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Despite Various Drugs, Cats Continue to Kill Mice[1]

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LEAF, R. C., D. J. WNEK, S. LAMON AND P. E. GAY. *Despite various drugs, cats continue to kill mice.* PHARMAC. BIOCHEM. BEHAV. 9(4) 445–452, 1978.—Amphetamines (d- at 0.5–4 mg/kg; l- at 2–4 mg/kg) inhibited spontaneous mouse killing by some, but not all cats. Various other drugs (drugs and maximum tested doses were: imipramine, 64 mg/kg; amitriptyline, 32 mg/kg; tranylcypromine, 2 mg/kg; tripelennamine, 4 mg/kg; scopolamine, 1 mg/kg; methyl scopolamine, 1 mg/kg; chlordiazepoxide 16 mg/kg; diazepam 4 mg/kg; meprobamate, 80 mg/kg; pentobarbital, 16 mg/kg; chlorpromazine, 8 mg/kg; and haloperidol, 0.5 mg/kg) did not reliably inhibit such killing. In contrast with rats, mouse killing by cats was not consistently blocked by antidepressants or amphetamines. When individual cats were inhibited, their reduction of killing seemed related to anorexia rather than to affective arousal.

Amphetamines Mouse killing Cats Aggression Antidepressants Tranquilizers Neuroleptics Species differences

KILLING of animals of one species by those of another is widespread in nature. Its frequency influences evolutionary selection. Despite this evolutionary function, relatively few studies have investigated how interspecies killing can be reduced by pharmacological treatments.

Only one type of intraspecies killing has been subjected to detailed study. Drugs that selectively block mouse killing by rats have been investigated fairly extensively, primarily because inhibition of killing has been related to the antidepressant effects of many of these drugs in humans [21]. d-Amphetamine has been the prototypic, most extensively studied, drug that inhibits mouse killing by rats. The inhibition it produces is specific to killing, and it appears to be related to the affect increasing actions of the drug. d-Amphetamine inhibits spontaneous mouse killing at doses that have minimal side-effects [4, 5, 21, 22]. The inhibition is separable from anorexic effects [18]. d-Amphetamine also selectively inhibits the killing of other prey, such as frogs and crickets [18]. It is more potent than l-amphetamine [16], and direct brain injections of microgram quantities are highly effective [34]. Finally, and most importantly, the selective inhibitory effects of d-amphetamine on killing seem to be shared by those drugs that have clinically effective antidepressant activity in humans [19, 21, 22, 33]. Reduction of spontaneous mouse killing by rats seems, therefore, to reflect a specific, selective, consequence of increased affective reactivity.

In addition to their inhibition of spontaneous mouse killing, amphetamines have inhibited mouse killing by rats that is not spontaneous, but elicited as a consequence of various drug injection treatments. d-Amphetamine inhibited killing induced by pilocarpine, both in neurologically normal [16,59] and in amygdala-lesioned rats [17]. It inhibited killing induced by chlordiazepoxide [35]. In addition, methamphetamine, when it did not potentiate stimulation-induced convulsions, seemed to inhibit "quiet biting" mouse attack produced by electrical stimulation of the rat hypothalamus [14].

Few studies have been carried out with other species. Evidence that d-amphetamine, which has been the most extensively studied inhibitor of killing by rats, also blocks spontaneous killing by mice has been reported [18,39]. No studies have examined the effect of d-amphetamine on spontaneous mouse killing by non-rodent species, however, so it is not clear whether the drug effects observed with rats are representative examples of general mammalian patterns (see [2, 6, 19, 26, 41, 56] for reviews).

With cats, some findings have indicated that d-amphetamine and tricyclic antidepressants may either facilitate [53] or have mixed effects [13, 14, 38] on reflex components of brain stimulation-induced attack and killing behavior patterns. It is not clear, however, whether there are differences between cats, on the one hand, and rats and mice, on the other, that are due to physiological differences

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in the mechanisms that control their killing. The reported experiments with cats are relatively meager when compared with the extensive literature on rats. Further, the brain stimulation procedures used to obtain killing, in previous studies with cats, differ from the spontaneous evocation procedures most commonly used to study drug effects on killing by rats. The reported differences may, therefore, be due to differences in the situations studied rather than to physiological differences between the species. Alternatively, of course, differences between the mechanisms that control killing by rats and cats may, in fact, exist [36].

