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. 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

**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
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.

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.

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

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...
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.

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.

**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.

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).
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
5. Data on file