CHAPTER

14

Behavioral Therapeutics

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OUTLINE

After diagnosing a behavioral problem, the veterinarian must plan a treatment and management program that is both practical and rational from the owner's perspective. If the program is too complex or time consuming, owners will have difficulty incorporating it into their daily lives and routines. If the program does not make sense to the owner, the owner is likely to disregard the advice. In either case, if the issue is not satisfactorily resolved, the cat may be relinquished or euthanized. It is essential that veterinarians spend time helping owners understand the problem and the reason it has occurred (the underlying causes) and then develop reasonable expectations.

The initial approach is to modify the environment and manage the owner's expectations so that further problems can be prevented. This may be a short-term remedy, but it may also be the best or only practical long-term solution for some owners and some problems. The owner can then be educated about how cats learn and how their behavior can be effectively modified; this knowledge will help the owner implement the program so that there is some resolution of their concerns.

There is no one-size-fits-all approach in resolving behavioral problems. Therefore every treatment and management program must be tailored to the individual pet and the household where it resides. If there is a safety issue, prevention of further injury is the first concern. Therefore an assessment of the owner, cat, problem, and household is essential not only for determining the prognosis but also for developing an effective treatment and management program.

In general, treatment and management programs for most behavioral problems consist of three key areas, the three M's: behavior modification, environmental management, and psychotropic medication. Medication is not always necessary, but long-standing, recurrent, or severe cases are unlikely to improve without medication. It should also be noted that delaying the use of medication has serious welfare implications for the cat, so if medication is indicated, then the sooner the medication is started the better.

BEHAVIOR MODIFICATION

Since first coined by Thorndike in 1911,[43] the term *behavior modification* has been used in many ways. Currently, it mainly refers to techniques for increasing adaptive behavior through reinforcement and decreasing maladaptive behavior through extinction or punishment (with much more emphasis on the former). This is because when aversive punishments are used (or misused), they can lead to more emotional distress and behavioral problems involving fear and anxiety. Most aversive techniques are inappropriate in context, duration, intensity, or time of application. Recent studies have confirmed that punishment-based training and confrontational techniques are more likely to lead to increased aggression and avoidance behaviors.

The aim of any behavior-modification program should always be to reward appropriate behaviors rather than to punish unwanted behaviors. Therefore rather than focusing on how to stop what is undesirable, the owner should first focus on providing a desirable alternative (e.g., where to sleep, where to climb, where to scratch).

Behavior modification in cats generally involves reward-based training, desensitization, counterconditioning, and response substitution. Therefore an

understanding of learning theory and the effects of operant and classical conditioning is essential before recommending treatment.

Classical conditioning is the pairing of an unconditioned stimulus with a neutral stimulus that results in a conditioned stimulus and a conditioned response. It does not use rewards, but the cat learns to pair an involuntary behavior with another neutral stimulus.

Classical conditioning can occur in both positive and negative ways. Examples of a positive conditioned emotional response are the pairing of a clicker with favored treats (for clicker training) or any sounds associated with feeding (e.g., filling the food bowl, opening the food cupboard, opening the refrigerator, shaking the package of treats).

Problems arise when a fearfully conditioned emotional response is established toward a previously neutral stimulus (visual, olfactory, auditory, animate, or inanimate) by repeatedly pairing it with a fear-producing stimulus. Once this occurs, the stimulus itself will elicit the fear response. Some examples might be the sound of a doorbell or a car pulling into the driveway that becomes paired with the visit of unfamiliar people (for cats that are fearful of visitors). Another example might be the sight of a grooming brush or nail clipper for a cat that is frightened by those procedures.

Operant conditioning involves the way actions result in consequences. The results either increase or decrease the likelihood of future responses. There are four types of behavior–consequence relationships. Reinforcement increases the likelihood that a behavior will be repeated, and punishment decreases the likelihood that the behavior will be exhibited. There can be both positive and negative reinforcement and punishment techniques. *Negative* refers to the removal of a stimulus, and *positive* refers to the application of a stimulus.

Counterconditioning occurs when a stimulus that evokes an unpleasant response is consistently and repeatedly paired with something that is highly positive until a positive association is made. To be successful, counterconditioning should be coupled with desensitization, wherein the intensity of the stimulus is minimized to a level that does not incite the fear response, such as by reducing volume, increasing distance, changing the environment, or modifying the stimulus to something less threatening.

Desensitization and counterconditioning are extremely time consuming. The exercises must be constantly repeated so that the response is altered to one that is positive. Clients often want both a quick fix and less work. However, moving too quickly provokes anxiety and sabotages any behavior-modification program.

