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Canine phobia

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Abstract: Phobia in dogs is one of the most frequent and difficult to diagnose behavioral pathologies; it is often confused with fear and anxiety, also because in some cases multiple pathologies may coexist. Furthermore, a fundamental role is played by the owner who often fails to understand their pet's behavior. Defining the type of pathology we are facing is the initial step from which to start to carry out an adequate therapeutic plan. The therapeutic aspect is also complex; it essentially consists of two parts: behavioral modification and a supportive drug therapy.

It is also essential to have a good owner's compliance.

Key Words: dog, phobia, behavior, noise.

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Introduction

"The fear emotion is highly conserved across species and evolved to detect threats and initiate the behavioral and physiologic response needed to survive them" (Ballantyne, 2018). This emotional response can be unconditioned or conditioned (Rosen, 2004). The unconditioned fear, also called innate fear, appears without learning (Marks, 2002). On the contrary, the conditioned fear, needs learning process. Both responses have a survival-related role in threatening situation triggering a range of defensive behaviors (Steimer, 2002).

The term "fear" is used interchangeably with "phobia" and "anxiety", but they refer to different emotional states and may have different neurobiological mechanisms (Ogata, 2016).

Fear is an emotional, behavioral, and physiologic response to a stimulus that the animal perceives as potential threat (Ballantyne, 2018). Anxiety is anticipation of a danger or threat and the stimulus for the response is not always identifiable or present (Ballantyne, 2018). Phobia has been defined as "an intense fear response that is out of proportion/excessive for the degree of threat in a given situation" (Beaver, 1999). The phobic response prevents the animal from adapting to the surrounding world since the behavioral reaction is elicited by stimuli which are not necessarily dangerous (Colangeli & Giussani, 2004).

Furthermore, the phobic state does not decrease with a gradual and controlled exposure over time to the triggering stimulus, but it increases in intensity with manifestations of panic and catatonia (Pageat, 1999); therefore, the evoked emotional state remains even after the stimulus has been removed even in the absence of the triggering stimulus (Palestrini, 2009).

Signs of fear in dogs include avoidance or hiding, lowered body posture with flat-tened ears and low tail position, pacing or excessive motor activity, hypervigilance, seeking out contact with humans or other animals, and aggression (Ballantyne, 2018). Physiological responses include tachycardia, hypersalivation, urination (Sherman, 2008; Blackwell et al., 2013; Dale et al., 2010;

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McCobb et al., 2001), defecation, mydriasis and anorexia are also present (Ballantyne, 2018).

Based on their origin, as in Human Medicine (American Psychiatric Association, 1994), phobias can be divided into ontogenetic and post traumatic phobias (Pageat, 1999).

Ontogenetic phobias have as a trigger a subject/object/situation that the animal has never encountered during the socialization period. They are therefore a consequence of inadequate behavioral development (Pageat, 1999; Gazzano et al., 2008).

The establishment of phobic behavior occurs through specific processes such as sensitization, anticipation and generalization (Pageat, 1999).

Sensitization is a learning process, consisting of a progressive increase of specific reactions to a stimulus. On the contrary, habituation consists in diminishing the response towards the stimulus; this process can be utilized during some stimuli introduction training technique (e.g. muzzle) presenting the stimulus with a low intensity and by providing to dog the possibility to avoid the stimulus itself (Pageat, 1999).

According to the French approach to behavior counseling (Pageat, 1999; Colangeli & Giussani, 2004), three stages of phobia are distinguished: simple phobia, generalized (or complex) phobia and pre-anxious state.

Simple phobia is the condition in which a single stimulus or more similar stimuli (generally, of a visual or acoustic nature) are clearly identifiable. This stage is characterized by: tachycardia, tachypnea, mydriasis, emotional peeing, trembling, attempts to escape, to avoid the stimulus, threats at a distance alternating with short exploratory phases, aggression (Colangeli & Giussani, 2004; Pageat, 1999).

In this phase the animal is still able to present and implement adaptive avoidance strategies. (Boyd et al., 2004).

The evolution of simple phobia can be categorized into three distinct circumstances (Overall, 2001):

- Spontaneous healing due to habituation to the phobogenic stimulus.
- Instrumentalization of aggressive behavior.
- Exacerbation of the phobic responses due to sensitization to the phobogenic stimulus.

