more time in the distinctive chamber. On the other hand, if the drug was aversive, the fish should spend less time there.

METHOD

For each experiment, 20 goldfish with a mean body weight of 4 g in Experiment A and 5 g in Experiment P were obtained from a local supplier. They were assigned to two groups of 10, equated in body weights. Each group was maintained in a 38-liter aquarium with filtered and aerated water (18.5±1°C) under a 12-hr light/dark cycle (lights on at 0800 hr). They were fed twice daily, once in the morning and again in the late afternoon. Experimental procedures were administered between 1400 and 1600 hr.

Training occurred in two distinctively different chambers that were formed by dividing each of 20 Plexiglas tanks (30×11×20 cm) into two equal-sized compartments with a Plexiglas barrier. In every tank, the external walls of one compartment were covered with white posterboard while the walls of the other compartment were left clear. In both experiments, one group of fish had the compartment with clear walls associated with the drug-induced hedonic state while the second group had the white compartment associated with the drug. On six training trials, each fish was injected intraperitoneally with the drug (0.02 mg of *d*-amphetamine sulfate

dissolved in 0.05 ml of 0.6% saline in Experiment A or 0.06 mg of pentobarbital in 0.05 ml of 0.6% saline in Experiment P) and then immediately placed in the appropriate compartment of one of the tanks for 30 min. On six other training trials, each fish was simply habituated to the other compartment for 30 min; no injections were given on these occasions. The two kinds of training trials were intermixed with rest days. Training trials were spaced 24–72 hr apart; at least 72 hr intervened between trials that involved injections of drug.

Several days after the last training trial, each fish was individually tested. The Plexiglas barrier was removed from the test tank, allowing free access to both compartments. At the beginning of the test, each fish was placed, head to tail, along the midline that separated the two compartments of the tank. In both groups, the amount of time spent in the clear compartment during a 10-min test was measured. The fish was visible to the experimenter only when it was in the clear compartment; it was considered to be in the clear side when the experimenter could see one of the fish's eyes.

RESULTS AND DISCUSSION

In Experiment A, the fish for which the clear compartment was associated with amphetamine spent on average 64% of the 10-min test in the clear compartment. In contrast, the fish for which the white compartment had been associated with amphetamine spent only 42% of the test period in the clear compartment. This difference between the two groups in the percentage of time spent in the clear compartment was significant ($p<0.001$, t-test) and indicates that the fish preferred the compartment paired with amphetamine. Thus, amphetamine has a rewarding effect in goldfish just as it does in humans, monkeys, and rats (4,12).

In Experiment P, the fish that had the clear compartment associated with pentobarbital spent on average 38% of the 10-min test in the clear compartment while those that had the white compartment paired with pentobarbital spent on average 58% of the test period in the clear compartment. This difference was significant ($p<0.05$, t-test) and indicates that the fish showed an aversion to the compartment associated with pentobarbital. Rats also show aversion to a place associated with pentobarbital (6). Unfortunately, the mechanism by which pentobarbital produces an aversive effect is unknown.

There is a large and convincing body of evidence that amphetamine produces a rewarding effect in mammals such as rats, monkeys, and humans by facilitating dopamine transmission in the part of the brain that mediates the hedonic effect of natural rewards such as food (7–11). Since the goldfish brain has neurons containing dopamine (3), the rewarding effect of amphetamine is probably produced by the same mechanism in goldfish, a teleost, as in mammals. If so, the shared characteristic of a dopaminergic component implies that the central reward system in teleosts and mammals evolved from a common ancestor.

ACKNOWLEDGEMENTS

We thank Maurice Kavanagh for his skillful technical assistance and also Eugene Fitzgerald and Kevin Keough for loaning us test tanks and aquaria. We are also indebted to Bill Montevecchi and Larry Crim for helpful advice and to Sam Revusky for reading and commenting on the manuscript. This work was supported by the Natural Sciences and Engineering Research Council of Canada.

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