Response substitution involves replacing an undesirable response with a desirable one. The process would be to use high-value rewards to teach desirable behaviors that have been selected as an acceptable and practical alternative to the undesirable behavior. However, if the behavior is part of the cat's natural repertoire (e.g., scratching), it can be particularly difficult to train the cat to perform alternative behaviors.

Training should always begin in the environment where success can be most readily achieved. The target behavior is for the cat to be quiet and calm. Therefore the owner must learn to read the look in the cat's eyes, its body posture, its facial expressions, and its breathing to be able to gradually shape the desired behavior. Training could then move to environments with increasing distractions and places where the problem is most likely to arise.

To replace the undesirable behavior with a desirable behavior, response substitution should be coupled with desensitization, by setting up exposure to low levels of the stimulus and practicing the target behaviors and relaxation exercises while reinforcing with the highest-valued rewards. If the cat is fearful or anxious, the focus should also be on classical counterconditioning so that each exposure to the stimulus is associated with only highly positive outcomes and no negative outcomes.

ENVIRONMENTAL MANAGEMENT

Environmental management is usually necessary to prevent exposure to the stimulus, prevent access to locations where problems might arise, or provide outlets for expression of the behavior. For example, cats may need to be confined to avoid exposure or access to other cats, so cat enclosures made of metal or mesh can be attached to a door or window to allow the cat access to outdoors and some or all of the yard (Figure 14-1). Another option might be to fence off the garden to keep the cat enclosed.

FIGURE 14-1 A cat enclosure attached to a door or window allows for safe access to a stimulating environment outdoors.

Management may also include physical and mental stimulation in the form of enrichment, which may reduce stress as well as help the cat cope with potential stressors in day-to-day living. There are many types of environmental enrichments that allow the cat to express normal behaviors in an acceptable way.

Any environmental enrichment program should be designed to provide sufficient outlets and opportunities for species-specific normal behavioral patterns, while offering the individual cat sufficient control and choices to be able to cope with challenges in a normal way. Therefore motivation, novelty, and complexity are important considerations when developing enrichment strategies.

The goal is an environment that the cat can use in a positive way, while reducing or eliminating abnormal behaviors. The enrichment program suggested must be individually tailored to the cat, its personality, and its behavioral problem so that the behavior is not inadvertently exacerbated. It should also be noted that too much enrichment (i.e., too many choices) can lead to increased stress in already anxious cats.

Studies have investigated disease rates among animals in enriched environments versus those in standard housing. Enriched environments were found to decrease the incidence of gastric ulcers in rats[35] and urinary tract disorders in cats[4] and to improve the immune functioning of animals.[39] Conversely, stress may alter immune function and has been shown to be a contributing or aggravating factor in gastrointestinal diseases, dermatologic conditions, respiratory and cardiac conditions, behavioral disorders, and a shortened life span.[12,31,44]

Enrichment might also delay the onset or lessen the effects of feline cognitive dysfunction. Studies in dogs and humans have shown that continued learning; physical exercise; and a change to a diet rich in antioxidants, essential fatty acids, and mitochondrial cofactors can have a positive effect on well-being,[26,29] and the same may be true for cats.[16]

Appropriate enrichment may prevent some behaviors that are of concern to owners[33,46] and lower stress, which may in turn lessen the chances of stress-related diseases such as interstitial cystitis.[3-5]

Enrichment can alleviate boredom and may play a role in preventing obesity and associated medical problems such as diabetes mellitus, hepatic lipidosis, and osteoarthritis.[33] Stress has a negative role in the development of skin conditions such as infections and pruritus, feline lower urinary tract disease (FLUTD), and conditions such as irritable bowel syndrome.[31,44] Addressing the environment of affected cats may help in reducing the number and severity of outbreaks of chronic diseases such as FLUTD.[21]

Any enrichment that is added to a cat's environment must take into account the species-specific behavior of cats and the preferences of the individual cat. An elderly cat that has lived most of its life without feline company will have different needs than a young cat living in a multicat household. As discussed in previous chapters, cats are small, solitary, ambush hunters that have a crepuscular activity pattern. They have complex and highly variable social systems, depending on the spread and amount of resources such as food and shelter.[9,11] Cats are territorial, with male territories overlapping several female territories.[10] Enrichment devices and activities must address the biological needs of cats as well as the individual preferences to have a positive effect on feline welfare.

Hunting and Foraging Behavior

Wild and feral cats spend a significant amount of their waking hours foraging and hunting for food. It is therefore unsurprising that pet cats investigate new objects in their environments and engage in play with small, prey-size objects.[17] Cats should not be allowed to play with human hands or feet because of the potential for injury resulting from their claws and teeth. However, toys that encourage the behaviors of the hunting sequence, such as stalking, rushing, pouncing, and biting, are popular with cats and their caregivers and provide opportunities for cats to engage in these normal behaviors. There are many types of toys that foster this type of play, including fishing rod–style toys and laser pointers. However, because the cat can never catch the light, some cats find laser toys frustrating. It can also be an issue for cats with the potential of developing an obsessive-compulsive disorder. Providing treats periodically during the game or afterwards may reduce frustration.

