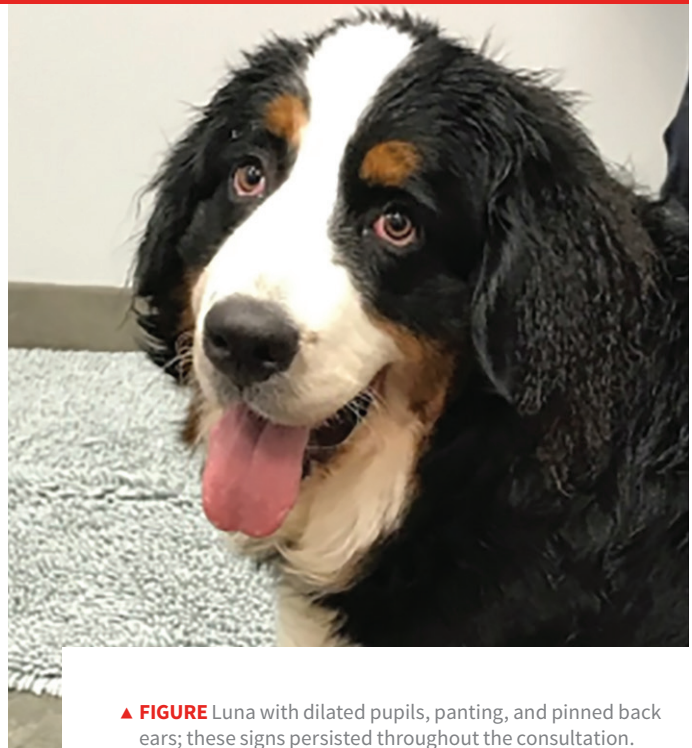


# Sudden Onset of Fear & Panic in a Bernese Mountain Dog

**Amy L. Pike, DVM, DACVB**  
*Animal Behavior Wellness Center*  
 Fairfax, Virginia



▲ **FIGURE** Luna with dilated pupils, panting, and pinned back ears; these signs persisted throughout the consultation.

Luna, a 9-month-old, 60-lb (27-kg) intact female Bernese mountain dog, had a sudden onset of severe fear and panic toward new elements in her environment, unfamiliar humans, and riding in a car after she fell from a moving vehicle at 4 months of age.

Prior to Luna falling out of the car, her owners reported that she was normal, quickly accepted unfamiliar humans, and appeared to enjoy riding in the car. After falling, Luna began to startle, back up, bark, and growl when encountering novel items (eg, a plastic bag blowing in the wind); pant, bark, growl, and attempt to hide when unfamiliar humans entered the home; and back up, cower, tremble, pant, and profusely drool when being lifted into and riding in the car. She also appeared fearful when walking underneath objects (eg, trees, entryways). These behaviors continued for the next 5 months,

at which time she was presented to a behavior clinic.

## Physical Examination & Diagnostics

Luna was initially presented to an emergency veterinary clinic after the fall. Diagnostic evaluation (including CBC, serum chemistry profile, and urinalysis) was performed, and all results were within normal limits. Because there was possible head trauma from the fall, she was also referred to a neurologist where a brain MRI was completed—results were also within normal limits.

Physical and neurologic examination findings at the time of presentation to the behavior clinic were also within normal limits. Behavior signs in the examination room included panting, pinning her ears back, cowering near her owners, and being unwilling to interact with staff or take treats during the consultation; her pupils were also dilated (*Figure*). An FAS (ie, Fear, Anxiety, and Stress) spectrum and pain algorithm was used (see *Suggested Reading*, page 71), on which Luna scored an FAS 4: severe.

## DIAGNOSIS: CHRONIC POST-TRAUMATIC STRESS DISORDER

Based on patient history, and because the behavior issues were persistent and did not resolve, chronic post-traumatic stress disorder (PTSD) was diagnosed.

Secondary diagnoses included generalized anxiety disorder (based on the patient spending most of her time in an anxious state), global phobia (ie, persistent and excessive fears that are potentially irrational in nature), neophobia (ie, exaggerated fear response to novel items), and fear-based aggression (ie, distance increasing body postures and vocalizations [eg, barking, growling, snarling, lunging, nipping, snapping, biting] toward unfamiliar humans and dogs).

### Treatment

Treatment for behavior issues should include environmental management, behavior modification, and medical therapy.

