

NEW RESEARCH

Managing Anxiety in Dogs

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Animal Health

Signs of anxiety

Physiologic signs

- Increased respiration
- Increased heart rate
- Vasomotor changes
- Trembling or paralysis
- Increased salivation
- Sweating
- Gastrointestinal signs

Behavioral signs

- Immobility
- Pacing
- Circling
- Restlessness
- Changes in appetite

Behavior problems caused by anxiety and fear may undermine the human-pet bond. Although the underlying neural and emotional systems differ, the terms anxiety, fear, and phobia are often used synonymously. In clinical practice the distinctions are of less concern. What is of concern is that fear and anxiety can lead to behavioral and physical problems.



Harmful effects of anxiety

Anxiety is the anticipation of danger, usually from unknown or imagined origin. Anxious animals are hypervigilant even in the absence of specific stimuli and exhibit physiologic responses. They may startle easily or show more subtle signs of yawning, tongue flicking, or licking. The earlier a fearful or anxious animal is treated, the more likely behavior problems can be resolved.

One mechanism of the cycle of fear and anxiety affecting a pet's health is stimulation of the hypothalamic-pituitary-adrenal axis, increasing release of noradrenalin and adrenaline. This process can lead to medical conditions including gastrointestinal, dermatologic, and urinary tract disorders as well as immunosuppression.¹ Effective management of anxiety is necessary for the health and welfare of the pet and maintenance of the relationship between pet and owner.

The effectiveness of a nutraceutical containing 99.95% pure L-theanine (*N*-ethyl-L-glutamine; ANXITANE® [L-theanine] Chewable Tablets, virbacvet.com/virbac_behavior) was assessed in a study of 21 healthy laboratory beagle dogs for the treatment of fear of unfamiliar humans.

- Blinded
- Placebo-controlled
- Objective behavioral markers of anxiety employed

Behavioral dermatology

The role of anxiety in health can easily be seen in the relationship between grooming, dermatologic conditions, and anxiety in pets. A medical condition may cause self-inflicted dermatologic lesions, and anxiety may continue the learned behavior of self-injury even when the medical condition has been successfully treated.



Managing anxiety

The first step in managing a fearful pet is to assess its physical health and obtain medical, nutritional, and behavioral histories to help determine if the behavior is a manifestation of a medical condition. Treatment for any medical condition should be instituted and the behavior reexamined. The behavior component should be treated initially with behavior modification programs and owner education, but medical intervention for the behavioral signs may be necessary as well. Combining anxiolytics with behavior modification can improve the rate and extent of improvement.

Both tests were identical to those successfully applied in the past, except that an unfamiliar human was used to exacerbate fearful behavior.



Rated behaviors exhibited by fearful dogs

- Moving to back of pen
- Hiding in or behind cage enclosures
- Circling
- Reduced activity
- Reduced interaction with unfamiliar humans
- Facial expression
- Body posture

The role of L-theanine

L-theanine is an amino acid that is found naturally in green tea and is known for its calming properties. When administered at therapeutic levels, it increases levels of gamma-aminobutyric acid (GABA), an inhibitory neurotransmitter. GABA regulates neuronal excitations in the central nervous system. L-theanine is also a structural analog of glutamate, an excitatory neurotransmitter. L-theanine attaches to glutamate receptors, blocking glutamate and dampening excitatory impulses.

The effectiveness of a nutraceutical containing 99.95% pure L-theanine (*N*-ethyl-L-glutamine; ANXITANE® [L-theanine] Chewable Tablets, virbacvet.com/virbac_behavior) was assessed in a blinded, placebo-con-

trolled study of 21 healthy laboratory beagle dogs.² Fourteen had been previously determined to show fear of humans based on their response when approached in their home pens³ and 7 served as nonanxious controls. (See **Box** below) Dogs were considered nonanxious if they approached and remained at the front of their home pens when visited by strangers and generally displayed greeting behaviors.

Fearful dogs were randomly selected to receive either half an ANXITANE Tablet (50- or 100-mg tablet based on

Study

ANXITANE® (L-theanine) Chewable Tablets for reducing fear of unfamiliar humans

- 21 laboratory-housed beagle dogs (4 dropped from study for demonstrated acclimation to human before treatment phase)
 - 10 with fear of unfamiliar humans
 - 7 nonanxious dogs as controls
- 5 anxious dogs received ANXITANE Tablets
- 5 anxious dogs received placebo

Results

- Dogs receiving ANXITANE Tablets showed greater human interaction than placebo group
- No side effects observed

patient weight) or an identical placebo twice daily. Treatment was administered for 57 days. Subjects were tested by open field and human-interaction behavioral measures during the final week of treatment in order to assess the effectiveness of the test article.⁴

Objective markers of anxiety

Using objective markers rather than subjective markers was essential to allowing the study to determine the effects of ANXITANE Tablets despite the small number of study subjects. The open field test was originally developed to examine the effects of age on general canine behavior in a con-

trolled environment, as well as to study the effects of various drugs on behavior. Both this test and the human-interaction test were identical to those successfully applied in the past, except that an unfamiliar human was used to exacerbate fearful behavior.

Results

Efficacy

Anxious dogs showed reduced interaction with an unknown human compared with nonanxious dogs, and ANXITANE Tablets improved measures of human approach and interaction as compared with placebo. Anxious dogs showed a significant reduction in time spent near the human and in frequency of interaction with the human, indicating that this was a sensitive measure of anxiety. Total distance traveled did not differ between fearful and normal dogs, suggesting that it is a less robust measure of anxiety than interaction with the human in these subjects. In placebo-treated dogs, there was a decrease in frequency and duration of interaction at the treatment phase over baseline.