Cats hunt in short bursts, so play sessions should mimic this natural behavior. The owner should provide toys of a size and texture that motivate the cat. Cats may quickly become habituated to and lose interest in a particular toy; studies have shown that play intensity may be heightened in the short term if play is repeated with three or four different toys that have slightly different characteristics. Owners should try to maintain the cat's role as the predator with the toy as prey by using sudden changes of speed and direction when manipulating the toy. Toys on strings should be used for supervised play only as when alone the cat may ingest the string, leading to severe intestinal damage and possible death. After play sessions the cat's interest in further play may remain heightened for 15 minutes or more, so it might be advisable to give the cat some food or treats to keep it occupied and perhaps simulate the feeding that might logically follow predatory activity in the wild.

Cats that hunt for food will chase, capture, and eat several small meals a day. Therefore some cats may benefit from more play sessions and multiple smaller, prey-size meals. This might be accomplished by using timed feeding dishes or making meal feeding more complex by placing canned food in ice cube trays, small

FIGURE 14-2 Feral cats frequently eat grass. Indoor cat gardens allow cats to carry out this normal behavior.

FIGURE 14-3 Appropriate hiding and perching places can reduce stress. If perches are placed near windows, cats can watch birds, butterflies, and other outdoor activities, which can be enriching for them. *(Courtesy Dr. Susan Little.)*

containers, or toys that require manipulation with paws or teeth to extract the food. A number of commercial toys are now available that require varying degrees of batting and rolling, dexterity, and mental activity to release the food.

Wild and feral cats frequently eat grass.[1] Cat grass offers a safe grazing choice for cats kept indoors (Figure 14-2). If the owner periodically moves the cat grass throughout the home, the cat will have to seek out the forage and therefore replicate natural behavior.

Resting Places

Cats spend an average of 2.8 hours resting and 7.8 hours sleeping during the day.[1] Comfortable, protected areas should be provided for cats to sleep and rest. Many cats like high positions and will gravitate to beds in high places, such as in cupboards or on shelves. In multicat homes cats are less likely to compete over prime space when there are several choices, such as window ledges, cat climbing frames, and furniture to which cats are allowed access. Every room that cats visit frequently should offer them appropriate hiding and perching places, which can reduce stress (Figure 14-3).[23] Cats are both predator and prey and may feel more secure in a place where they can watch activities without being watched themselves.

Scratching

Scratching is a normal behavior for cats. A cat's motivation to scratch includes maintenance grooming of the claws and deposition of an olfactory mark to convey temporal cues regarding the cat's proximity or passage.[25] Cats often scratch when they are excited (e.g., when their owners come home or during play) and after sleeping.[25] Old and new objects will be scratched, although older, frequently used scratching posts seem to continue to maintain interest for many cats.[25]

Owners should provide suitable outlets for scratching that are easily accessible and attractive and make unacceptable targets, such as furniture, less attractive. When a cat's scratching appears to be excessive in frequency, location, or duration, the possibility that the marking is related to stress or anxiety (as with urine marking) should be considered. In this case increased environmental enrichment, identification and removal of potential stressors, and possibly pheromone therapy may be necessary.

It is advisable to have at least one scratching post in the room most frequented by family members and in other well-traveled places in the home. More posts are needed in multicat homes. Ideally, vertical scratching posts should be tall enough for the cat to stand on its back legs and reach up to scratch. Posts should also be sturdy and stable. Cats have individual preferences regarding the materials and orientation (vertical or horizontal) of the posts. Therefore owners can be both proactive and reactive in providing scratching posts that appeal to the cat's tastes in type, texture, and location.

Cats can be encouraged to scratch by using an interactive toy (e.g., a fishing pole–type toy with feathers) and waving it over the post or attaching a dangling toy to the post. Once a cat's scent is deposited on the post, the cat is more likely to return. Cats can also be clicker trained to scratch at the posts.