## DESENSITIZATION & COUNTERCONDITIONING FOR A TRIGGER

To address Luna's fear of plastic bags, the distance at which she had no negative reaction toward the bag was determined. The bag was presented to her at that distance, her owner fed her a high-value reward, and the bag was removed when she stopped feeding. Once Luna developed a positive emotional response to the presence of the bag (as a result of receiving a high-value reward), criteria were increased, including bringing the bag closer to her or having the bag make noise or move. Luna was kept under threshold for reaction, and focus was kept on creating a positive emotional response before moving to next steps.

DSCC = desensitization and counterconditioning

NT = neurotransmitter

PTSD = post-traumatic stress disorder

### Environmental Management

Environmental management is important for elimination of unwanted behavior, as well as elimination (as much as feasible) of fear, anxiety, and frustration that are often the underlying cause of behavior concerns. Learning can only take place when the patient is not experiencing a high level of emotional arousal; thus, environmental management is the first step in treatment, before behavior modification can be started.

Luna's owners were instructed to attempt to avoid triggering situations during the treatment period, including not having guests in the home, not driving Luna in the car, and taking Luna on walks during nonpeak hours. Her owners were told to remove her from triggering encounters as quickly as possible.

### Behavior Modification

Behavior modification involves either teaching an alternate incompatible behavior to replace the unwanted behavior or altering the emotional state from one that is negative to one that is positive or neutral (ie, desensitization and counterconditioning [DSCC]).

Initial behavior modification techniques were focused on additional management strategies, including teaching Luna to wear a basket muzzle and perform an emergency U-turn (ie, a 180-degree turn away from the trigger/stimulus). Further behavior modification was delayed until Luna's anxiety was low enough to remain under threshold (ie, the level at which emotional arousal is too high and a negative reaction occurs). Once Luna's anxiety was under control, DSCC for her triggers could begin (see *Desensitization & Counterconditioning for a Trigger*).

### Medical Therapy

Environmental management alone is impractical, and complete compliance is difficult in patients with numerous triggers, as with Luna and most patients with this set of diagnoses. Anxiolytic medication is thus necessary. Medical therapy is often multimodal, targeting  $\geq 1$  neurotransmitters

(NTs) involved in fear and anxiety and includes serotonin (ie, coping NT), dopamine (ie, pleasure/activation NT),  $\gamma$ -aminobutyric acid (ie, inhibitory NT), and norepinephrine (ie, NT involved in fight/flight modulation).

Treatment for dogs with chronic PTSD and other phobias can be challenging, and the correct medications and products are needed for behavior modification.

Luna was started on the following:

- ▶ Sertraline (25 mg twice daily [ $\approx 1$  mg/kg PO every 12 hours]), which was chosen because it is a selective serotonin reuptake inhibitor that targets serotonin and dopamine increases via inhibition of reuptake in the postsynaptic cleft.<sup>1</sup> In humans, sertraline is approved for use in patients with PTSD and social phobias.<sup>2-4</sup>
- ▶ Alprazolam (1-3 mg PO prior to or immediately after any panic-inducing situation [ $\approx 0.04$ -0.1 mg/kg PO every 6-8 hours as needed]), which is shown to be effective in treating dogs with noise phobia and often useful for treatment of other phobia disorders (eg, noise phobia)<sup>5,6</sup>
- ▶  $\alpha$ -casozepine (450 mg; used as directed based on patient weight), which is used for calming effects in dogs with anxiety disorders<sup>7</sup>
- ▶ Pheromone collar (used as directed by the manufacturer); maternal-appeasing pheromones have been shown to help dogs with noise phobias and other anxiety disorders (eg, travel anxiety).<sup>8-10</sup>

Nutraceuticals and pheromones may augment medical therapy and potentially improve outcomes when combined with other treatment modalities.<sup>11</sup>

After 4 weeks, sertraline was increased to 50 mg twice daily ( $\approx 2$  mg/kg PO every 12 hours) based on an  $\approx 60\%$  reduction in intensity of fear and anxiety, as well as a continued need for improvement. All other drugs and products were continued at the starting dosages. Luna's owners reported a decrease in the intensity of reactions to triggers and slightly decreased time of recovery, but attempts at DSCC were still unsuccessful. Manage-

ment was still difficult due to the numerous triggers Luna experienced daily; this was partly due to living in an apartment complex in a major metropolitan area and the need to walk Luna for elimination purposes on a busy street.

### Prognosis & Outcome

Once Luna's anxiety was lowered and she was able to be under threshold while at a reasonable distance from triggering situations, a program of DSCC to specific triggers (eg, riding in a car, meeting new people, going through thresholds and under trees) was implemented.