In order to examine this question more carefully, a series of studies was carried out to examine the possible inhibitory effects of drugs on spontaneous mouse killing by cats.

d-Amphetamine, in the experiments described below, did inhibit spontaneous mouse killing by cats. Although these results at first appeared similar to the well established findings with rats, the inhibition of killing by cats does seem to differ from that seen with rats. d-Amphetamine does not block killing, at any dose, in all cats. Although it is more potent than l-amphetamine, and probably inhibits killing by a central nervous action, tricyclic antidepressant drugs do not produce similar inhibition. The inhibitory action in cats, unlike that in rats, seems present in only some individuals and is closely associated with the anorexic effects of the drug. Further, d-amphetamine induced conditioned aversions could not be established in cats, even though aversions that completely block killing are readily established in rats [16,17]. It seems, therefore, that there may be real species differences in the mechanisms by which d-amphetamine inhibits killing by rats and cats. These results, together with others described below, suggest that feeding mechanisms play a major role in regulating killing by cats and that affective mechanisms are more important for rats.

EXPERIMENT 1: EFFECTS OF d-AND l-AMPHETAMINE ON SPONTANEOUS MOUSE KILLING BY CATS

The purpose of Experiment 1 was to determine whether or not d-amphetamine inhibited spontaneous mouse killing by cats and, if it did, whether it was more potent than l-amphetamine. A group of cats that spontaneously killed mice reliably was selected, and a dose-effect study was carried out with both d- and l-amphetamine.

METHOD

Animals

Five adult male and five adult female laboratory-bred cats that spontaneously killed mice during every one of ten pretests, described below, were selected for this experiment.

Experimental Design, Apparatus, and Procedure

The cats were separated by sex and housed with others (not all of which were used in this study) in groups of 4–8 in separate rooms. Each room was 2.43 m×3.05 m in floor area and 2.43 m in height. Each room contained tiered shelves, open stainless steel cages, and resting mats. Lights in the rooms were on from 8:00 a.m. to 11:00 p.m. daily and off otherwise. Tap water and Purina Cat Chow, plus daily dietary supplements of varied canned and commercial fish and meat cat foods were provided *ad lib*.

Cats were tested for killing every other day. Each test was carried out by placing the cat together with a single adult male Swiss-Webster albino mouse in one of the stainless steel cages in its housing room, and closing the cage. If the cat killed the mouse, the test was terminated and the cat and mouse carcass were removed from the cage; if no kill occurred within 0.5 hr, however, the cat and live mouse were removed and the test was scored as a non-killing instance.

Each cat was pretested ten times. Those selected for this experiment not only killed a mouse during every pretest but, by the end of the pretest series, did so within 1 min after the test began.

Ten tests, each of which was preceded by an injection 20 min before the start of the test, followed the selection pretests. This procedure presumably produced high stable brain levels of d-amphetamine throughout each test [32]. All injections were given IP in 0.2 cc/kg solutions of 0.9% NaCl. Each cat's series of 10 injections contained each of 5 doses (0, 0.5, 1, 2 and 4 mg/kg) of d-amphetamine sulfate (d-amphetamine), and each of 5 doses (0, 0.5, 1, 2, and 4 mg/kg) of l-amphetamine sulfate (l-amphetamine); one of the 2 control doses (0 mg/kg) were arbitrarily assigned to each of the 2 isomers, before testing began, to provide statistically independent evaluation of each isomer's dose-effect function separately from that of the other, if that should prove desirable. The 10 doses were administered to the 10 cats in an order that corresponded to a counterbalanced 10×10 Latin Square.

RESULTS

d-Amphetamine blocked mouse killing in a dose-related fashion, as shown in Fig. 1. All cats killed when they received control injections, but some inhibition was apparent even at the 0.5 mg/kg dose of d-amphetamine, and the frequency of killing progressively decreased as the dose increased. l-Amphetamine, in contrast, was much less effective. Killing was never blocked except at the very highest doses, of 2 and 4 mg/kg. Interestingly, the 3 cats that failed to kill when given 4 mg/kg l-amphetamine were the same 3 cats that were inhibited after 0.5 mg/kg d-amphetamine. The reduction in kills per cat produced by d-amphetamine was significantly greater than that produced by l-amphetamine (sign test, $p<0.05$; all statistical significance levels shown in this report are two-tailed, unless otherwise noted). d-Amphetamine clearly inhibited spontaneous mouse killing by cats, and it was several times as potent as l-amphetamine, which suggests that its mechanism of action probably was a central one. These results are similar to previous findings with rats.