Viewing Places

Watching birds, butterflies, and other things can be enriching for cats. However, the presence of other free-roaming cats in the vicinity can be stressful for some indoor cats and result in frustration and redirected aggression toward other family members, both human and feline.[26]

Novelty

For cats that have all of their basic needs met, exploratory behavior becomes a greater priority.[46] Because most pet cats do not have to spend several hours a day hunting, novelty plays an important role in enriching a well-fed and rested cat's time. The owner can increase this novelty by using different feeding techniques, such as placing food in treat balls, scattering dry food over a wide area for the cat to hunt, and putting food in different locations; offering new toys; and rotating toys every few days. Another option is providing new objects with which the cat can interact, such as a box or tunnel. Objects and toys can be moved around the space the cat occupies to create the appearance of a new environment. Cats can become used to hunt-and-chase toys within a few minutes, necessitating the introduction of a few different items within and between play sessions.[17]

Social Interaction

Cats are social creatures[3] and are often found in the vicinity of people with whom they are bonded. Cats enjoy not only human companionship but also that of members of their own and other species. However, there can be extensive individual variation depending on genetics, early experiences, and previous encounters. Just because a cat has a healthy social relationship with one or more cats does not mean that the cat will tolerate an unfamiliar cat being added to the household.

Brushing and hand grooming can be a form of enrichment for cats that enjoy physical contact and attention. Positive reinforcement training can also be enriching to cats[45] and can be used to train a number of simple behaviors, such as "sit," "roll over," and "come here." One useful and effective form of training for cats is clicker training. Training enhances the human–animal bond in dogs[2] and is likely to do the same in cats.

Environmental enrichment takes effort but should be considered as an important part of caring for companion cats, regardless of whether they have behavioral problems.

PSYCHOTROPIC MEDICATION

Medication for behavioral problems should not be viewed as a quick fix or a silver bullet. The decision to use medication depends on the diagnosis, and this should include a thorough physical workup, blood work, and a behavioral assessment. Medications are not generally indicated for problem behaviors (often normal behaviors that are problematic for the owners), only for behavioral problems, so it is important that veterinarians understand the rationale for prescribing psychotropic medication.[40]

Many of the medications in common usage are not registered for this purpose in animals. As more and more medications are registered for use in animals, it is increasingly important that veterinarians be familiar with these medications and the research that supports their use. This allows veterinarians to make an informed decision about which medication to use, as well as why and when to use it.

Much information regarding psychotropic medication is derived from human-medicine literature. When used in animals, the medication may have different effects, different side effects, and different therapeutic and toxic levels, and these factors may also vary with the species. It is the veterinarian's responsibility to be familiar with these factors before prescribing medication.

Medications do not change the relationship with the stimulus, and concurrent behavior modification will also be necessary to desensitize, countercondition, and train the cat in desirable responses. Clients must understand that behavior modification and environmental management are necessary if medication is used. Clients should be informed that the cat may require medication for the rest of its life, similar to chronic therapy for diseases such as diabetes. Once the behavior is managed to the owner's satisfaction, a lifelong commitment from the owner and continued support from the veterinarian may be necessary.

In veterinary medicine there is limited opportunity to perform evidence-based studies on the use of medication in cats, and much of the information has therefore been extrapolated from human-medicine literature.[24] This information should be interpreted with care because drug metabolism and receptor effects vary among species. This variation can lead to inaccurate assumptions with respect to dose, duration of effect, contraindications, and side effects. Therefore medications that are licensed for use in cats (e.g., clomipramine) should be considered first because data regarding safety, efficacy, side effects, contraindications, toxicity, and pharmacokinetics are available. In addition, the manufacturer can provide additional expertise, which is especially important should an adverse event occur.

When medication is used for longer than 8 weeks, it is prudent to consider a gradual weaning to determine the lowest effective dose and minimize potential withdrawal effects.

Why Use Psychotropic Medication?

The rationale for using psychotropic medications is based on their purported neurochemical actions in the brain. Many medications have now been used to modify behavior in humans and companion animals. Medications may influence neurotransmitters in three main ways:

1. They may act presynaptically and affect the presynaptic action potential, synthesis, storage, metabolism, release, or reuptake.
2. They may act on the enzymes that deactivate the neurotransmitter.
3. They may act postsynaptically and affect binding to receptors by acting as agonists or antagonists or actually modify receptors.

Obtaining the results of blood tests before prescribing medication is always recommended, especially in very old or young animals and those with a previous history of medical problems. A minimum database should include a complete blood count (CBC), biochemistry panel, and urinalysis. Because most of the medications are metabolized through the liver and then excreted through the renal system, liver and kidney function monitoring is important both before and during treatment.

It may be necessary to repeat these tests, often at 4 to 6 weeks after starting medication, depending on the cat, the medication, and the effects seen. All cats on long-term medication should be reassessed and have blood work re-evaluated every 6 to 12 months, depending on the cat's age and medical history.

It is also important to question owners about any other medications that they may be administering to their cat. This includes the use of natural remedies or homeopathic medications; many owners do not realize that these may also have significant effects on their pet and interact with the medications prescribed by the veterinarian.

