Updates in the management of noise aversion in dogs

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1.Definitions:

Fear

Response to **actual presence** of perceived unpleasant trigger

Adaptive

Anxiety

Response to **anticipated exposure** to perceived unpleasant trigger

Level can range from normal to abnormal

Phobia

Fear response **out of proportion** to actual level of danger presented by trigger

Maladaptive, interfere w normal functioning

Noise phobia, Storm phobia

Aversion

Distressed, try to avoid, uncomfortable

Noise aversion

Refer to all anxious, fearful or phobic responses to sounds

Noise phobia

fear of loud noises, commonly gunshots or fireworks, or other unexpected loud noises such as those experienced during car travel, in the veterinary clinic, animal shelters

Thunderstorm phobia

fear of thunder and associated contextual cues with storms (rain, wind, lightning, darkening skies, barometric pressure change, etc.)

Associated with generalized anxiety and hypervigilance

2. Noise aversion is a common problem worldwide, in the USA, ~ 44-67% of dogs(1-4).

However, only a small percentage of owners seek out help from their veterinarian.

If left untreated, it generally will get worse over time. This impacts the human animal bond (5,6)

3. When considering comorbidities with noise aversion, there is variable data available.

3.1. Some data suggests those dogs with separation related problems are also more likely to have noise aversion, while others do not (3,7).

3.2. More recent studies have investigated the association between musculoskeletal pain and noise aversion (8,9)**.** Dogs with concurrent musculoskeletal pain are more likely to show signs of noise aversion later in life (2 yrs of age vs 6 yrs of age), they are more likely to have their fear of noises generalize to other noises, and they are also more likely to avoid other dogs.

3.3. Additional data from Zoetis (10) describes a high overlap of noise aversion and motion sickness. (82% of dogs with motion sickness also showed noise aversion, and 60% of dogs with noise aversion showed signs of motion sickness.)

3.3. This is the reason we must continue to focus on the whole animal in front of us and not try to separate behavior from medical problems- they are both problems in the body, and very often co-morbid or exacerbators of the other. We veterinarians are in the best position to treat all aspects contributing to the owner's behavioral complaint and therefore improve our patients' welfare and help preserve the human animal bond (HAB).

4. Noise aversion itself is generally a straightforward diagnosis based on descriptions or video of the patient demonstrating intense fear related behavior in response to specific noises, such as hiding, restlessness or vocalizing when the noise event occurs. However, sometimes the patient is presented for other behaviors that the owner is more likely to pick up on, such as housesoiling, destructive behavior or escape attempts.

5. Pathophysiology

5.1. Because this is a neurobiological event, the patient experiences the noise stimulus and the response starts in the locus coeruelus in the brainstem stimulating a physiologic stress response and consequently behaviors intended to help the patient gain safety in the face of the stimulus

(fight, flight, freeze, fidget.) Once the stimulus ends, the body and brain should return to its normal homeostatic setpoint via autoregulatory control.

5.2. However, with prolonged or repeated exposure without time to return to baseline, the patient's brain and body sensitize to the stimulus and the physiologic and behavioral responses become more and more intense with prolonged recovery and increased conditioning of contextual cues, now new triggers for the fear response.

5.3. Clinical Signs

5.3.1. Signs of physiologic response via the sympathetic nervous system include mydriasis, tachycardia, tachypnea, panting, piloerection, hypersalivation, trembling, urination, defecation and anal gland expression.

5.3.2. The behaviors observed that are the body's attempts to regain safety include hiding, avoidance, escape attempts, destructive behaviors associated with the former, pacing, whining, howling, barking, seeking attention or solace from the owner, inappetance, behavioral inhibition, freezing, and even learned helplessness in severe situations.

6. Treatment is often easiest to follow when split into immediate/ short term management and longer term interventions.

6.1. Short term management includes environmental control, counter conditioning, and behavioral medications.

6.2. Longer term intervention is all of the above with additional behavior modification and possibly other behavior medications added in.

6.1. Short Term Management:

6.1.1. Create a Safe Spot- this is generally an interior room, away from window, with comfortable bedding for the patient. Windows should be covered, the lights should be on, and ambient noise added (bathroom fan, white noise machine, music playing.) The patient should be introduced to this area outside of a noise event and be taught relaxed behaviors there using positive reinforcement. My rule of thumb is that the Safe Spot is prepared and ready to go when there is 40% or greater chance of inclement weather. Reimer (2020) (9) demonstrated that up to 69% of owners reported that teaching relaxation techniques had a positive effect on their pet during a noise event.