The overt effects of both isomers were qualitatively similar. The principal overt effects with the doses, duration, and setting conditions used in Experiment 1, in agreement with previous reports [58], consisted primarily of changes in autonomic, affective and behavioral reactivity. The cats sat and moved about in a generally normal manner, even at the highest doses, but they tended to be overreactive to mice, human handlers, and other features of their environment. These reactions were qualitatively appropriate whether they were positive (e.g., purring) or negative in (e.g., hissing) affective tone. Under these conditions, persistent, stereotyped, motor activity was not observed, in agreement with previous studies of similar doses in cats [50].

EXPERIMENT 2: EFFECTS OF IMIPRAMINE AND AMITRIPTYLINE ON SPONTANEOUS MOUSE KILLING BY CATS

Despite the fact that some cats continued to kill, the fact

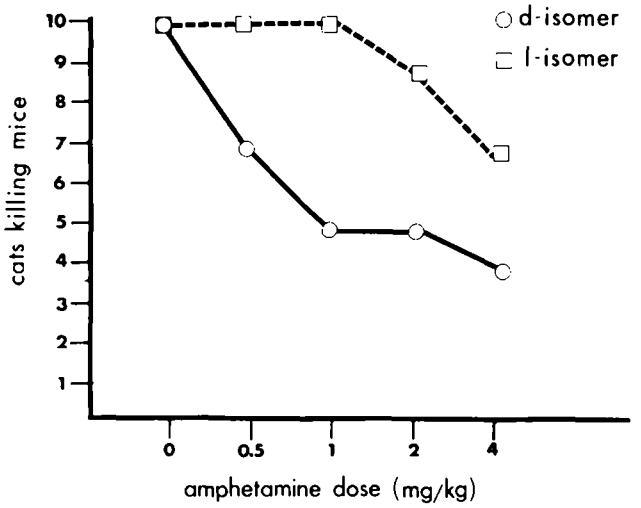

FIG. 1. Effects of *d*- and *l*- isomers of amphetamine sulfate on the number of cats that spontaneously killed mice during Experiment 1.

that d-amphetamine did inhibit mouse killing by cats suggested that the pharmacological mechanisms for inhibiting spontaneous killing by rats and cats might be basically alike. If so, tricyclic antidepressant drugs, would be expected to inhibit spontaneous mouse killing by cats. Experiment 2 tested for such an action. It should be noted, however, that tricyclic antidepressants (like d-amphetamine) do *not* reliably inhibit brain-stimulation induced killing by cats [13,14]. If such induced killing is, in fact, like spontaneous killing [7], tricyclics would *not* be expected to inhibit spontaneous mouse killing by cats. Previous findings, therefore, do not permit a clear prediction about what results would be most likely from this study.

METHOD

Animals

Two adult male and three adult female laboratory-bred cats, selected in the same fashion as those of Experiment 1, were used for this experiment.

Experimental Design, Apparatus, and Procedure

The cats were separated by sex and housed with others (not all of which were used in this study) in groups of 4–8 in chain-link pens. Each pen had a 2.43 m×1.22 m floor area and a height of 2.43 m. The pens contained tiered shelves, open stainless steel cages and resting mats. In all other respects conditions for housing maintenence and testing were identical to those used for Experiment 1.

Drug test series 2A, 2B, 2C, 2D, 2E, and 2F were conducted sequentially after the pretests for selection of animals. These tests included initial drug (d-amphetamine) and placebo (vehicle) control injections to show that these cats, like those of Experiment 1, could be weakly inhibited by d-amphetamine and that they were not inhibited when undrugged. These control tests were followed by 3 series of tests with various, progressively higher, ranges of imipramine doses; a series of tests with a range of amitriptyline doses; and a final brief retest with the drug and placebo control injections.