When to Use Psychotropic Medication

Psychotropic medications have proved to be useful in several categories of behavioral problems. These include anxiety-related problems (including fears and phobias), obsessive–compulsive behaviors, some types of aggression, and geriatric behavioral problems.

The treatment of nonspecific signs (e.g., excessive vocalization, aggression, inappropriate elimination) by using medication is not acceptable, and this approach will ultimately lead to treatment failures.

What if the Medication Does Not Work?

Owners may sometimes believe that the medication has been ineffective. Reasons include the following:

- No diagnosis was made.
- An incorrect diagnosis was made.
- The incorrect medication was selected.
- An inadequate length of time was allowed for the treatment program to take effect.
- Medication has been used as stand-alone therapy when it should have been combined with a behavior-modification program.
- The owner was unable to medicate the pet.
- The owner has unrealistic expectations regarding the influence of the medication.

In some cases the effects of medication can be seen only when the medication has been stopped. It is important to advise owners that medication should never be suddenly stopped except under veterinary advice. The patient should always be weaned off the medication slowly and monitored by a veterinarian.

What Owners Need to Know About Psychotropic Medication

- Medication may take 6 to 8 weeks to reach therapeutic blood levels. Owners must understand that the effects will not be immediate.
- It may be necessary to change the medication or the dose as the management and treatment progresses.
- The minimum time required for a cat to receive medication is usually 6 months.
- Medication may be needed for the duration of the cat's life. This should be discussed with the owner before the medication is prescribed.
- Medication should never be suddenly stopped. The cat should always be weaned off it gradually to avoid a rebound affect. Owners should be warned of the danger of sudden cessation whenever medication is prescribed.
- Changing the dose, discontinuing the medication, or changing the type of medication should occur only with veterinary advice and under veterinary supervision.

Dosing and Compliance

Because many owners cannot administer pills, they are often reformulated into compounded liquids, flavored tablets, and transdermal medications. For compounded medications it is necessary to determine the stability and storage of these products. To date, no data support the efficacy of transdermal medication for behavior-modifying drugs in cats. One study found that the bioavailability of transdermal doses of fluoxetine was 10%

compared with oral dosing.[7] In another study systemic absorption of both amitriptyline and buspirone was poor compared with that conferred by the oral route.[28]

Common Psychotropic Medications

Medications that have anxiolytic action include the benzodiazepines, tricyclic antidepressants (TCAs), antihistamines, barbiturates, selective serotonin reuptake inhibitors (SSRIs), and beta blockers, and these have proved useful in some cases. Commonly used medications and dosing are summarized in Table 14-1 and Box 14-1.

Antidepressants cause little or no sedation and are unlikely to inhibit learning or memory. There is extensive evidence on the efficacy of clomipramine and fluoxetine for treating anxiety disorders, obsessive–compulsive disorders, and urine marking in dogs and cats; however, despite their use in the treatment of aggression, there is minimal evidence supporting efficacy.

TABLE 14-1 Drug Doses for Behavior-Modification Therapy in Cats

Drug	Dose
Alprazolam	0.125 to 0.25 mg/cat every 8, 12, or 24 hours
Diazepam	0.2 to 0.5 mg/kg every 8 to 12 hours
Oxazepam	0.2 to 0.5 mg/kg every 12 to 24 hours
Clonazepam	0.02 to 0.2 mg/kg every 12 to 24 hours
Lorazepam	0.025 to 0.05 mg/kg every 12 to 24 hours
Amitriptyline	0.5 to 1 mg/kg every 24 hours
Clomipramine	0.3 to 0.5 mg/kg every 24 hours
Fluoxetine	0.5 to 1 mg/kg every 24 hours
Paroxetine	0.5 to 1 mg/kg every 24 hours
Buspirone	0.5 to 1 mg/kg every 12 hours

BOX 14-1
Characteristics of Commonly Used Behavior-Modifying Medications in Cats

Tricyclic Antidepressants

- Clinical uses: urine spraying, feline lower urinary tract disease, overgrooming, anxiety, intercat aggression, impulsivity, obsessive–compulsive disorders[22,27,41]
- Side effects: short-term lethargy or sedation, mild and intermittent vomiting (usually transient), increases or decreases in appetite, dry mouth, constipation, urine retention (especially at higher doses),[37] tachycardia, cardiac arrhythmia, decreased tear production; high doses have been associated with increased liver enzymes, hepatotoxicity
- Contraindications and precautions: cardiac dysrhythmias, urinary retention, narrow-angle glaucoma, seizures, or within 2 weeks of a monoamine oxidase inhibitor drug; these medications may interfere with thyroid function and should be used with caution in affected patients
- Examples: amitriptyline, clomipramine, doxepin