Generalized phobia is generally considered an evolution of the simple phobia, but it can occur suddenly, without the first stage, as it happens in post-traumatic phobia (Colangeli & Giussani, 2004). This stage is the result of emotional anticipation process and during this phase the phobogenic stimuli are no more clearly recognizable.

Generalized phobia is characterized by increased activity of the dopaminergic system with a marked avoidance behavior and concomitant neurovegetative manifestations (Colangeli & Giussani, 2004; Pageat, 1999). The animal's avoidance behavior leads to a total isolation from reality, making it phobic towards any stimulus associated with the initial triggering stimulus (Boyd et al., 2004).

The evolution of generalized phobia can lead to anxiety, instrumentalization of the aggression, or pre-anxious state; rarely a spontaneous remission can occur (Pageat, 1999).

Anxiety is an emotional state presenting neurovegetative symptoms with activation of the serotoninergic system. There is a state of almost persistent fear determined by the anticipation and generalization of the phobogenic stimulus, which lead the dog not to leave the place considered "safe" (Colangeli & Giussani, 2004; Pageat, 1999).

Research on canine phobia

In canine behavioral medicine, several studies have been carried out on phobia, especially about the predisposing factors and the genetic predisposition.

The stimuli that are most often able to give rise to a phobia are the auditory ones (fireworks,

thunder, gunshots and engine noises) (Levine, 2009). From a recent study (Iimura et al., 2007) conducted on 2577 dogs it emerged that the fireworks phobia was the most represented (32%) followed by the thunderstorm's phobia (31%).

It should be considered that the noise reactivity is often confused with anxiety; in fact, when the event occurs in the absence of the owner, it is not easy to determine, based on symptoms (e.g. inappropriate eliminations), what is the emotional response of the dog. Furthermore, in some cases fear and anxiety can coexist (Sherman & Mills, 2008).

Regarding the phobia of thunderstorms, a study conducted on 781 dogs showed that 49% of subjects exhibited phobic behavior during thunderstorms; neutered dogs were more phobic (38%) unlike not neutered subjects (26%), with a higher incidence in castrated females (58%). In addition, the incidence of thunderstorm phobia was higher in dogs adopted from a kennel (43%) or found abandoned (44%), especially within the first year of life (34%). Finally, to underline a possible social contagion of the phobia, 36% of phobic dogs lived with one or more dogs, compared to 27% who lived without other animals in the house (Mengoli et al., 2012).

Regarding the breed, a study conducted on 17 dog breeds, for a total of 5257 dogs, showed significant differences between the Norwegian Buhund, Soft Coated Wheaten terrier, Lagotto Romagnolo which showed a greater noise reactivity compared to Boxer, Chinese Crested and Great Dane. Also, in this research, females and castrated dogs were more insecure (Storengen & Lingaas 2015).

In other studies, it emerges that shepherd dogs (German shepherds, Australian shepherds, Border collies) have a high incidence of developing aversion to noise (Ballantyne, 2018; McCobb et al., 2001; Whal, 2008).

In a study conducted in 2016 (Overall et al., 2016), 3 breeds of shepherd dogs (Australian shepherds, Border collie and German shepherds) were observed. Owners were given a questionnaire about dog aversion to specific noisy stimuli (thunder, gunfire, fireworks and others). Reactivity to noise was found to segregate in some family lines. The presence and intensity of reactivity as represented by Anxiety Intensity Rank scores varied by breed but only with age. Source and / or purpose of dog may also affect severity of affliction.

In a study performed by Branson (Branson, 2008), the association between paw preference, as a measure of brain lateralization, and noise phobia in the domestic dog was investigated. A significant and positive correlation was found between the questionnaire responses on the dogs' reactivity to thunderstorms and fireworks and direct observations of the dogs' behavior in response to audio playback of the sounds of thunderstorms, fireworks, and white noise. Ambilateral dogs showed fear responses compared to dogs with a significant left-paw or right-paw preference, indicating that non-lateralization of neural functions may be associated with intense emotional responses.