6.1.2. Behavior Modification- The owner should be advised to not reprimand or punish the patient for the behaviors demonstrated during a noise event. These behaviors are motivated out of fear and anxiety and adding more fear and anxiety is likely to make the problem worse and further damage the HAB. Comforting the patient during a fear response has historically been not recommended in the attempt to avoid inadvertent conditioning of a fear response via positive reinforcement. However, when one breaks down the types of learning that are occurring in these contexts, classical (Pavlovian) conditioning is more likely to be pre-eminent and even potentially over-ride operant conditioning, and it is almost impossible to reinforce a fear response (associated with high sympathetic nervous system arousal) with something pleasant (which by default if engaged in would stimulate the parasympathetic nervous system.) These two systems counter-balance each other, so if the patient is responding to petting, treats or play, it is more likely learning that the noise is not as frightening rather than their fear response being operantly reinforced. Therefore, the first and easiest behavior modification technique recommended is (classical) Counter conditioning. The goal is to change the emotional perception of the frightening event by pairing it with something pleasant. This is an unconscious physiologic response, stimulating the parasympathetic nervous system. Reimer (2020) (9) noted that over 70% of clients responded that counterconditioning was considered effective for reducing fear of fireworks in their dogs.

6.1.3. Medications - These can be used to help improve treatment success by increasing the number of patients that respond and the rate of response (5). This also helps to improve the quality of life for the patient and helps to preserve the HAB. This helps keep the pet alive and in the home. Gruen, et al. (2020) (6) reported that owners often feel frustration (42%), stress (46%), guilt (42%) and/ or sadness (75%) due to their dog's fear of noises.

6.1.3.1. Situational medications are typically fast acting within hours to minutes after a single dose and last for a finite amount of time, usually several hours. These are best administered prior to an anticipated noise event for optimal effect.

6.1.3.1.1. Examples of common medications of this classification include the benzodiazepines, trazodone, an SARI; gabapentin, pregabalin and imepitoin, historic antiepileptic medications; and clonidine, guanfacine and dexmedetomidine, alpha-2 agonists.

6.1.3.2. Sometimes a longer term chronic baseline antidepressant is used. These must be dosed every day for several weeks before beneficial effects are expected, but they also give consistent anxiety control for 24 hours, 7 days a week. These are often recommended during times of frequent and/ or unpredictable exposure.

6.1.3.2.1. Examples here include fluoxetine and sertraline, SSRIs; clomipramine, a TCA; or other classes such as venlafaxine, a SNRI.

These two groups of medication (situational and longer term baseline) can be combined together. Additional data on responses to commonly prescribed behavior medications can be found in Reimer (2020).

6.1.4. Regarding clinical updates, we will focus on dexmedetomidine (Sileo) and imepitoin (Pexion.)

6.1.4.1. Imepitoin (Pexion) was first reported for use in control of epilepsy in dogs, but then trialed for its anxiolytic properties. These are similar to the BZDs, as this medication is a central acting partial agonist of GABA-a receptor. Engel et al. (2019) (11) noted that the odds ratio of having a positive response for controlling noise phobia in dogs was 4.5 as compared to a placebo. However, at the doses used, which were the same as reported for epilepsy control, ataxia and sedation were common side effects. Additionally, this medication is labeled to be dosed orally every 12 hours starting two days prior to a noise event, and through the day of the event. A similar study was performed using lower doses for storm phobia in the US that were then titrated up for effect (12). Measures of fear (anxiety scores) were reduced with chronic daily imepitoin use during storm season, and side effects were less at lower doses, supporting the recommendation for lowered starting doses and titrating up to effect. Currently this medication is not available in the USA.