Series 2A consisted of control injections of either vehicle alone, or of 4 mg/kg d-amphetamine, in an order that was randomly determined for each animal. Series 2B consisted of 5 doses (0, 2, 4, 8 and 16 mg/kg) of imipramine HCl (imipramine). The 5 doses were administered to the 5 cats in an order that corresponded to a 5×5 Latin Square. Series 2C was identical to Series 2B except that the doses used were 0, 4, 8, 16 and 32 mg/kg imipramine, and a different Latin Square was used to assign their order. Series 2D was, once again, identical to Series 2B and 2C except that the doses used were 0, 8, 16, 32 and 64 mg/kg imipramine, and another Latin Square was used. Series 2E consisted of 5 doses (0, 4, 8, 16 and 32 mg/kg) of amitriptyline HCl (amitriptyline), in still another Latin Square. Series 2F was identical to series 2A except that 6 mg/kg of d-amphetamine was used.

RESULTS

The results of Experiment 2 were simple and clear. No cat ever failed to kill except after injections of d-amphetamine. Two of the 5 cats failed to kill after either 4 or 6 mg/kg of d-amphetamine and 3 cats killed even when given d-amphetamine. Every cat killed every mouse at every dose of imipramine and amitriptyline that was tested.

The highest doses of the tricyclics had clear pharmacological and acutely toxic effects even though they never blocked killing. At 64 mg/kg imipramine, for example, one cat had convulsions (after it killed its mouse) and had to be given supportive veterinary treatment. The failure of these drugs to block spontaneous killing was, therefore, not attributable to a lack of pharmacological activity at the doses tested. The tricyclics were, in fact, *less* effective in blocking spontaneous killing than they had been in blocking brain-stimulation induced killing by cats [14].

These results contrast sharply with those previously reported with rats. The ED_{50}'s for block of spontaneous mouse killing by rats were 8.0 mg/kg for imipramine and 5.1 mg/kg for amitriptyline [22], and both compounds are typically more potent in cats than in rats. The weak inhibitory effects of d-amphetamine were not shared at all by the tricyclic antidepressants. Neither d-amphetamine nor either of the tricyclics inhibited spontaneous killing at all in several cats. Thus, there does not seem to be any association between the clinical antidepressant action of drugs in humans and the inhibition of mouse killing by cats.

EXPERIMENT 3: EFFECTS OF d-AMPHETAMINE ON SPONTANEOUS MOUSE KILLING AND EATING BY CATS

If the inhibition of spontaneous mouse killing by d-amphetamine in some cats is not associated with its affect stimulating action, the question of what action it might be associated with, when it does occur, seems particularly important. The anorexic effects of d-amphetamine are an obvious possibility, but several considerations weigh against that suggestion. No simple association between readiness to eat and readiness to kill has been apparent in rats [55], in spite of controversial claims to the contrary [45,46]. In addition, d-amphetamine has proven a powerful tool for *dissociating* mouse killing and eating in the rat, because the ED_{50} for inhibition of mouse eating is much lower than the ED_{50} for killing those same mice [18]. There is no pre-experimental reason to expect different results in cats because, from the

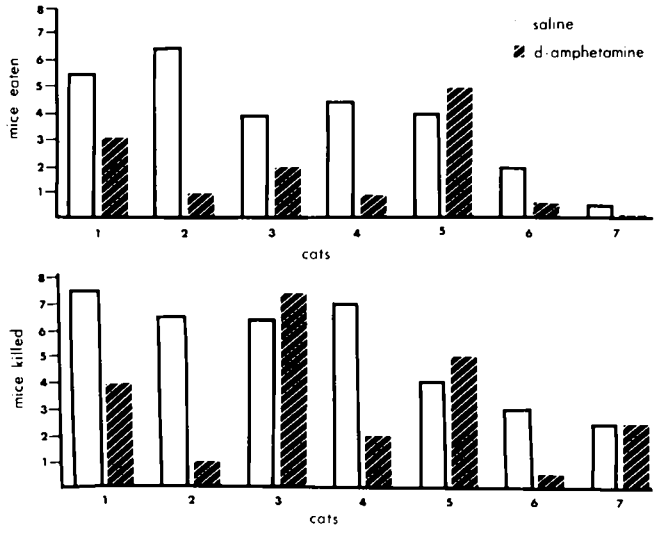

FIG. 2. Effects of placebo and d-amphetamine injections on the number of mice killed and the number of mice eaten by cats during Experiment 3.

results of Experiment 1, the ED_{50} for inhibition of killing appears quite high when compared to previously reported ED_{50} values for anorexic effects of d-amphetamine in cats [1]. The possibility that cats might be inhibited by d-amphetamine for different reasons than rats must, nevertheless, be considered.