Selective Serotonin Reuptake Inhibitors

- Clinical uses: urine spraying, some types of aggression, obsessive–compulsive disorders
- Side effects: liver changes, gastrointestinal disturbances, rashes; nausea, weight loss, tremors, and agitation have been reported in humans
- Contraindications and precautions: should not be used concurrently with monoamine oxidase inhibitors (may cause serotonin syndrome), and at least 2 weeks should be allowed as a washout period between selective serotonin reuptake inhibitor and monoamine oxidase inhibitor therapy (a 5-week washout period should be allowed for fluoxetine)
- Examples: fluoxetine, paroxetine

Benzodiazepines

- Clinical uses: urine spraying, overgrooming, fear-related aggression
- Side effects: increased appetite, transient ataxia, paradoxical hyperactivity, increased friendliness, increased vocalization, fatal idiopathic hepatic necrosis, interference with memory and learning, disinhibition of suppressed behaviors such as aggression
- Contraindications and precautions: not recommended for patients with liver or kidney failure or in obese cats, and use with caution in aggressive cats
- Examples: diazepam, alprazolam, oxazepam, clonazepam

Azapirones

- Clinical uses: mild fear; long-standing anxiety-related problems, including urine marking or spraying and inappropriate urination[19] and overgrooming
- Side effects: bradycardia and tachycardia, nervousness, gastrointestinal disturbances, stereotypic behaviors; restlessness has been reported in humans
- Contraindications and precautions: may lead to increased aggression as the disinhibitory effects of fear are decreased
- Example: buspirone

Although antidepressants reach peak plasma levels within hours, this does not reflect their therapeutic effect because reuptake inhibition may induce downregulation of postsynaptic receptors. Therefore 4 to 8 weeks of therapy is generally recommended to fully assess therapeutic effects.

TCAs and SSRIs should not be used concurrently with other antidepressants or monoamine oxidase (MAO) inhibitors such as selegiline and amitraz and should be used cautiously in pets with seizures. Because SSRIs inhibit cytochrome P450 enzymes, they can lead to increased toxicity if combined with other drugs that are metabolized by these enzymes.

Tricyclic Antidepressants

The primary mechanism of action of TCAs such as clomipramine and amitriptyline is to block the reuptake of serotonin and, to a lesser extent, noradrenaline. The degree of serotonin and noradrenaline reuptake blockade, as well as anticholinergic, antihistaminic, and alpha-adrenergic effects, varies among TCAs. Clomipramine is the most selective inhibitor of serotonin reuptake of the TCAs. It also inhibits noradrenaline reuptake and has mild anticholinergic and antihistaminic effects, which might account for some its side effects, such as lethargy, dry mouth, and gastrointestinal upset.

Clomipramine may help facilitate training in cats that are fearful of unfamiliar people or animals and may be useful for a variety of fear- and anxiety-based behavioral problems, alone or in combination with other anxiolytic agents.

Selective Serotonin Reuptake Inhibitors

As the name implies, SSRIs are selective for serotonin and lack the anticholinergic and cardiovascular side effects of the TCAs.

SSRIs are selective in their blockade of the reuptake of the neurotransmitter 5-hydroxytryptamine (5-HT) into the presynaptic neurons. Because they are selective for serotonin reuptake, they may have fewer side effects than TCAs, including fewer cardiac effects and less hypotension.[42] They may also be preferable where urine retention, increased intraocular pressure, sedation, or anticholinergic effects might be a concern. Paroxetine is mildly anticholinergic.

In a study of generalized anxiety disorders, fluoxetine and paroxetine were effective when combined with behavioral therapy. The primary side effect is decreased appetite, which may resolve with decreased dose.

For intercat aggression sertraline, paroxetine, or an anxiolytic might be used to increase confidence in the victim cat, and the aggressor may be treated with fluoxetine. Fluoxetine may also be effective in the treatment of feline urine marking.[18,38]

Benzodiazepines

Benzodiazepines potentiate the effects of gamma-aminobutyric acid (GABA), an inhibitory neurotransmitter. They cause a decrease in anxiety and hyperphagia and induce muscle relaxation. They reach peak effect shortly after each dose and can be used alone or in combination with other drugs on an as-needed basis. Diazepam may be effective for feline urine marking.[8] Because clonazepam, oxazepam, and lorazepam have no active intermediate metabolites, they may be safer when hepatic function is compromised. Benzodiazepines must be dosed frequently, and there may be a rebound effect if withdrawal is not gradual. They can cause paradoxical excitability and can have an amnesic effect. They are useful for counterconditioning because they decrease anxiety and increase appetite; however, diazepam has been reported to cause rare cases of fatal hepatotoxicity in cats.[6] Benzodiazepines can also be used for drug desensitization.

