Frequency of nonspecific clinical signs in dogs with separation anxiety, thunderstorm phobia, and noise phobia, alone or in combination

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Objective—To determine the frequency of nonspecific clinical signs in dogs with separation anxiety, thunderstorm phobia, noise phobia, or any combination of these conditions and determine whether these conditions are associated in dogs.

Design—Case series.

Animals—141 dogs.

Procedure—Diagnoses were established using specific criteria. Owners of dogs completed a questionnaire on how frequently their dogs exhibited destructive behavior, urination, defecation, vocalization, and salivation when the owners were absent and the types and frequency of reactions to thunderstorms, fireworks, and other noises.

Results—Associations of the 3 conditions and of various nonspecific clinical signs within and between diagnoses were nonrandom. The probability that a dog would have separation anxiety given that it had noise phobia was high (0.88) and approximately the same as the probability it would have separation anxiety given that it had thunderstorm phobia (0.86). However, the probability that a dog would have noise phobia given that it had separation anxiety (0.63) was higher than the probability that it would have thunderstorm phobia given that it had separation anxiety (0.52). The probability that a dog would have noise phobia given that it had thunderstorm phobia (0.90) was not equivalent to the converse (0.76).

Conclusions and Clinical Relevance—Results suggested that dogs with any of these conditions should be screened for the others. Interactions among these conditions are important in the assessment and treatment of dogs with > 1 of these conditions. Responses to noise were different from those to thunderstorms, possibly because of the unpredictability and uncertainty of thunderstorms. (*J Am Vet Med Assoc* 2001;219:467–473)

Separation anxiety is one of the most common and devastating behavioral conditions in pet dogs. It has been estimated, for instance, that at least 14% of dogs examined at typical veterinary practices in the United States have signs of separation anxiety.[1] Unfortunately, as is true for most behavioral conditions, signs associated with separation anxiety are nonspecific, making an accurate diagnosis difficult. Dogs with separation anxiety usually destroy objects in the house, destroy sections of the house, or urinate, defecate, vocalize, or salivate when they are left alone.[2-4] Dogs with profound separation anxiety can be left alone for no more than minutes before they begin to panic and exhibit the behaviors associated with separation anxiety. In the absence of treatment, affected dogs are often relinquished to a humane society or shelter, abandoned, or euthanatized.[5,6]

Elimination, destruction, and vocalization are the most obvious and, hence, the most commonly reported behaviors associated with separation anxiety.[2,3] It is important, however, to realize that clients complain about these behaviors most often because they are easy to recognize and cause problems for the client themselves. Dogs that exhibit less obvious signs of distress such as withdrawal, inactivity, salivation, whimpering (or louder vocalizations if there are no nearby neighbors), and pacing may not be identified as having separation anxiety, even though they are equally affected, and owners of such dogs seldom seek treatment for their pets, because the dogs' behaviors are not problems for the clients. Including dogs with these less obvious signs, the population of dogs with separation anxiety, although unknown, is likely to be quite large, and all dogs with separation anxiety can benefit from treatment.

Noise and thunderstorm phobias are among the most commonly recognized disorders associated with panic or phobic responses in dogs, although no data exist on relative incidences of these problems. In our experience, dogs with signs of separation anxiety frequently also have signs of noise phobia or thunderstorm phobia. This observation suggests 4 avenues of investigation that merit exploration: whether the development or expression of noise phobia, thunderstorm phobia, and separation anxiety are codependent, with the extent to which they covary suggesting differences in mechanisms for thresholds of anxiety-related disorders; whether reactions to noises may predispose dogs to other anxiety-related conditions; whether the interactions among these disorders may have time penetrance, such that the longer a dog has been affected with 1 of these conditions, the more at risk it may be either for a more complex form of that condition (eg, a greater number or intensity of signs) or for other anxiety-related conditions; and whether the incidence and comorbidity (ie, the cooccurrence of separate, but possibly related, conditions) of these conditions may be underestimated, particularly in the absence of a questionnaire or evaluation tool that systematically explores all responses to anxiety-related situations in all dogs.

Specific criteria for the diagnosis of noise phobia, thunderstorm phobia, and separation anxiety in dogs have been published.[7] The use of such criteria allows examination of the distribution of nonspecific signs of anxiety-related disorders independent of diagnosis.[8-10] Nonspecific signs may be uniquely important for assessing psycho-pathologically distinct groups,[11] and an improved understanding of the intensity, duration, and age of onset of certain signs may improve our understanding of the variable behavioral phenotypes associated with these conditions.[12] The use of explicit diagnostic criteria is key to ensuring that observed heterogeneity is not an artifact of careless classification. Use of explicit diagnostic criteria is also a powerful tool for examining phenotypes and endophenotypes (ie, components of complex phenotypes) and avoids the underdiagnosis of comorbid conditions that is prevalent when somatic signs are used instead of independent diagnostic criteria.[9,10] This type of approach is essential for elucidating any underlying genetic susceptibility for behavioral or psychiatric conditions.[10] In cases where there are strong genetic influences on different facets of temperamental expressions such as fearfulness, the biological correlates of the behaviors can be considered as related endophenotypes for anxiety.[13,14]

The purposes of the study reported here were to evaluate the covariation (ie, the nonrandom association) of nonspecific signs of separation anxiety, thunderstorm phobia, and noise phobia and determine the comorbidity of these conditions in dogs.