Experiment 3 was therefore designed to test the relationship between inhibition of killing and inhibition of eating in cats. Spontaneously killing cats were given mice to kill and eat every 0.25 hr for 2 hr after either vehicle or low doses of d-amphetamine. It seemed likely that the cats, under somewhat satiating test conditions, would reduce either the amount that they ate mice or the amount that they killed them, or both.

METHOD

Animals

Five adult male and two adult female laboratory-bred cats, selected in the same fashion as those of Experiment 1, were used for this experiment.

Experimental Design, Apparatus, and Procedure

The cats were housed and maintained like those of Experiment 2. Drug test Series 3A and 3B were conducted sequentially after the pretests for selection of animals. Series 3A consisted of 2 tests, one each after PO injections of either distilled water vehicle or of 1 mg/kg d-amphetamine at a volume of 1 cc/kg. Series 3B consisted of 2 more tests, one each after injections of either vehicle or of 2 mg/kg d-amphetamine. The test procedure in each case consisted of presentations of 8 mice, one at a time, every 0.25 hr, for 1.75 hr, to each cat. The mice were removed whether alive or dead at the end of each 0.25 hr period, unless they had been killed and completely eaten. Dead mice were scored as either eaten (more than 25% of the carcass consumed) or uneaten when they were removed, and the presence or absence of eating behavior after each kill was also observed and recorded.

RESULTS

The data for individual animals from the 2 drug tests were quite similar even though 2 different doses had been used, and the data for individual animals on the 2 control tests were also quite similar. The 2 drug and 2 control tests for each animal were therefore separately combined and averaged, to increase statistical reliability. These data are shown in Fig. 2. As Fig. 2 indicates, d-amphetamine clearly inhibited both killing and eating by 4 of the cats, but it seemed to inhibit only eating and to have little effect on killing by the other 3 cats. When all 7 cats were considered together, d-amphetamine decreased killing from 5.29 mice per control session to 3.21 mice per drug session, a difference of 2.07 mice ($t = 1.99$, $df = 6$, $p < 0.05$).

The decrease in killing exactly paralleled the decrease in eating for the group as a whole, and it tended to do so for a bare majority of individual animals, as well. Some individual animals reduced their eating without reducing killing, suggesting that a dissociation like that seen in rats may have occurred with these individuals. It is fair to say, however, that d-amphetamine either had no effect on killing by individual cats, or it had one that was associated with anorexia. The parallel reductions in killing and eating contrast strikingly with the consistent dissociation between effects of d-amphetamine on killing and eating in rats [18,42].

EXPERIMENT 4: AN ATTEMPT TO PRODUCE A d-AMPHETAMINE-INDUCED CONDITIONED AVERSION TO MOUSE KILLING BY CATS

d-Amphetamine can block killing by rats in two ways. Both types of inhibition may involve its affect-stimulating actions. d-Amphetamine can block killing when it is injected before a mouse is presented, as described above. Experiment 1 tested for this action in cats. It can also block mouse killing by rats when it is injected after each kill, in which case it induces a gradually acquired conditioned aversion [16,17]. Experiment 4 was a test for this latter action in cats.

The conditioned aversions produced by d-amphetamine seem to differ from those due to treatments that produce toxic gastrointestinal disturbances [11, 42, 47]. d-Amphetamine conditioned killing (and taste) aversions seem to involve different (possible affect related) brain mechanisms from those that mediate illness-induced aversions in rats [10,17]. Further, they occur after dose levels that can also reinforce antecedent behavior [10, 12, 54]. Finally, these aversions are acquired with doses which do not seem to produce gastrointestinal disturbances. It is likely, for all these reasons, that d-amphetamine conditioned killing aversions in rats (perhaps unlike other drug-induced conditioned aversions) are more related to the drug's affect-stimulating than its gastrointestinal actions [10,42].