As regarding sex and age, it has been showed that the incidence of phobia is higher in females (24.9%) compared to males (21.2%) (Storengen & Lingaas, 2015); the incidence of noise phobia increases with increasing age (Storengen & Lingaas, 2015; Blackwell et al., 2013; Ballantyne, 2018).

In addition, dogs living with their own breeders develop noise sensitivity more rarely than dogs that are adopted or have changed owners. This indicates the importance of the environment where the puppy's first stages of development take place and the correct exposure to certain stimuli, especially acoustic (Blackwell et al., 2013; Sherman & Mills, 2008). Moreover, a social contagion of the phobia is also possible: a research on 283 dog owners has shown the existence of social transmission in 22.6% of dogs (Sherman & Mills, 2008).

Finally, a comorbidity between noise phobia and separation anxiety may be present (Overall, 2001).

Prevention and therapy of phobia

In prevention, the puppy socialization period is the most critical for the development of dog's behavioral pattern and it is precisely in this period that as many stimuli as possible must be correctly presented to the puppy. It is therefore recommended to carry out socialization classes (puppy party and puppy class), interspecific social contacts with a high variability of people, correct exposure to all kinds of noise, and basic education techniques.

The treatment of phobia in dogs proposed by Karen Overall (2001) includes:

- General clinical visit to exclude systemic metabolic diseases
- Identification of phobogenic stimulus or stimuli
- Behavior modification program
- Pharmacological support to the behavior modification program

Before implementing a behavioral modification therapy, the animal must be "put in safety", that is, measures must be implemented to prevent the disease from worsening further (Shaw & Martin, 2016).

For example, not leaving the animal alone in unfamiliar environments during thunderstorms or outbursts of fireworks; darken glass to prevent the association between the lights of fireworks and the noise; try to distract the dog and not punish him; make comfortable the place considered by the animal as a "safe place" with kennels, blankets, pheromones (Bowen, 2005).

Among the various behavioral modification techniques, desensitization and counterconditioning are the most used strategies for treating dog phobias.

A behavioral modification technique that must be avoided is "flooding", which consists in exposing the animal to the phobogenic stimulus at a high intensity, with no possible escape routes, maintaining exposure until the fear response disappears (Young, 1982; Shaw & Martin, 2015). This technique is very traumatic from a psychological point of view and often causes an increase in fear and phobia (Levis, 1980; Rachman, 1974; Rachman & Levitt, 1988; Shaw & Martin, 2015).

Drug therapy is used to support behavioral therapy (Overall, 2001). The drugs used have the purpose of carrying out a "pharmacological desensitization" when the intensity of the stimulus is too high or there are too many stimuli that do not allow the control of the animal; in this way the implementation of the behavior modification program is made possible, also increasing the compliance of the owner who finds a less stressful starting point (Shaw & Martin, 2015).

Before implementing a drug plan, it is recommended to perform a clinical examination, urinalysis, a complete blood count, chemistry (basic metabolic) panel and a thyroid panel. Moreover, there must be an accurate diagnosis or in any case a list of differential diagnoses (Overall, 2004; Landsberg et al., 2013).

Based on drug mechanism of action, protocols can be divided into short-term (they help the subject to endure a limited phobogenic stimulus over time) and long-term therapy (generally lasting weeks or months in support of behavioral modification techniques) (Bowen & Heat, 2005).

The classes of drugs most frequently used in behavioral medicine during phobia are (Bowen & Heat, 2005; Overall, 2001; Shaw & Martin, 2015):

- Neuroleptic drugs: Acepromazine → short term
- Anxiolytics: Benzodiazepines → short term
- Alpha2-agonists (Clonidine, Dexmedetomidine) → short term
- Antidepressants: tricyclics (Clomipramine), selective serotonin reuptake inhibitors (Fluoxetine), monoamine oxidase inhibitors (Selegiline), serotonin antagonist and reuptake inhibitors (Trazodone) → long term

Acepromazine is mainly used for the sedative effect characterized by reduction of motor activity and reactivity due to blocking of dopamine D2 receptors (Shaw & Martin, 2015; Bowen & Heat, 2005; Overall, 2001). The anxiolytic effect remains mild because the animal remains mentally active and alert. Moreover, Acepromazine could increase the fear response since this drug makes

the animal unable to avoid/escape the stimulus. Possible side effects are hypotension, excessive sedation and possible lowering of the seizure threshold (Shaw & Martin, 2015; Overall, 2001). Acepromazine is not recommended in epileptic, brachycephalic, respiratory / hepatic and renal patients (Bowen & Heat, 2005). The recommended dose is 0.55-1.1 mg / kg po, 0.055-0.11 mg / kg IM, SC, IV (Overall, 2001).