Azapirones

Buspirone, an azapirone, is a serotonin (5HT1A) receptor agonist and a dopamine (D_2) agonist. It is nonsedating, does not stimulate appetite, and does not appear to inhibit memory. It takes a week or more to reach effect and is therefore not useful for situational anxieties. Higher doses may have more immediate effect. Adding buspirone to an SSRI or a TCA might help ensure an adequate serotonin pool.

Synthetic Pheromone Analogs

Pheromones are released during facial rubbing on objects when cats feel comfortable in their environment. A synthetic feline facial pheromone (Feliway, Ceva Animal Health) has been developed as an aid in the treatment for anxiety-related disorders. Several studies have documented a significant decrease in urine-spraying behavior when the pheromone is sprayed in a cat's environment.[13,20,30,32] Other documented uses include reduction of stress during handling, hospitalization, or transport and treatment of intercat aggression in multicat households.[14,15,34,36] There are no reported side effects associated with use of Feliway, although caution should be exercised when using the product around cats with asthma or in the presence of birds.

References

1. Beaver B: *Feline behavior: a guide for veterinarians*, ed 2, St Louis, 2003, Saunders Elsevier.
2. Bennett PC, Rohlf VI: Owner–companion dog interactions: relationships between demographic variables, potentially problematic behaviours, training engagement and shared activities, *Appl Anim Behav Sci* 102:65, 2007.
3. Buffington CA: External and internal influences on disease risk in cats, *J Am Vet Med Assoc* 220:994, 2002.
4. Buffington CA, Westropp JL, Chew DJ et al: Clinical evaluation of multimodal environmental modification (MEMO) in the