Despite moderate improvement in fear intensity and ability to recover when triggered, Luna's owners chose to relinquish her because they lived in an urban area in which she was exposed to triggers daily and because they were first-time dog owners who felt overwhelmed by her continued need for behavioral care. Luna's breeder assisted in rehoming her with a family in a suburban area in which management could be more easily accomplished. Luna had significant progress with the new family, presumably due to the combined effect of being in a new environment, ongoing medical therapy, and the new owner's commitment to the prescribed behavior modification plan. Alprazolam was rarely

### TREATMENT AT A GLANCE

- ▶ Any possible medical etiology should be ruled out, especially in patients with a sudden change in behavior.
- ▶ Strict environmental management should be implemented to avoid unwanted behavior and keep the patient under threshold during treatment.
- ▶ Appropriate psychotropic medications and products should be considered to help reduce fear, anxiety, and stress.
- ▶ Behavior modification, including DSCC, with the assistance of a board-certified veterinary behaviorist or other qualified positive-reinforcement-based trainer can be helpful.

needed; however, her owners continued sertraline and other products because of Luna's progress and the owner's hesitance for potential setbacks.

## Discussion

Canine PTSD is diagnosed based on the patient experiencing a potentially traumatizing event and subsequently developing signs like hypervigilance, aggression, compulsive disorders, sleep disturbance, increased startle response, fear, avoidance, and/or withdrawal. These signs persist >1 month after the traumatic event and are not present prior to the event. Similar experiences in humans should be used as criteria when diagnosing PTSD. Prevalence of PTSD in dogs is widely unknown due to lack of retrospective studies.<sup>12</sup>

Sudden onset of behavior is usually an indicator that a thorough medical workup is needed. Once medical etiologies have been ruled out and diagnostic criteria for behavior disorders are met, treatment can be started to alleviate and modify signs. ■■■

## TAKE-HOME MESSAGES

- Medical etiologies should always be considered and ruled out when there is a sudden change in behavior.
- Traumatic events can cause PTSD in companion animals similar to that seen in humans.<sup>12</sup>
- Treatment for PTSD and other behavior problems should include a 3-part approach (ie, environmental management, behavior modification, medical therapy).
- Behavior modification, which is key for behavior disorders, cannot proceed until triggers do not immediately push the patient over their threshold.
- Psychotropic medications and products can positively impact patient well-being.
- Some owners may be unable or unwilling to care for a patient with behavior disorders.
- Improved living environment can impact treatment outcomes.

See page 71 for references and suggested reading.

PTSD = post-traumatic stress disorder

# Mirataz<sup>®</sup>

## (mirtazapine transdermal ointment)

For topical application in cats only. Not for oral or ophthalmic use.

**CAUTION:** Federal law (USA) restricts this drug to use by or on the order of a licensed veterinarian.

**Before using this product, please consult the product insert, a summary of which follows:**

**INDICATION:** Mirataz is indicated for the management of weight loss in cats.

**DOSE AND ADMINISTRATION:** Administer topically by applying a 1.5-inch ribbon of ointment (approximately 2 mg/cat) on the inner pinna of the cat's ear once daily for 14 days. Wear disposable gloves when applying Mirataz. Alternate the daily application of Mirataz between the left and right inner pinna of the ears. See **Product Insert for complete dosing and administration information.**

**CONTRAINDICATIONS:** Mirataz is contraindicated in cats with a known hypersensitivity to mirtazapine or to any of the excipients. Mirataz should not be given in combination, or within 14 days before or after treatment with a monoamine oxidase inhibitor (MAOI) [e.g. selegiline hydrochloride (L-deprenyl), amitraz], as there may be an increased risk of serotonin syndrome.

**HUMAN WARNINGS:** Not for human use. Keep out of reach of children. **Wear disposable gloves when handling or applying Mirataz to prevent accidental topical exposure.** After application, dispose of used gloves and wash hands with soap and water. After application, care should be taken that people or other animals in the household do not come in contact with the treated cat for 2 hours because mirtazapine can be absorbed transdermally and orally. However, negligible residues are present at the application site and the body of the cat at 2 hours after dosing. In case of accidental skin exposure, wash thoroughly with soap and warm water. In case of accidental eye exposure, flush eyes with water. If skin or eye irritation occurs seek medical attention. In case of accidental ingestion, or if skin or eye irritation occurs, seek medical attention.