The Italian Association of Veterinary Experts in Animal Behavior (A.V.E.C.) has recently published a recommendation against the use of acepromazine as a therapy for noise phobia since it increases the sensitivity of dogs to noise and it alters the dog's ability to process and understand the noise and its response (Piotti et al., 2019).

Benzodiazepines enhance the effects of GABA inhibitors, binding the GABA receptor (Mayes, 1979; Shaw & Martin, 2015), resulting in a dose-dependent sedative, anxiolytic, muscle relaxant and antiepileptic effect. Generally, benzodiazepines are administered 3-4 hours before the phobogenic event and, when necessary, repeated every 3-6 hours (Overall, 2001). Otherwise, in long-term therapy, a weaning plan from the drug is necessary before the suspension, i.e. reducing the dose by 25-30% every week (Shaw & Martin, 2015; Schwartz, 2005).

The possible side effects there are: amnesia, paradoxical effect as excitability and hyperactivity, disinhibitory effect and therefore possible exacerbation of aggression (Shaw & Martin, 2015; Bowen & Heat, 2005; Overall, 2001). Flumazenil can be used as antidote (Overall, 2001).

In a recent study, the anxiolytic effect of the anticonvulsant drug Imepitoin, partial agonist for the benzodiazepine binding site on the GABA receptor, was evaluated (Engel et al., 2018; Engel et al., 2019; McPeack & Mills, 2017). The authors concluded that Imepitoin can be used as an anxiolytic drug (at a dosage of 10-30 mg / kg BID) without the side effects of benzodiazepines, such as sedation and disinhibition.

Clonidine is commonly used as an anxiolytic drug due to the agonism on the pre-synaptic α2 receptor. Peripheric effects of the Clonidine are hypotension, bradycardia, reduction of intestinal peristalsis, reduction of insulin release, increased diuresis. Recommended dosage: 0.015 mg / kg / day (Habran, 2005; Landsberg et al., 2013).

Recently, dexmedetomidine, an Alfa2 agonist more selective than clonidine, was shown to be effective on noise-associated acute anxiety and fear in dogs (Korpivaara et al., 2017).

Tricyclic antidepressants (TCAs) inhibit the reuptake of norepinephrine and serotonin, increasing the synaptic concentrations of these neurotransmitters. The most used TCA is clomipramine, particularly to treat noise phobias, anxiety and compulsive disorders (i.e. licking dermatitis) (Bowen & Heat, 2005; Overall, 2001). These drugs also have adrenergic effects (sedation or syncope), anticholinergic effects (dry mouth, mydriasis, constipation, urinary retention, tachycardias and arrhythmias) (Shaw & Martin, 2015; Overall, 2001). Moreover, it was shown that clomipramine can affect the thyroid function (Crowell-Davis & Murray, 2006). The systemic effects must be closely monitored.

TCAs should not be associated with monoamine oxidase inhibitors (MAOIs) and at least fourteen days of suspension are necessary when switching from a TCA to a MAOI. The recommended dosage of clomipramine is 1 – 2 mg/kg q12h (Landsberg, 2013). The effects of this drug normally appear after 4-6 weeks from the beginning of treatment (Overall, 2001) and a pharmacological weaning is necessary in suspending the therapy (Shaw & Martin, 2015).

Selective serotonin reuptake inhibitors (SSRIs) inhibit the reuptake of serotonin at the synaptic level. Three/four weeks could be required to have the desired therapeutic effect and the interruption requires a pharmacological weaning program. SSRIs should not be associated with MAOIs but at least wait five weeks of suspension are necessary before introducing a MAOI. Possible side effects are dysorexia, nausea, vomiting, sedation, emotional instability and impulsivity mainly in the first days of administration due to a 5HT1 and 5HT2 receptor down regulation. The most widely used active substance is fluoxetine, at a dosage of 1-2 mg/kg/day in a single administration (Landsberg, 2013).

