

PIECE OF THE PUZZLE

While nutritional interventions can be helpful in decreasing feline stress, no diet or supplement alone can eliminate stress in cats.

NUTRITION NOTES

Nutritional Intervention for Feline Stress

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“Stress” is a term that is routinely used in many contexts and has several meanings. It can mean typically temporary and normal neurophysiologic states of being, the external or internal causes of such states, or the sequelae of long-term exposure to the mediators involved. All 3 terms are commonly considered together in discussions of stress and the states are physiologically related as corticotropin-releasing hormone receptor density in the amygdala and receptor variations may mediate adaptation to anxiety and stress.¹ In this article, the following definitions are used.²

Acute stress response is the host of neurophysiologic and behavioral responses involving the hypothalamic-pituitary-adrenal and sympathetic-adreno-medullary axes, which result in the final mediators classically associated with stress (cortisol, epinephrine, norepinephrine) as well as many other mediators (e.g., other glucocorticoids, prostaglandins, β -endorphins, endocannabinoids, met-enkephalin, melanocyte-stimulating hormone, vasopressin, glucagon). This response is typically allostatic, creating changes that ultimately return the animal to homeostasis, predictively or reactively.

Pathologic stress responses can be outside the normal reactive range (sometimes called homeostatic overload)

or prolonged (chronic stress). This response may result from a single prolonged stressor or the summation of multiple stressors over time, resulting in lack of return to baseline. The line between acute and chronic stress is subject to species and individual variation, making objective differentiations between acute and chronic stress challenging.

Stressor is a stimulus or condition that causes a stress response and includes physical homeostatic threats (e.g., heat, cold, hunger, thirst) and emotional homeostatic threats (e.g., anxiety, fear). Anxiety (anticipation of future danger) and fear (perception of threat at the moment) are separate emotional and physiologic states that can be considered stressors.³ They include multiple overlapping neurochemical cascades and behaviors.

FELINE STRESS

Needs and Potential Stressors

Cats are the domestic species most capable of breeding, birthing, raising their young, and living without human care; thus, many consider them less domesticated than dogs.⁴ Human-friendly environments that fail to meet all of cats' species-typical behavioral needs may increase



stress loads. Cats need spaces for perching, hiding, and scratching. They also need core areas separate from other cats, with food and water located separately and cat-appropriate litter that is separate from both.^{5,6} Scratching is a normal behavior (performed for stretching, strength, nail care, and social signals), which cats will do with or without human-approved targets in cat-approved locations.⁷⁻⁹ Lack of preferred substrates may decrease scratching but may also increase stress load. Cats benefit from several small bursts of predatory-like (object) play in sessions of 2 to 10 minutes.¹⁰

Situations that humans have become habituated to or are even excited about (e.g., fireworks, champagne corks, sports event cheering) and environmental changes (e.g., moves, new furniture, new flooring, construction) can serve as stressors for cats. Separation-associated problems are being increasingly recognized in cats as well.^{11,12} Unfamiliar or nonpreferred cats or animals can be stressors. Outside of human influences, cats may elect to live in matrilineally related groups.^{13,14} With human influence, cats may find themselves living with cats that are neither related nor desired. Newcomers are not readily welcomed in cat colonies inside home ranges as large as hectares/acres, let alone 1-bedroom apartments.¹³

Signs of Stress

Feline behaviors that could be related to stress and are readily recognized by clients include hiding, slinking, hissing, swatting, undesirable elimination, urine marking, and undesirable scratching. More subtle are avoidance behaviors, such as not being in the same room as another animal or person, cats not grooming each other or not sleeping touching each other, or moving in a large arc around people/animals/objects. Often overlooked are pain signals such as limping; however, veterinary professionals are increasingly aware that they suffer from chronic osteoarthritis pain.¹⁵⁻¹⁸

REDUCING STRESS

Often the best way to reduce a cat's stress is to mitigate the stressor itself; however, that is not always feasible either in its entirety or sufficiently to achieve baseline (e.g., noises from outside the apartment, a new baby in the household, having moved for a job, generalized anxiety, separation anxiety if the client works outside the home). For cats in these situations, further support in the form of medication or nutrition is necessary.

Because anything that makes our feline patients feel less well can exacerbate stress, medical conditions should be ruled out first, even in the face of an obvious trigger.