Test methods

Open field test

- Dogs placed in 9 ft × 12 ft room
- Room sanitized to reduce olfactory cues
- Path/distance traveled measured digitally
- Trained observer scored behavior/bouts of inactivity

Human interaction test

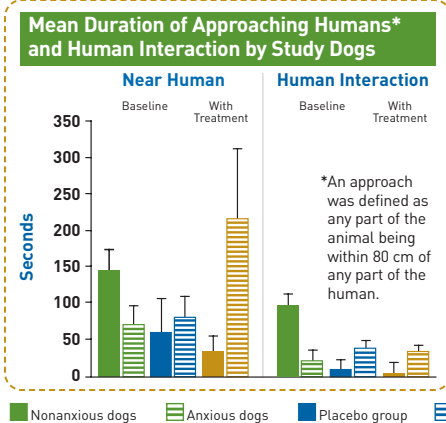
- See above methodology
- Unfamiliar human at center of room
- Touching, sniffing, approaching human rated for frequency/duration

This may be explained by a phenomenon of sensitization to the presence of the human over time and suggests that treatment would benefit these subjects. Additional study to substantiate these implications is needed.

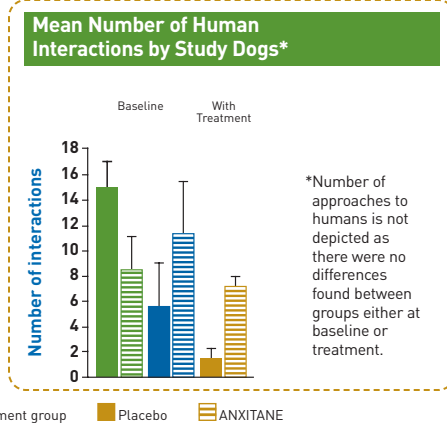
Safety

Trained technicians observed the dogs twice a day for motor stimulation and sedative effects as well as other potential side effects. In addition, 24-hour activity collars were used to track day-to-day activity levels and potential sedative effects of treatment. None was found. In addition, a study specifically addressing tolerance was conducted

Fearful dogs showed reduced interaction with an unknown human compared with normal dogs, and ANXITANE Tablets improved measures of human approach and interaction as compared with placebo.



Mean duration of interaction was significantly reduced in anxious dogs compared with normal dogs. Mean duration of time spent near the human and of interaction with the human were significantly higher in the treatment group at the treatment time-point compared with the placebo group.



Mean frequency of interaction with the unknown human was significantly higher in the treatment group compared with the placebo group at treatment, although both groups showed mean reductions compared with baseline (to a greater extent in the placebo group).

Trained technicians observed the study dogs twice a day for the duration of the study for motor stimulation and sedative effects as well as other potential side effects. None was found.

using 5 times the recommended dosage for a period of 2 months. No effect was observed on appetite, sleep, or general activity. Biochemical and hematologic values remained within normal ranges.⁵

Implications for practice

Consideration of ANXITANE Tablets as a first-intention treatment for dogs exhibiting anxious behaviors in

response to unfamiliar humans and other stimuli is warranted in view of its demonstrated efficacy and apparent lack of side effects. ANXITANE Tablets are not recommended for treating separation anxiety and its accompanying nuisance behaviors (destructiveness, vocalization, etc). It can be considered for use with other anxiolytics and can be used for life-long treatment, if necessary.

Commentary



Dogs affected with anxiety disorders are commonly presented to both veterinary practitioners and behavior specialists. Such disorders represent a welfare issue, negatively affecting the dog's quality of life and optimal health. They may also erode the all-important human-animal bond, as frustrated and conflicted clients conclude that, despite their attachment, they can't continue to sustain the emotional and financial burden. This is a critical consequence, since it may lead to relegation outside, rehoming, abandonment, relinquishment, or even euthanasia of the affected dog. In such cases, the dog is lost as a companion by its family and as a patient from its veterinary practice. Thus, there are negative goodwill and economic consequences to practitioners. For all these reasons, veterinarians need to be proactive in recognizing and treating anxiety-related behavioral disorders of dogs.

L-theanine (ANXITANE Chewable Tablets) is an important addition to our armamentarium of agents helpful in the treatment of canine anxiety disorders. Well-tolerated and palatable, it may be used on a daily basis for ongoing problems, such as generalized anxiety; on an as-needed basis for anxiety-producing events, such as car travel or veterinary visits; or both. In addition, in severe or treatment-resistant cases, L-theanine may be administered in combination with conventional pharmacologic treatments, such as fluoxetine or clomipramine, to enhance treatment outcome.—*Barbara L. Sherman, PhD, DVM, Diplomate ACVB, Clinical Associate Professor, Department of Clinical Sciences, North Carolina State University College of Veterinary Medicine; President, American College of Veterinary Behaviorists*

References

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2. **Anxitane tablets reduce fear of human beings in a laboratory model of anxiety-related behavior.** Araujo JA, de Rivera C, Ethier JL, et al. *J Vet Behav* 5:5, 2010.
3. **The development of laboratory models for the objective evaluation of anxiolytics in dogs.** Landsberg GM, Araujo JA, de Rivera CM, Milgram NW. *Proc Am Vet Soc Anim Behav*, 2009.
4. **Effect of age and level of cognitive function on spontaneous and exploratory behaviors in the beagle dog.** Siwak CT, Tapp PD, Milgram NW. *Learn Mem* 8:317-325, 2001.
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Indications for ANXITANE® Chewable Tablets

- Encounters with unfamiliar people
 - On walks
 - Veterinary visits
 - Groomer appointments
- Situational anxiety from environmental or family changes (birth, adoption, house visitors, death, divorce, moving, etc)
- Travel
- Fear of loud noises (thunderstorms, fireworks, gunfire, etc)

This summary is based on research findings as reported in the references cited.