management of cats with idiopathic cystitis, *J Feline Med Surg* 8:261, 2006.
5. Cameron ME, Casey RA, Bradshaw JW et al: A study of environmental and behavioural factors that may be associated with feline idiopathic cystitis, *J Small Anim Pract* 45:144, 2004.
6. Center SA, Elston TH, Rowland PH et al: Fulminant hepatic failure associated with oral administration of diazepam in 11 cats, *J Am Vet Med Assoc* 209:618, 1996.
7. Ciribassi J, Luescher A, Pasloske K et al: Comparative bioavailability of fluoxetine after transdermal and oral administration to healthy cats, *Am J Vet Res* 64:994, 2003.
8. Cooper L, Hart BL: Comparison of diazepam with progestin for effectiveness in suppression of urine-spraying behavior in cats, *J Am Vet Med Assoc* 200:797, 1992.
9. Crowell-Davis S, Curtis T, Knowles R: Social organization in the cat: a modern understanding, *J Feline Med Surg* 6:19, 2004.
10. Crowell-Davis SL, Barry K, Wolfe R: Social behavior and aggressive problems of cats, *Vet Clin North Am Small Anim Pract* 27:549, 1997.
11. Curtis T, Knowles R, Crowell-Davis S: Influence of familiarity and relatedness on proximity and allogrooming in domestic cats *(Felis catus)*, *Am J Vet Res* 64:1151, 2003.
12. Dreschel NA: Anxiety, fear, disease, and lifespan in domestic dogs, *J Vet Behav* 4:249, 2009.
13. Frank DF, Erb HN, Houpt KA: Urine spraying in cats: presence of concurrent disease and effects of a pheromone treatment, *Appl Anim Behav Sci* 61:263, 1999.
14. Gaultier E, Pageat P, Tessier Y: Effect of a feline appeasing pheromone analogue on manifestations of stress in cats during transport. In *Proceedings 32nd Congress of the International Society for Applied Ethology*, Clermont-Ferrand, 1998, p. 198.
15. Griffith CA, Steigerwald ES, Buffington CA: Effects of a synthetic facial pheromone on behavior of cats, *J Am Vet Med Assoc* 217:1154, 2000.
16. Gunn-Moore D, Moffat K, Christie LA et al: Cognitive dysfunction and the neurobiology of ageing in cats, *J Small Anim Pract* 48:546, 2007.
17. Hall SL, Bradshaw JWS, Robinson IH: Object play in adult domestic cats: the roles of habituation and disinhibition, *Appl Anim Behav Sci* 79:263, 2002.
18. Hart B, Cliff K, Tynes V et al: Control of urine marking by use of long-term treatment with fluoxetine or clomipramine in cats, *J Am Vet Med Assoc* 226:378, 2005.
19. Hart B, Eckstein R, Powell K et al: Effectiveness of buspirone on urine spraying and inappropriate elimination in cats, *J Am Vet Med Assoc* 203:254, 1993.
20. Hunthausen W: Evaluating a feline facial pheromone analogue to control urine spraying, *Vet Med* 95:151, 2000.
21. Ibanez M, Dominguez C, Martin M: Cats showing comfort or well-being in cages with an enriched and controlled environment. In *Proceedings of the 3rd International Congress on Veterinary Behavioural Medicine*, 2001, p. 50.
22. King J, Steffan J, Heath S et al: Determination of the dosage of clomipramine for the treatment of urine spraying in cats, *J Am Vet Med Assoc* 225:881, 2004.
23. Kly K, Casey R: The effects of hiding enrichment on stress levels, behaviour and time to homing of domestic cats in a rescue shelter in the UK. In *Proceedings of the Companion Animal Behaviour Therapy Study Group study day*, Birmingham, England, 2004.
24. Kochevar DT, Fajt V: Evidence-based decision making in small animal therapeutics, *Vet Clin North Am Small Anim Pract* 36:943, 2006.
25. Landsberg G: Feline behavior and welfare, *J Am Vet Med Assoc* 208:502, 1996.
26. Landsberg G, Hunthausen W, Ackerman L: *Handbook of behavior problems of the dog and cat*, ed 2, St Louis, 2003, Elsevier Saunders.
27. Landsberg GM, Wilson AL: Effects of clomipramine on cats presented for urine marking, *J Am Anim Hosp Assoc* 41:3, 2005.
28. Mealey KL, Peck KE, Bennett BS et al: Systemic absorption of amitriptyline and buspirone after oral and transdermal administration to healthy cats, *J Vet Intern Med* 18:43, 2004.
29. Milgram NW, Head E, Zicker SC et al: Long-term treatment with antioxidants and a program of behavioral enrichment reduces age-dependent impairment in discrimination and reversal learning in beagle dogs, *Exp Gerontol* 39:753, 2004.
30. Mills DS, Mills CB: Evaluation of a novel method for delivering a synthetic analogue of feline facial pheromone to control urine spraying by cats, *Vet Rec* 149:197, 2001.
31. Nagata M, Shibata K, Irimajiri M et al: Importance of psychogenic dermatoses in dogs with pruritic behavior, *Vet Derm* 13:211, 2002.
32. Ogata N, Takeuchi Y: Clinical trial of a feline pheromone analogue for feline urine marking, *J Vet Med Sci* 63:157, 2001.
33. Overall K, Rodan I, Beaver B et al: Feline behavior guidelines from the American Association of Feline Practitioners, *J Am Vet Med Assoc* 227:70, 2005.
34. Pageat P, Tessier Y: Usefulness of the F3 synthetic pheromone Feliway in preventing behaviour problems in cats during holidays. In *Proceedings 1st International Veterinary Behavior Meeting*, Birmingham, 1997, p 231.
35. Pare WP, Kluczynski J: Developmental factors modify stress ulcer incidence in a stress-susceptible rat strain, *J Physiol Paris* 91:105, 1997.
36. Patel G, Health S, Coyne K et al: Pilot study to investigate whether a feline pheromone analogue reduces anxiety-related behavior during clinical examination of cats in a rescue shelter, *J Vet Behav* 5:33, 2010.
37. Pfeiffer E, Guy N, Cribb A: Clomipramine-induced urinary retention in a cat, *Can Vet J* 40:265, 1999.
38. Pryor P, Hart B, Cliff D et al: Effects of a selective serotonin reuptake inhibitor on urine spraying behavior in cats, *J Am Vet Med Assoc* 219:1557, 2001.
39. Schapiro SJ, Nehete PN, Perlman JE et al: A comparison of cell-mediated immune responses in rhesus macaques housed singly, in pairs, or in groups, *Appl Anim Behav Sci* 68:67, 2000.
40. Seksel K: Behaviour modifying drugs. In Maddison J, Page S, Church D, editors: *Small animal clinical pharmacology*, St Louis, 2008, Saunders.
41. Seksel K, Lindeman M: Use of clomipramine in the treatment of anxiety-related and obsessive-compulsive disorders in cats, *Aust Vet J* 76:317, 1998.
42. Steinberg MI, Smallwood JK, Holland DR et al: Hemodynamic and electrocardiographic effects of fluoxetine and its major metabolite, norfluoxetine, in anesthetized dogs, *Toxicol Appl Pharmacol* 82:70, 1986.
43. Thorndike E: *Animal intelligence*, Cambridge, Mass, 1911, Harvard University Press.
44. Westropp JL, Kass PH, Buffington CA: Evaluation of the effects of stress in cats with idiopathic cystitis, *Am J Vet Res* 67:731, 2006.
45. Yin S: *Low stress handling, restraint and behavior modification of dogs and cats*, Davis, Calif, 2009, Nerd Books.
46. Young R: *Environmental enrichment for captive animals*, Oxford, 2003, Blackwell Science.