NUTRITIONAL MANAGEMENT OF STRESS

Client and veterinarian comfort with psychoactive medications varies widely. Many people are concerned about using medications of any sort, especially psychoactive medications.¹⁹ It is the veterinary professional's job to advocate for patients and educate clients when experience, data, and training indicate that a medication is best; however, adherence by clients with negative expectations may be low.²⁰

Some clients consider supplements that are "Generally Recognized As Safe" by the Food and Drug Administration (GRAS status) to be less synthetic and/or less threatening. If these products are the only option that will find its way into the cat, they become the best option at the time.

α -Casozepine

This product, tryptic bovine α S1-casein hydrolysate (Zylkene; Vetoquinol, vetoquinolusa.com), is a lactose-free milk-derived protein that most likely interacts with the γ -aminobutyric acid type A (GABA A) benzodiazepine binding site.^{21,22} Two multicenter placebo-controlled trials have shown it to decrease stress-related behaviors.^{23,24} One of these studies, a double-blind trial, evaluated 34 cats after administration of α -casozepine at 15 mg/kg over 3 veterinary visits (days 0, 28, 56) and by phone questionnaires.²³ A standardized Cat Emotional Scale was used to evaluate interactions with unfamiliar and familiar people, other fears, organic signs (e.g., displacement behaviors), and autonomic signs (not defined but presumed to be pupil dilation, piloerection, drooling, increased heart and respiratory rates). Veterinarians' scores for autonomic signs improved across visits for only the α -casozepine group. Client-rated changes during visits did not differ between groups. Fearful behavior with nonfamiliar and familiar people decreased in the treatment group compared with the placebo group. Aggression was lumped together across contexts (familiar and nonfamiliar people) and did not differ statistically across groups or times. In the other study, 20 cats in each of 3 groups were given 225 mg of α -casozepine, 75 mg of α -casozepine, or placebo.²⁴ For those that received high-dose

α -casozepine, paw sweating while in the examination room decreased. However, during or after each visit, no significant differences were noted for fecal cortisol scores, pupil dilation, respiratory rate, or vocalization.

L-Tryptophan

This amino acid is a natural precursor to serotonin. To the author's knowledge, only 1 abstract/proceedings reports the effect of L-tryptophan supplementation alone.²⁵ In the placebo-controlled trial, 25 cats in multicat households were observed for 3.5 months; after a 4-week baseline, they received supplementation at 12.5 mg/kg for 8 weeks. After cats were given the supplement, stereotypies, vocalization, house soiling, and conflicts between cats, as well as sustaining or maintenance behaviors (e.g., grooming, scratching), decreased.

Royal Canin Calm Therapeutic Diet

This diet (royalcanin.com) contains α -casozepine with L-tryptophan as well as marigold (*Tagetes erecta*), which is purported to be serotonergic.^{26,27} Effects are noticed 2 to 4 weeks after initiation of feeding.²⁸ This diet is also available with Royal Canin urinary SO (anti-stone) index and Satiety Support formulations. In a placebo-controlled trial with 21 cats, fearful behavior in an open field test and around novel humans decreased after 8 weeks of feeding,²⁸ as did urine cortisol concentrations;²⁹ however, plasma cortisol in response to veterinary handling did not decrease.²⁹

Hill's c/d Multicare Stress and Metabolic Diet

This diet (hillspet.com) is typically labeled as milk protein hydrolysate but is cross-listed as α S1-casein.³⁰ The diet is enriched with omega-3 fatty acids and glucosamine/chondroitin. In a placebo-controlled trial of 31 cats, original Hill's c/d Urinary Stress led to decreased hematuria and stranguria by 89% compared with a control diet.³¹ In a masked, uncontrolled trial of 18 cats, in which environmental management recommendations were recommended, the cats were scored by using a modification of the Cat Emotional Scale; 3 of 5 emotional scales and 4 of 5 lower urinary and behavior signs improved over 8 weeks.³² A study in the Netherlands evaluated 31 cats fed Hill's c/d Urinary Stress or the cat's original diets over 5 weeks.³³ Clients were allowed to use rescue doses of meloxicam (0.04 mg/kg q24h up to 7 days). For cats eating the

Hill's diet, the odds ratio for short-term recurrence was 8.8 times lower than that for cats fed their original diet. No other variables affected odds ratios.