6.1.4.2. Sileo (dexmedetomidine oromucosal gel) is a novel administration system of this alpha-2 agonist via transmucosal absorption to avoid first pass metabolism. This allows a microdose to be delivered to target the dosing range ideal for anxiolysis but lower than sedation for most individuals. It is labeled to be given 1 hour prior to a noise event, at the first sign of noise, or when the signs of fear occur. It takes ~ 20-30 minutes to take effect and lasts for 2-3 hours in most dogs. It is labeled to be redosed every 2-3 hours as needed up to 5 times in a 24 hour period. In my experience, patients rarely need repeated dosing during a prolonged event, and if they do, one dose is usually sufficient. The greatest niche that this drug has is that it can be given after the fear response has already started and still have some beneficial effect on the patient. All of the other oral situational options have dramatically poorer efficacy if given after fear has already begun. An interesting phenomenon was noted after initial release where some dogs who received Sileo for repeated noise events began to have less and less of a fear response to their noise trigger. A few were even asymptomatic at the start of the next noise season. This suggested true drug desensitization. Gruen, et al. (2020) (6) investigated this further, looking at the behavioral response over 10 noise events. 50% of the dogs received Sileo

for all 10 noise events, and 50% received Sileo for six to nine events. Within this, for each subsequent event, the odds that the owner would administer Sileo decreased by 25%, and 50% of the dogs were perceived by their owners to not need Sileo for at least one event.

6.2. Longer Term Interventions:

The goal of this is to help to reduce the intensity of the fear response with each successive season of noise using the steps in the Short Term Management plan in addition to some additional behavior modification and potentially other medications.

6.2.1. Systematic desensitization and counter conditioning is the mainstay of this treatment. However, it is crucial that this step not be attempted during the noise event season. For example, in the Midwest and Mid-Atlantic region of USA, this should only be performed during winter months when storms are not expected, or outside of football season if the fear is of fireworks.

6.2.1.1. The patient is exposed to a recording of the noise trigger at volumes low enough they are almost imperceptible. They are then given time to habituate to the sound at that volume. When they are not reacting with fear, and emotionally they are relaxed, the volume can be increased by one notch. This is gradually increased, over several sessions, as the dog remains relaxed until the volume is at the same level as a real noise event. The sound can be made more realistic by using surround sound and making a recording of the noise event in the patient's environment. Not all dogs will respond to the recording, so this strategy will not work for all patients.

6.2.2. The process can be sped up by pairing systematic desensitization with classical counter conditioning and operant counter conditioning (response substitution).

6.2.2.1. Classical counter conditioning is used by pairing each clap of thunder or pop of firework with a high value food treat in the recording.

6.2.2.2. Operant counter conditioning is added by asking the patient to settle in a relaxed down and rewarding this behavior while the recording is playing. This was reported to be effective in ~ 54% of patients in Reimer's 2020 study (9).

This exercise is also limited in that the patient may only learn that the stimulus is less frightening in a specific location or context, because this type of learning can be difficult to generalize. Baseline medications can be added at this stage to help facilitate faster learning and giving a more realistic starting point, especially if the patient also experiences panic and/or generalized anxiety.

6.2.3. Other tools such as wearables and supplements have shown lower response rates in a variety of studies, although generally they also have lower risk to the patient. In Reimer (2020), (9) these were found to have a rate of ~ 27-35% effectiveness. However keep in mind that a standard rate of response with placebo is expected to be ~ 37% (13).

6.2.4. Calmer Canine Loop by Assisi (Pulsed electromagnetic frequency - PEMF- therapy):

This therapy has been around for a while in other species, especially humans and horses, and has historically been particularly focused on musculoskeletal pain such as fractures, wound healing, edema, post-operative and osteoarthritic pain.

It has been used to treat refractory anxiety in people with success. However, it has not been as thoroughly investigated in dog. The Calmer Canine sends electromagnetic pulses of a specific frequency that targets the amygdala in the brain. The hypothesis that some of the maladaptive fear response is due to inflammation in that part of the brain, and this treatment modality is intended to help reduce inflammation. A case series treating canine separation anxiety demonstrated all enrolled patients improved by 4 weeks, and signs in more than half of patients resolved by 6 weeks (14).

A placebo controlled clinical trial by Pankratz et al. (2019) (15) demonstrated that at 6 weeks, 30% of the dogs in the control group and 55% of dogs in the treatment group were reported as successes for separation related disorders. Both of these studies were focused on separation related distress. Though there are not yet studies of its use in noise aversion, clinically it has been used successfully in several cases for noise aversion treatment.

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