MAOIs increase the dopamine concentration at the synaptic level by inhibiting monoamine oxidase. The most used drug in behavioral medicine is Selegiline. It is used both for its anxiolytic effects and for its neuroprotective effects by reducing oxidative damage; for this last reason it is administered to treat animals affected by Cognitive Dysfunction Syndrome. At high dosages, due to the increased concentration of dopamine, stereotyped behaviors can occur; furthermore, an increase in motor activity may occur due to the production of intermediate metabolites with amphetamine-like effects; therefore, it is recommended to take it in the morning. Vomiting, diarrhea, disorientation and restlessness can occur as side effects. It is important to remember that it should not be associated with TCAs and SSRIs otherwise the serotonin syndrome could occur when the concentration of serotonin at the central level reaches toxic effects. Symptoms of this syndrome are nausea, tremors, hypersalivation, muscle rigidity, hyperthermia up to leading to seizures, coma and death (Shaw & Martin, 2015; Overall, 2001).

Recently, the effectiveness of Trazodone, a serotonin antagonist and reuptake inhibitor, was tested to treat anxiety (Gruen & Sherman, 2008) and thunderstorm phobia in dogs (Ogi, 2018).

In addition to the classes of drugs mentioned above, some research has evaluated the effectiveness of synthetic pheromones, similar to the appeasing pheromones produced by the sebaceous glands of the bitch's intermammary sulcus during lactation.

Their calming properties have been demonstrated during travel, cage or kennel containment, veterinary visits, fireworks or thunderstorm, introduction of puppies into new environments, separation from the owner (Mills et al., 2003; 2006; Tod et al., 2005; Sheppard et al., 2003; Levine et al., 2007; 2008; Gaultier et al., 2008; 2009; Estelles, 2006).

In a study was examined the effectiveness of 2 different dosage levels of a fish hydrolysate, a natural supplement derived from fish protein, in reducing fear and anxiety in beagle dogs. The test compound showed some effectiveness in reducing emotional response to thunder and in reducing the cortisol levels (Landsberg et al., 2015).

In association with behavioral therapy other substances such as L-theanine (Michelazzi et al., 2010; Araujo et al., 2010) and alpha-casozepine, have also shown anxiolytic effects (Beata et al., 2007).

Diet manipulation could be used to produce a rise in plasma and, consequently, intracerebral tryptophan concentrations, leading to the synthesis and release of a greater amount of serotonin. This could have positive effects on behavioral problems resulting from an altered function of serotoninergic systems (Gazzano et al., 2018; Gazzano et al., 2019).

Finally, the effectiveness of the Anxiety Wrap, a product designed to apply pressure to a dog's torso, on canine thunderstorm phobia was investigated by comparing owner-reported Thunderstorm Anxiety Scores before and after the use of this product. The mean Thunderstorm Anxiety Score associated with the fifth use of the Anxiety Wrap was 47% lower than the mean anxiety score that was generated before the use of the Anxiety Wrap ($P = 0.001$) (Cottam et al., 2013).

Conclusion

Phobia in dogs is one of the most frequent and most difficult to diagnose behavioral pathologies; it is often confused with fear and anxiety, also because in some cases multiple pathologies may coexist. Furthermore, a fundamental role is played by the owner who often fails to interpret their pet's behavior well. Defining well the type of pathology we are facing is the initial step from which to start to carry out an adequate therapeutic plan.

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La fobia nel cane

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Sintesi

La fobia nel cane è una delle patologie comportamentali più frequenti e di più difficile diagnosi: essa è spesso confusa con la paura e l'ansia, anche perché in alcuni casi possono coesistere patologie multiple.

Un ruolo fondamentale è inoltre svolto dal proprietario che spesso non è in grado di intrepretare nel modo corretto il comportamento del proprio animale.

Il primo passo per instaurare un piano terapeutico adeguato è quindi quello di definire correttamente il tipo di patologia.

L'approccio terapeutico è assai complesso e consiste essenzialmente di due parti: interventi di modificazione comportamentale e terapia farmacologica di supporto. È anche essenziale riuscire a stabilire un'efficace alleanza terapeutica con il proprietario.

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