Anxitane

Anxitane (Virbac, virbac.com) contains L-theanine as its active ingredient, a nonstimulant, green tea derivative, structurally similar to the amino acid glutamine. It increases release of GABA, serotonin, and dopamine and decreases anxiety responses in mice.^{34,35} Research is sparse; however, an open-label, multicenter trial of 33 cats showed that cats receiving 25 mg of Anxitane exhibited reduced inappropriate elimination (the most improved variable), followed closely by reduced digestive or grooming problems.³⁶ The least-improved variables were fear-induced aggression, hypervigilance, and scratching behaviors.

Solliquin

This product (solliquin.com) by Nutramax (nutramaxlabs.com) contains L-theanine, α -lactalbumin, a high-tryptophan-content protein (the amino acid from which serotonin is derived), and 2 plant products (*Magnolia officinalis* and *Phellodendron amurense*). These whole plants are not listed in the original GRAS database, but proprietary extracts may well have GRAS status. In a case series of 2 cats and 19 dogs, only 1 cat finished the 8-week trial, reportedly showing improved response to fear, stress, and anxiety.³⁷

Purina ProPlan Calming Care

Bifidobacterium longum (BL999) is a well-researched probiotic supplement for dogs,³⁸ which has been extrapolated into a feline supplement product (proplanvetdirect.com). To the author's knowledge, there are no peer-reviewed papers on this product, but white paper research done at Colorado State University includes statistical analysis for a placebo-controlled trial in feline herpesvirus-1-positive cats.³⁹ Over 12 weeks, cats receiving this product showed decreased sneezing, pacing, and cortisol, and increased contact seeking.^{39,40}

Composure and Composure Max Liquid

These 2 Vetriscience (vetriscience.com) products contain L-theanine and Colostrum Calming Complex (C3). Despite no peer-reviewed publications describing efficacy in cats, the packaging reports 73% effectiveness



according to owner-reported scores for their cats. This percentage was achieved by multiplying the number of cats with scores of 0 (not effective), 1 (mildly effective), 2 (effective), or 3 (very effective). Those multiplicative factors were then added and divided by total possible points.⁴¹ Vetriscience did not report any statistics, potentially because a chi-squared distribution of scores results in a (*P*) value of 0.157. The above information does not mean that Composure does not work; it means only that specific data are lacking. Vetriscience also offers an option containing L-tryptophan, Composure Pro.

Water

Some studies have found that increased water intake (via consumption of wet food) improves feline idiopathic cystitis,^{42,43} but others have not.^{31,44,45} Effects of water intake on non-urinary tract indicators of stress have not been evaluated.

CHOOSING A NUTRITIONAL INTERVENTION

One choice to address feline stress is whether to recommend a supplement or a diet. **TABLE 1** describes

TABLE 1 Findings Associated With Nutritional Interventions for Feline Stress

INTERVENTION	DOSAGE	BEHAVIORS IMPROVED
α-Casozepine	15 mg/kg q24 for 56 days	<ul style="list-style-type: none"> Fearful behavior with nonfamiliar and familiar people per Cat Emotional Scale²³
	225 mg/cat q24h 3–6 days before veterinary visit	<ul style="list-style-type: none"> Decreased sweaty paws in examination room; no change in fecal cortisol, pupil dilation, respiratory rate, or vocalization²⁴
L-Tryptophan	12.5 mg/kg q24h for 8 weeks	<ul style="list-style-type: none"> Stereotypies, vocalization, house soiling, scratching, and conflict decreased compared to 4-week baseline²⁵
Royal Canin Calm Therapeutic Diet	<ul style="list-style-type: none"> α-Casozepine proprietary levels^a to mimic Zylkene dosing (J. Grither, pers. comm., April 2022) L-Tryptophan <ul style="list-style-type: none"> Original formulation: 100 mg/100 kcal New formulation: 80 mg/100 kcal^b Marigold proprietary levels 	<ul style="list-style-type: none"> Decreased fearful behavior with novel humans in open field test²⁸ Decreased urine cortisol²⁹
Hill's c/d Multicare Stress	<ul style="list-style-type: none"> α-Casozepine proprietary levels L-Tryptophan <ul style="list-style-type: none"> Chicken Dry: 91 mg/100 kcal Chicken & Vegetable Stew: 201 mg/100 kcal + Metabolic Weight Chicken: 228 mg/100 kcal 	<ul style="list-style-type: none"> Decreased duration of hematuria and stranguria 89% versus placebo³¹ Improved pollakiuria, dysuria, stranguria, and overgrooming³² 8.8× fewer FIC recurrences³³
L-Theanine	25 mg q24h	<ul style="list-style-type: none"> Greatly improved: inappropriate elimination, digestive and grooming problems Minimally improved: fear-induced aggression, hypervigilance, scratching³⁶
Solliquin	Per chew <ul style="list-style-type: none"> L-Theanine: 75 mg α-Lactalbumin (whey concentrate): 35 mg <i>Magnolia officinalis</i> + <i>Phellodendron amurense</i>: 75 mg 	<ul style="list-style-type: none"> Reported improvement at or more than improvement after previous receipt of L-theanine supplement³⁷
Purina ProPlan Calming Care	1 × 10 ⁶ CFU <i>Bifidobacterium longum</i> (BL999)	<ul style="list-style-type: none"> Decreased sneezing, pacing, cortisol; increased contact seeking^{39,40}
Composure	Per chew <ul style="list-style-type: none"> Thiamine: 67 mg Colostrum Calming Complex: 11 mg L-Theanine: 10.5 mg 	<ul style="list-style-type: none"> 5 very effective, 2 effective, 3 mildly effective⁴¹
Composure Max Liquid	Per ½ tsp (2.5 mL) <ul style="list-style-type: none"> Thiamine: 134 mg Colostrum Calming Complex: 22 mg L-Theanine: 21 mg 	

