

Selected References

Aronson L. (1995) Animal behavior case of the month. A dog was evaluated because of extreme fear. J Am Vet Med Assoc.;215(1):22-4.

Benton. D,. Danohoe. R-T. Sillance. B. and Nabb. S. (2001) The influence of phosphatidylserine supplementation on mood and heart rate when faced with an acute stressor. Nutr. Neurosci. 4(3), 169-178

Berteselli GV, Michelazzi M. (2007) Use of L-Theanine tablets (Anixitame™) and behavior modification for treatment of phobias in dogs: a preliminary study. Poster. 6th IVBM, Riccione, IT.

Dramard V, Kern L, Hofmans J. (2007) Clinical efficacy of I-theanine tablets to reduce anxiety-related emotional disorders in cats: a pilot open-label clinical trial. In Landsberg et al (eds) Proc 6th IVBM/ECVBM-CA. Fondazione Iniziative Zooprofilattiche e Zootechniche. Brescia, IT, 114-115 Farber, S. (2002) Sports Medicine for Dogs Part 2: Introduction to Treatment: The Anxiety Wrap.

Gomez-Ramirez M, Kelly SP, Montesi JL, Foxe JJ. (2008) The Effects of L-theanine on Alpha-Band Oscillatory Brain Activity During a Visuo-Spatial Attention Task. Brain Topogr.

Hellhammer J, Fries E, Buss C, Engert V, Tuch A, Rutenberg D, Hellhammer D. (2004) Effects of soy lecithin phosphatidic acid and phosphatidylserine complex (PAS) on the endocrine and psychological responses to mental stress. Stress. June;7(2):119-26.

Juneja L, et al. (1999) L-theanine – A unique amino acid of green tea and its relaxation effect in humans. Trends in food science technology. v. 10(6/7) p. 199-204.

Kimura K, Ozeki M, Juneja LR, Ohira H. (2007) L-Theanine reduces psychological and physiological stress responses. Biol Psychol.Jan;74(1):39-45. 2006 Aug 22.

Kimura R, et al. (1986) Effect of theanine on norepinephrine and serotonin levels in rat brain. Chem Pharm Bull (Tokyo). July;34(7):3053-7. Kobayashi A, et al. (1998) Effects of L-theanine on the release of a-waves in human volunteers. Nippon Nogeikagaku Kaishi. Vol. 72, 153-157. Kronen PW, Ludder JW, Erb HN, Moon PF, Gleed RD, Koski S. (2006) A synthetic fraction of feline facial pheromones calms but does not reduce struggling in cats before venous catheterization. Vet Anaesth Analg. July 33(4):258-65.

Mero, A., Miikkulainen, H., Riski, J.; Pakkanen, R.; Aslto, J., Takala (1997), Effects of bovine colostrum supplementation on serum IGF-I, IgG, hormone, and saliva IgA during training. Journal of Applied Physiology 83(4):1144-1151.

Nitsch, A. and Nitsch, F.P. (1988) The clinical use of bovine colostrum. The Journal of Orthomolecular Medicine. 13(2):110-118, Second Quarter 1988. Nozawa, A. et al. (1995) Theanine, a glutamate analog, stimulates NMDA-receptors by suppressing excitatory effect of caffeine in cortical neurons. Society for Neuroscience Abstracts., Vol. 21, No. 1-3, p. 835.

Pageat P. Gaultier E. (2003) Current research in canine and feline pheromones. Vet Clin North Am Small Anim Pract.; 33(2):187-211.