**PRECAUTIONS:** Do not administer orally or to the eye. Use with caution in cats with hepatic disease. Mirtazapine may cause elevated serum liver enzymes (See **Animal Safety** in the product insert). Use with caution in cats with kidney disease. Kidney disease may cause reduced clearance of mirtazapine which may result in higher drug exposure. Upon discontinuation of Mirataz, it is important to monitor the cat's food intake. Food intake may lessen after discontinuation of mirtazapine transdermal ointment. If food intake diminishes dramatically (>75%) for several days, or if the cat stops eating for more than 48 hours, reevaluate the cat. Mirataz has not been evaluated in cats < 2 kg or less than 6 months of age. The safe use of Mirataz has not been evaluated in cats that are intended for breeding, pregnant, or lactating cats.

**ADVERSE REACTIONS:** In a randomized, double-masked, vehicle-controlled field study to assess the effectiveness and safety of mirtazapine for the management of weight loss in cats, 115 cats treated with Mirataz and 115 cats treated with vehicle control were evaluated for safety. The vehicle control was an ointment containing the same inert ingredients as Mirataz without mirtazapine. The most common adverse reactions included application site reactions, behavioral abnormalities (vocalization and hyperactivity), and vomiting. See **Product Insert for complete Adverse Reaction information.** To report suspected adverse events, for technical assistance or to obtain a copy of the SDS, contact Dechra at 888-933-2472. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at <http://www.fda.gov/reportanimalae>.

**EFFECTIVENESS:** The effectiveness of Mirataz (mirtazapine transdermal ointment) was demonstrated in a randomized, double-masked, vehicle-controlled, multi-site field study involving client-owned cats of various breeds. Enrolled cats were ≥ 1 year of age and had existing documented medical history of ≥ 5% weight loss deemed clinically significant. The most common pre-existing conditions included renal insufficiency, vomiting, and hyperthyroidism. Some cats had more than one pre-existing condition. Cats were randomized to treatment groups in a 1:1 ratio of Mirataz to vehicle control. A total of 230 cats were enrolled and received either Mirataz (115 cats) or a vehicle control (115 cats) containing the same inert ingredients without mirtazapine. The cats were 2.8-24.6 years of age and weighed 2.1-9.2 kg. The dosage was a 1.5-inch ribbon (approximately 2 mg/cat) mirtazapine or vehicle ointment administered topically to the inner pinna of the cat's ear. A total of 177 cats were determined to be eligible for the effectiveness analysis; 83 cats were in the Mirataz group and 94 cats were in the vehicle control group. The primary effectiveness endpoint was the mean percent change in body weight from Day 1 to the Week 2 Visit. At Week 2, the mean percent increase in body weight from Day 1 was 3.94% in the mirtazapine group and 0.41% in the vehicle control group. The difference between the two groups was significant (p<0.0001) based on a two-sample t-test assuming equal variances. A 95% confidence interval on the mean percent change in body weight for the Mirataz group is (2.77, 5.11), demonstrating that the mean percent change is statistically different from and greater than 0.

**STORAGE:** Store below 25°C (77°F). Multi-use tube. Discard within 30 days of first use.

**HOW SUPPLIED:** Mirataz is supplied in a 5 gram aluminum tube.

**MANUFACTURED FOR:**  
Dechra Veterinary Products  
7015 College Boulevard, Suite 525  
Overland Park, KS 66211 USA

US Patent 10,603,272

Approved by FDA under NADA # 141-481  
NDC 86078-686-01

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**... TO YOUR PATIENTS**

Key pearls to put into practice:

- 1** Steroid therapy may result in insulin resistance and DM in cats. Most (64.3%) cats that developed DM in this study required insulin therapy and/or reduction of the steroid dosage for management of DM.
- 2** Although DM can occur at any time, most cats developed DM within the first 3 months of prednisolone therapy. It is important to educate owners on how to monitor for polyuria, polydipsia, and polyphagia, so cats that develop DM can be identified. Unlike dogs, cats do not normally exhibit polyuria/polydipsia with corticosteroid therapy.
- 3** Tapering to the lowest effective steroid dosage as soon as possible may help reduce the risk for secondary DM; however, this requires further evaluation.

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CASE IN POINT ► CONTINUED FROM PAGE 86

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**Suggested Reading**

FAS spectrum and pain algorithm. Fear Free website. <https://fearfreepets.com/fas-spectrum>. Accessed November 2020.