CFU=colony-forming units; FIC=feline idiopathic cystitis.

^aLevels are published for food produced in other countries with different labeling requirements (e.g., Belgium), but these are not guaranteed to be the levels in food produced in the United States.

^bNew formulation as of 2022, confirmed by Royal Canin.

dosage recommendations and behaviors reportedly improved by supplements and diets listed in this article.

Supplements

Commercially available supplements for stress all have a protein-derived flavor base, which makes them easy to give. However, the flavoring also poses risks for cats with hydrolyzed protein-responsive chronic enteritis or cutaneous adverse food reactions. For these cats, options are limited to generic L-theanine powder, which has not been specifically studied for absorption or efficacy. Although Zylkene and the flavoring in Calming Care are hydrolyzed, extrapolation from studies of dogs assumes that a small portion of cats may still have an immune response.⁴⁶ A better choice for cats that exhibit urinary signs of stress or have osteoarthritis may be diets with omega-3 fatty acids and glucosamine/chondroitin. In the absence of head-to-head comparison studies, if the cat's comorbidities are excluded, the choice often comes down to what each cat will consume without added stress. Cats that "only eat red triangles" or receive specialized diets for a variety of reasons (dental disease, cardiac disease, facial shape) may more successfully ingest the contents of Zylkene capsules or Calming Care on top of their kibble or wet food. Cats that like crunchy dry treats may be more likely to eat Anxitane, whereas those that enjoy meaty chews may more willingly eat Solliquin.

Diets

Choosing to change a patient's diet (or adding calories from a nutraceutical chew) provides an excellent opportunity to do a complete nutritional assessment and calculate estimated resting energy requirement.⁴⁷ Veterinarians can then inform clients of the precise amount of new food (including calories from supplements or treats) needed to meet any weight goals (loss, management, gain). Weight control is particularly critical for patients with osteoarthritis.

In addition to providing potential physiologic change and support for patients based on diet content, food can also be an excellent source of enrichment. Cats in the wild spend time hunting, successfully and unsuccessfully, a far cry from the always-full food dish of many indoor cats. Clients can simulate hunting for their cats by placing food in puzzles that require the cat to fish pieces out, by moving the puzzle itself, or by hiding pieces of food in a variety of locations to imitate forage feeding. The transition to food enrichment is

best conducted slowly or even partially and by customizing the plan for each patient by taking into account their food preferences, play preferences, and any environmental considerations (location, stairs, financial constraints, other cats).⁴⁸ Starting with the easiest option and monitoring the cat for signs of frustration is critical, especially when the food bowl is empty. Some cats prefer a free meal despite health benefits to the contrary.⁴⁹

TAKE-HOME POINTS

- Although nutritional interventions are a helpful adjunct for decreasing feline stress, the best intervention is removing the stressor(s).
- Nutritional interventions coupled with a complete nutritional assessment enable veterinary professionals to meet many feline-specific needs of their patients.
- Clients should be counseled that no nutraceutical supplement or diet alone is going to cure fear or anxiety and that, despite these interventions, they should do their best to remove the stressor(s) and enrich the cat's environment. **TVP**

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