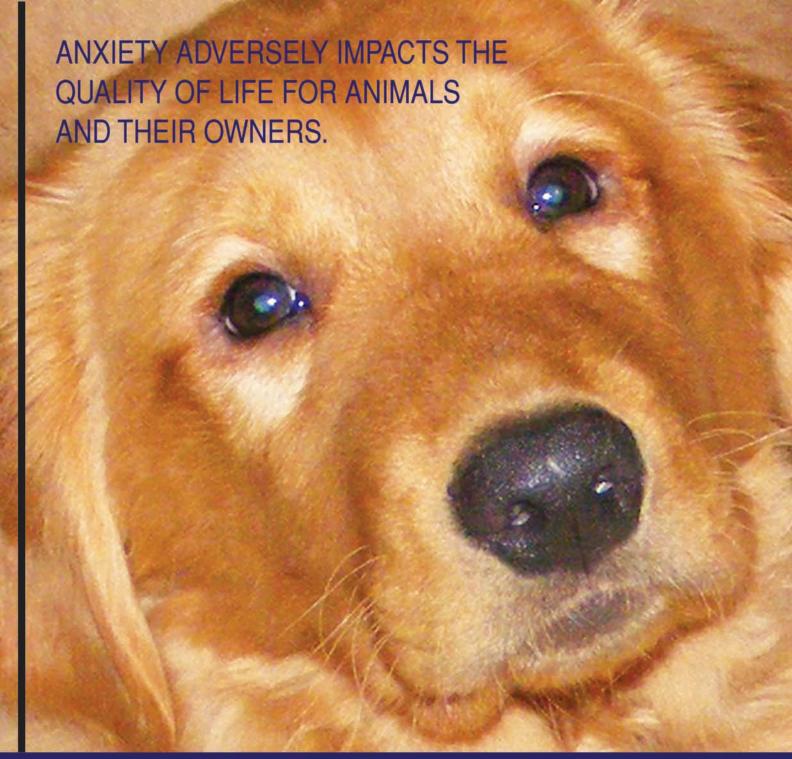
Russo S, Kema IP, Fokkema JR, Boon JC, Willemse PH, de Vries EG, den Boer JA, Korf J. Tryptophan as a link between psychopathology and somatic states. (2003) Psychosom Med. 65(4):665-71.

Wells DL. (2006) Aromatherapy for travel-induced excitement in dogs. J Am Vet Med Assoc;229(6):964-7

Yokogoshi H, et al. (1998) Theanine-induced reduction of brain serotonin concentration in rats. Biosci Biotechnol Biochem; 62(4): 816-17.

Yokogoshi H, et al. (1998) Effect of theanine, r-glutamylethylamide, on brain monoamines and striatal dopamine release in conscious rats. Neurochem 23(5): 667-73.

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Now you have choices



According to current shelter statistics, behavior problems – many due to anxiety – are still the number one cause of euthanasia in the United States.

CHOICES FOR HANDLING BEHAVIORAL ISSUES

Anxiety and negative behavior in companion animals can range from mild to extreme. While stress-induced anxiety is difficult to quantify in dogs and cats, the consequence of ongoing anxiety to the pet's health and the owner's peace of mind can be monumental.

Causes of anxiety:

Signs of anxiety may include: Treatment of anxiety:

- Genetic predisposition
- Inconsistent discipline or training
- Stressful changes in the environment/boarding
- Changes in animals or people residing in the house
- Visitors
- Conflict with other animals in the household
- Separation from owner/travel
- + Fear of thunderstorms or other natural causes
- + Hyper-attachment to owner
- Eliminating in the house
 Destruction of objects in the environment
- * Agitation, nervousness, panting, salivation
- Barking, growling or other aggressive behavior
- Fighting with other animals in the house
- Remove triggersBehavior modification
 - Chemical anxiolysis:
 - Drug therapies
 - Non-drug therapies



Non-Drug Therapies:

Colostrum Derived Bioactive Proteins Colostrum has been studied extensively for its health-building properties in both humans and animals. Colostrum contains immune-enhancing immuno globulins, essential growth factors, cytokine inducers and other classes of proteins (Mero 1997, Nitch 1988). Once many of these dietary proteins are broken down in the gastrointestinal tract, they produce bioactive peptides that display a wide range of activities ranging from antimicrobial properties, antioxidant activity as well as anxiolytic characteristics. Colostrum contains precursors to neurological important molecules that can affect mental alertness, cognitive function and calming in stressed animals. Evaluations of specific protein fractions derived from bovine colostrum in both dogs and cats have shown a reduction in adverse behavior patterns and enhanced calming.