Whether or not d-amphetamine can produce conditioned killing aversions has not previously been tested with cats. Experiment 4 was designed to test for development of such aversions. Spontaneously killing cats were pretested, to determine whether or not d-amphetamine injected before mouse presentation would block killing. Some cats that were inhibited during this pretest and some that were not inhibited were included in each of 2 groups, for subsequent aversion conditioning. Cats from 1 of these groups were given d-amphetamine after each of a series of killing tests, and those from the other groups were given control injections.

METHOD

Animals

Six adult male and four adult female laboratory-bred cats, selected as in the same fashion as those of Experiment 1, were used for this experiment.

Experimental Design, Apparatus, and Procedure

The cats were housed and maintained like those of Experiments 2 and 3, and tested daily for mouse killing with procedures like those of Experiments 1, 2, and 3.

Drug test series 4A, 4B, and 4C were conducted sequentially after the pretests for selection of animals.

These tests included drug (d-amphetamine) and placebo (vehicle) control injections *before* daily tests, to confirm the comparability of these cats to the previous experiments; drug and placebo injections *after* daily tests to test for acquisition of conditioned aversions; and a final series of control injections *before* daily tests.

Series 4A and 4C were identical for all cats. Both series consisted of two tests given after 0.2 cc/kg IP injections, as in Experiments 1 and 2. One of these injections was of 0.9% NaCl vehicle and the other was 2 mg/kg d-amphetamine, with the order of the 2 treatments randomly determined for each animal during each series.

Series 4B consisted of 10 tests given before the daily injections. During Series 4E, the cats were divided into 2 groups, each of which contained 3 males and 2 females; and each of which included 3 cats that had killed and 2 cats that had not killed when given d-amphetamine during Series 4A. Cats of one group, Group A, were given daily 0.2 cc/kg IP injections of 2 mg/kg d-amphetamine immediately after each daily killing test. When the test was terminated because of a kill, this injection was always completed within 1 min after the kill had occurred. Cats of the other group, Group S, were given daily injections of 0.9% NaCl vehicle, but otherwise treated identically to those of Group A.

RESULTS

The results of Experiment 4 were almost as simple as those of Experiment 2. During Series 4B, only 1 cat ever failed to kill a mouse. That cat, which was in Group S, failed to kill on 3 occasions. Every cat in Group A and all the other cats in Group S, continued to kill within 1 min during every daily test of Series 4B. No evidence that the cats of Group A were developing a conditioned killing aversion was found.

All the cats in both groups killed mice during the placebo control tests of both Series 4A and 4C. As noted above, 3 cats in each group did not kill when given d-amphetamine before the drug control tests of Series 4A. After the cats in Group A had become somewhat tolerant to the affects of amphetamine during Series 4B, however, only 1 of these cats failed to kill when given the drug before the control test of Series 4C. Four of the cats in Group S, in contrast, were inhibited sufficiently enough so that they did not kill during the control d-amphetamine test of Series 4C. These nonkillers included all 3 cats that had not killed during the Series 4A drug test and the one that had failed to kill three times during Series 4B.

Some tolerance to the effects of d-amphetamine may, therefore, have developed in the Group A cats during Series 4B. It should be noted that the tolerance did not completely block the inhibitory effects of d-amphetamine during Series 4C in every cat. Further, daily doses of d-amphetamine do not block the development of conditioned killing aversions in rats [16,17]. The tolerance that occurred, therefore, probably cannot account for the complete absence of any evidence of conditioned inhibition of killing.

EXPERIMENT 5: EFFECTS OF VARIOUS OTHER DRUGS ON SPONTANEOUS MOUSE KILLING BY CATS

The notion that mechanisms that inhibit killing in rats may be missing in cats predicts a series of negative results, and it is therefore necessary to examine a large body of data before either accepting or rejecting it. As noted above, relatively little data on the effects of psychotropic drugs on spontaneous mouse killing by cats is available. In order to permit a more definitive acceptance or rejection of the notion that cats lack a homolog of mechanisms present in rats, a wide variety of psychotropic drugs was studied. Experiment 5 was designed to test the effects of drugs that either (a) were known to be effective inhibitors of spontaneous mouse killing by rats (e.g., tripelennamine and tranylcypromine), (b) had been reported as possible inhibitors of spontaneous mouse killing by cats (e.g., diazepam, [13]), (c) could inhibit a possible cholinergic system [27] that might mediate the induction of killing (e.g., scopolamine, or (d) could markedly influence mood or affective reactivity (e.g., chlordiazepoxide or chlropromazine). These drugs were tested, over a wide range of pharmacologically active doses for each drug, in selected cats, in which amphtamine reliably inhibited killing. Negative findings, therefore, could not be attributed to the possibility that these cats were generally insensitive to drug effects on killing.

METHOD

Animals

Five adult male and five adult female laboratory-bred cats selected from a larger group of 22 cats, after pretests to assure that they killed reliably after placebo injections and inhibited killing after d-amphetamine injections, were used for this experiment.

Experimental Design, Apparatus, and Procedure

The cats were housed and maintained like those of Experiments 2, 3 and 4, and tested daily for mouse killing with procedures like those of the previous Experiments.

Drug tests series 5A, 5B, and 5C were conducted sequentially. Series 5A and 5C both consisted of drug tests after (d-amphetamine) and placebo (vehicle) control injections, identical to the procedures used for Series 4A and 4C of Experiment 4. Series 4A served as a pretest for animal selection. Only those cats that killed after the placebo injection and did not kill after the 2 mg/kg d-amphetamine injection were used for Series 5B and 5C.

The cats were divided into 2 groups of 5 for Series 5B. Each group was tested with each of 5 doses (including a placebo dose) of each of 5 drugs. The 5 drugs were assigned to each of the 5 cats in an order that corresponded to a 5×5 Latin Square. The 5 doses of each drug were administered in 5 successive tests, in a different Latin Square order for each drug. All 5 tests with each drug were completed before the next drug was tested, in order to avoid drug interaction effects. The drugs and doses used for Series 5Ba were Haloperidol (0, 0.0625, 0.125, 0.25 and 0.5 mg/kg), Chlordiazepoxide HCl (0, 2, 4, 8 and 16 mg/kg), Tripelennamine

HCl (0, 0.5, 1, 2 and 4 mg/kg), Scopolamine HBr (0, 0.125, 0.25, 0.5 and 1 mg/kg), and Na Pentobarbital (0, 2, 4, 8 and 16 mg/kg); those used for Series 5Bb were Chlorpromazine HCl (0, 1, 2, 4 and 8 mg/kg), Meprobamate (0, 10, 20, 40 and 80 mg/kg), Diazepam (0, 0.5, 1, 2 and 4 mg/kg), Tranylcypromine SO_4 (0, 0.25, 0.5, 1 and 2 mg/kg), and Scopolamine Methylbromide (0, 0.125, 0.25, 0.5 and 1 mg/kg). Water soluble test drugs were given in 1 cc/kg 0.9% NaCl vehicle and insoluble drugs were given in 0.9% NaCl plus Tween 80.

Each cat, therefore, was given 29 tests. The first 2 tests with drug and placebo control injections served to select animals. Then 25 tests, one with each of 5 doses of each of 5 drugs, were given. Finally, 2 postests were given with the drug and placebo control injections.

RESULTS

The results of Series 5B were fairly uniform. In general, no dose of any test drug produced any inhibition of killing except when it produced debilitating side effects, including anorexia. No dose of any test drug inhibited killing in all cats, although d-amphetamine did so both during the selection pretests of Series 5A and the posttests of Series 5C. No inhibition was seen with any dose of Chlorpromazine, Chlordiazepoxide, Diazepam, Pentobarbital, Scopolamine, or Methyl Scopolamine. One cat failed to kill after 0.5 mg/kg of Haloperidol, one failed to kill after 1 mg/kg of Tranylcypromine, and one failed to kill after 40 mg/kg of Meprobamate. Two cats failed to kill after 2 mg/kg of Tranylcypromine and 4 cats failed to kill after 4 mg/kg of Tripelennamine. In all cases when inhibition did occur, the cats seemed acutely ill and they failed to eat for some hours thereafter.

DISCUSSION

With respect to drug-induced inhibition of mouse killing, the major phenomena that have been observed with rats are *not* evident with cats. Although components of killing patterns can be inhibited in some cats ([38], Experiments 1 and 3), d-amphetamine does not inhibit, and may even facilitate, killing by many other cats ([38,51], Experiments 1 and 3). Individual differences were clear. Some cats were easily inhibited by d-amphetamine and others never were, even when dose levels approached those that produced stereotyped motor behavior. Very few cats were ever inhibited by any other drug, even when toxic doses were used with amphetamine-sensitive cats. In individuals in which d-amphetamine and other drugs did inhibit killing, their effects seemed related to readiness to eat (Experiments 3 and 5). Many cats continued to kill even when they would not eat. In general, no drug selectively inhibited killing in all cats.