L-Theanine (N-ethyl-L-glutamine and L-glutamic acid —monoethylamide or gamma-glutamylethylamide) is a unique, non-protein-forming amino acid found in the leaves of the tea plant (Camellia sinensis) and in a single non-edible mushroom (Xerocomus badius). It has been approved in Japan since 1964 for flavoring a variety of foods as it provides the umami flavor that is thought to be a main component of the taste of tea. Rat studies suggest that L-Theanine does have calming properties. The compound apparently binds selectively to glutamate receptors, competitively inhibiting the binding of L-Glutamic Acid. EEG studies on people have shown that I-Theanine affects alpha brain waves in ways characteristic of relaxation responses without inducing drowsiness (Junega 1999). It also plays a beneficial role in focusing attention on difficult tasks (Gomez-Ramirez 2008) and may reduce anxiety responses while attending to acutely stressful tasks (Kimura 2006). The efficacy of L-Theanine as compared with placebo was tested in cats with storm phobia. In combination with a desensitization program, the L-Theanine resulted in reduced signs of anxiety (Dramard, in Landsberg 2007). (Berteselli, 2007).

Lecithin is a purified substance called phosphatidylcholine that belongs to a category of fat-soluble substances called phospholipids. A similar substance (soy lecithin phosphatidic acid and phosphatidylserine complex) has been shown in people to reduce stress responses and researchers involved theorize that the effect is mediated through the pituitary-adrenal axis (Hellhammer 2004, Benton 2001). Gindin (1993) also demonstrated enhanced memory and mood in seniors taking phosphatidylserine and phosphatidic acid.

Pheromones Feline cheek pheromone (F3) is deposited when cats rub their faces on objects in the environment to mark boundaries, thereby providing emotional stability (Pageat 2003). Synthetic F3 (Feliway) may be effective in reducing anxiety in multi-cat households, during transport and in veterinary clinics (Kronen 2006). DAP is a synthetic version of an intermammary appeasing pheromone in the lactating bitch. It has been suggested to help reduce excitement during puppy classes, reduce anxiety in veterinary clinics and shelters, help puppies adapt to new homes, reduce fear of fireworks and reduce transportation anxiety.

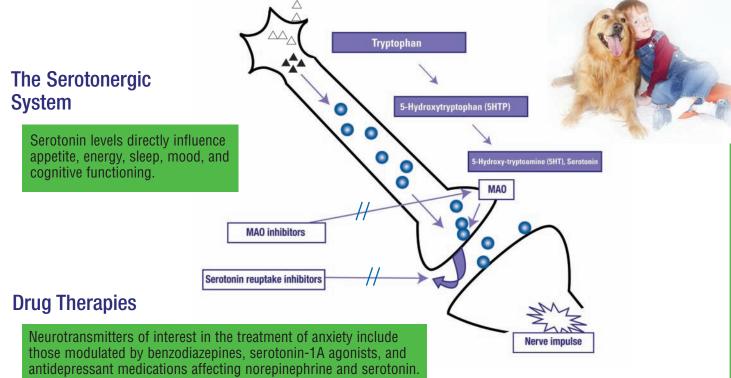
Melatonin is a serotonin derivative produced in the pineal gland and may inhibit dopamine. It has been recommended as a sleep aid and to reduce signs of thunderstorm phobia (Armson 1999). Sedation from high doses has been described anecdotally.

Tryptophan is the precursor of serotonin, and serotonin catabolism is enhanced under the influence of hormones, stress, and inflammation. Human research has shown exaggerated anxiety responses when tryptophan is depleted (Russo 2003). In people taking tryptophan, agitation, dizziness, drowsiness, dry mouth, headache, nausea, poor coordination, and twitching have sometimes been reported.

Lavender As part of traditional aromatherapy techniques, lavender has been used as an anxiolytic herb (Wells 2006) without reported adverse effects.

"Maintained Pressure" Anxiety wrap, Tellington Touch methodology: Sensory receptors located in the sensory organs as well as other organs, connective tissue, joints and muscles integrate information from the environment for interpretation by the brain (Shereen 2002). Touch is one of the earliest sensory inputs to develop, and the animal utilizes constant feedback to normalize touch responses. Maintained pressure is thought to suppress hypersensitivity in touch receptors that is facilitated by chronic sympathetic stimulation that lowers the threshold required to fire these sensory receptors. No adverse effects are known.

Summary: Behavior modification should be combined with either drug or non-drug therapy in the treatment of anxiety. Because the potential for adverse effects and abuse by clients exist when drug therapy is prescribed, non-drug therapy may be a viable first option. Using natural methods for reducing anxiety related behavior patterns may offer a potential solution with minimal disruption of the animal's normal activity.



Drug	Mechanism of Action	Adverse Effects
Alprazolam Diazepam Oxazepam Clonazepam Lorazepam	Lorazepam Benzodiazepines potentiate the transmission of GABA, an inhibitory neurotransmitter. They cause muscle relaxation, decrease motor activity, reduce anxiety and may cause hyperphagia.	Paradoxical excitability, amnesic effect on learning and behavior, rebound effects can be seen. In cats, rare instances of hepatotoxicity and death have been reported. Anxiolytic drugs can cause aggression due to disinhibition.
Amitriptyline Clomipramine Imipramine Doxepin	Tricyclic antidepressants (TCAs) block re-uptake of serotonin and noradrenaline. Depending on the drug, some have anti-cholinergic, anti-histaminic and alpha-adrenergic activity.	Lethargy, dry mouth or gastrointestinal signs. TCAs are contraindicated with cardiac disease (with the exception of amitriptyline and clomipramine), glaucoma or where urine retention may be a concern.
Fluoxetine Paroxetine Sertraline	Selective serotonin re-uptake inhibitors (SSRIs) block re-uptake of 5HT1A into pre-synaptic neurons.	Lethargy and anorexia. Because these drugs affect serotonin levels only, they are preferred to TCAs if cardia disease, urine retention, increase intraocular pressure, sedation or anti-cholinergic effects may be issues.
Buspirone	Buspirone acts as a serotonin (5HT1A) receptor agonist and a dopamine (D2) agonist. It may take a week or more to reach effect.	Should be used with caution in patients with hepatic or renal disease. Bradycardia, GI disturbances and stereotypic behaviors have been reported.
Selegiline	MAO B inhibitors enhance catecholamine transmission. A controlled trial showed that dogs treated with selegiline performed better in learning tasks.	Adverse effects may include vomiting, salivation, anorex and diarrhea; diverse CNS effects that may include lethargy, restlessness, repetitive movement. Diminished hearing/deafness, licking, pruritus, and trembling have been reported. Contraindicated for use with MAO inhibitors, TCA, SSRI, opioids, or amitraz.
Cabergoline	Dopamine-2-receptor agonists have anti-prolactin effects and may be used in dogs with signs of pseudo-pregnancy including aggression, and in post-spay aggression.	Contraindications include pregnancy and liver disease. Metoclopramide or phenothiazines are D2 dopamine antagonists that may reduce the efficacy of cabergoline. Because cabergoline may have hypotensive effects, avoiduse with other hypotensive agents.
Acepromazine	Phenothiazines are used for sedation but do not reduce anxiety.	Phenothiazines have anti-cholinergic activity, so should be used in patients with liver disease, seizures, or heart disease.

Sources: Gary M. Landsberg, BSc, DVM, DACVB (Behaviour), MRCVS. Treating Canine and Feline Anxiety: Drug Therapy and Pheromones. British Small Animal Veterinary Congress, April 3-6, 2008.