In addition, antidepressant drugs did not produce even the weak inhibitory effects seen with d-amphetamine in cats ([13,14], Experiments 2 and 5). Finally, d-amphetamine did not produce conditioned killing aversions in cats (Experiment 4). In contrast, d-amphetamine, tripelennamine and antidepressants are potent, selective and consistent inhibitors of killing by rats. The mechanisms by which drugs inhibit killing in cats, in contrast to rats, may be vestigial ones that are not universally present in all cats.

The differences between rats and cats in inhibition of killing seem to parallel differences that have been observed in initiation of killing. Rats initiate killing after repeated injections of pilocarpine, in spite of its potent anorexic actions and other marked side effects [40, 57, 59] but cats do not do so [36]. Pilocarpine administration and other treatments that produce anorexia seem to consistently inhibit mouse killing by some cats ([36], Experiments 1, 3 and 5) even though they have only weak inhibitory effects on mouse killing by rats [16,47]. In contrast, treatments that produce marked affective stimulation inhibit mouse killing by rats, but they do not inhibit mouse killing by cats (Experiment 3 of [36]; Experiments 2 and 4 above). In general, readiness to kill in cats, unlike rats, seems, in some individuals, somewhat sensitive to drugs that reduce readiness to eat; and readiness to kill seems consistently insensitive to drugs that enhance affective reactivity.

Domesticated cats do not necessarily need to kill in order to eat, but their carnivore ancestors clearly did so. Mice are frequently attacked by domestic cats and by their carnivorous, necessarily predatory, wild feline relatives [37]. Although wild rats also kill mice [25], they do not need to kill prey in order to eat, the the dentition of their omnivorous rodent ancestors and relatives does not seem to reflect an evolutionary history of specialization for killing [30]. Species differences in effects of drugs on killing may reflect the different evolutionary backgrounds of rats and cats. The naturally selected mechanisms that control killing by cats could be more extensively influenced by or overlap with the mechanisms that control their eating than those of rats [24]. Drugs that act on the mechanisms that control eating may, therefore, sometimes act on vestigial mechanisms that control killing by cats [36]. Because felines have a rich affective repertoire that has little to do with eating, however, the mechanisms that control cat affective reactivity might be highly distinct from those that control their killing behavior (Experiment 4). Rats, in contrast, kill frequently under conditions that seem to have extensive and varied affective functions. Rats kill competitors for the resources of their own ecological niches, and their mouse killing may be related to reduction of competition [23,42]. In consonance with this possibility, novelty seems to be a particularly critical parameter of mouse killing by rats [3,16]. Further the degree to which a novel mouse evokes affective reactions seems to be highly related to both inhibition and initiation of killing by rats [15].

The fact that d-amphetamine does not induce conditioned killing aversions in cats may be important for understanding such aversions, in general, as well as for understanding killing behavior. Conditioned killing aversions can be established in rats that do not acquire taste aversions [29, 43, 44], and prey taste aversions can be established in ferrets without suppressing killing [49]. Killing aversions based on taste aversions can be established in wild predators from insects to coyotes and wolves [8, 9, 20], but, in every case, the killing aversions seem to be acquired in a second stage of conditioning after the taste aversions are separately acquired [42]. In fact, in spite of earlier suggestions to the contrary [52], the conditioning of taste and killing aversions seem, in general, to be separate and dissociable processes. This may be true because the functional relationships between killing, feeding and affective reactivity are not consistent across species with differing problems of adaptive specialization.

In sum, the differences between the pharmacological mechanisms that control mouse killing by rats and cats could be due to different functions that such killing has served during omnivorous rodent and carnivorous feline evolution.

Whatever their origins, it is now clear that there are major differences between the pharmacological mechanisms that control killing by rats and cats. The experiments reported

here, together with those reported previously [13, 14, 36, 38, 53], indicate that differences are apparent whether one considers initiation or inhibition of killing. Mechanisms that readily control killing by rats do not all seem to have homologs in cats.

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