Materials and Methods

For the purposes of this study, the necessary conditions for a diagnosis of separation anxiety[7] were physical or behavioral signs of distress exhibited by the dog only during an actual absence of the owner (ie, when the owner is not at home) or a virtual absence of the owner (ie, when the owner is home, but the dog is denied access to the owner by a door or some similar barrier). Sufficient conditions for a diagnosis of separation anxiety were consistent intensive destruction, elimination, vocalization, or salivation exhibited only during an actual or virtual absence of the owner, with these behaviors most severe close to the time of separation and many anxiety-related behaviors (eg, autonomic hyperactivity, increased motor activity, and increased vigilance and scanning) becoming apparent as the owner exhibits behaviors associated with leaving.

Necessary and sufficient conditions for a diagnosis of noise phobia[7] were sudden profound nongraded extreme responses to noise that were manifest as intense active avoidance, escape, or anxiety behaviors associated with activities of the sympathetic branch of the autonomic nervous system. Such behaviors could include catatonia or mania concomitant with decreased sensitivity to pain or social stimuli. Repeated exposure resulted in an invariant pattern of response.

Necessary and sufficient conditions for a diagnosis of thunderstorm phobia[7] were sudden profound nongraded extreme responses to thunderstorms or any aspect of thunderstorms (eg, wind, noise, lightning, changes in barometric pressure, rain, darkness, changes in ozone concentration) that were manifest as intense active avoidance, escape, or anxiety behaviors associated with activities of the sympathetic branch of the autonomic nervous system. Such behaviors could include catatonia or mania concomitant with decreased sensitivity to pain or social stimuli. Repeated exposure resulted in an invariant pattern of response.

The present study was conducted in 2 parts. In the first part, medical records of 51 dogs that met the stated criteria for separation anxiety, noise phobia, or thunderstorm phobia and in which the diagnosis had been made during a 6-month period in 1997 were reviewed. Information on presence and frequency of attendant nonspecific signs was collected. The Pearson product-moment correlation method was used to identify significant pair-wise correlations for suites of behaviors and nonspecific signs.

Since 1998, owners of all dogs examined at the Veterinary Hospital of the University of Pennsylvania Behavior Clinic have been asked to complete a questionnaire[a] on behaviors exhibited by their dogs during actual and virtual absences of the owners. The questionnaire asked owners to indicate whether their dogs exhibited any of 5 behaviors (destructive behavior, urination, defecation, vocalization, and salivation) during actual or virtual absences of the owners (yes, no, unknown) and, if their dogs did exhibit any of these behaviors, to indicate how frequently they did so (100% of the time, < 100% but > 60% of the time, 40 to 60% of the time, > 0 but < 40% of the time). In addition, the questionnaire asked owners to indicate whether their dogs reacted to thunderstorms, fireworks, or other noises (yes, no, unknown) and, if their dogs did react, how frequently they did so (100% of the time, < 100% but > 60% of the time, 40 to 60% of the time, > 0 but < 40% of the time) and what responses they exhibited (salivating, defecating, urinating, destroying, escaping, hiding, trembling, and vocalizing).

In the second part of the present study, records for 141 dogs (81 males and 60 females) examined between January 1999 and January 2000 that were determined to have separation anxiety, noise phobia, or thunderstorm phobia and for which responses to at least 1 of the items on the screening questionnaire were positive were reviewed. Ambiguous data or client responses that were based on only a singular occurrence of a particular behavior were excluded from the relevant analyses.

Independence of diagnoses and nonspecific signs (ie, client responses to the screening questionnaire) was evaluated by use of **Cochran-Mantel-Haenszel (CMH)** χ^2 tests and by comparing results of these tests with results for a series of 1,000 CMH tests applied to randomized data sets generated by Monte Carlo simulation assuming complete independence of all diagnoses and client responses. For all analyses, values of $P < 0.05$ were considered significant.

Results

In the first part of the study, 25 dogs had separation anxiety alone, 5 dogs had noise or thunderstorm phobia alone, and 21 dogs had separation anxiety and noise or thunderstorm phobia. The probability that a dog had separation anxiety given that it had noise or thunderstorm phobia [P(SA|N)] was 0.81 [(21/51)/(26/51)], whereas the probability that a dog had noise or thunderstorm phobia given that it had separation anxiety [P (N|SA)] was 0.46 [(21/51)/(46/51)]. Frequencies with which dogs exhibited nonspecific anxiety-related signs (always [100% of the time], mostly [< 100% but > 60% of the time], consistently [40 to 60% of the time], seldom [< 20% of the time], and never [0% of the time]) were not independent of the nonspecific signs or of the specific condition, regardless of whether dogs had only 1 or multiple conditions. Owners of dogs that always reacted in situations associated with noise phobia were more likely to

Table 1—Frequency of various nonspecific clinical signs in dogs with separation anxiety alone, noise or thunderstorm phobia alone, or separation anxiety and noise or thunderstorm phobia

Frequency	Percentage of dogs					
	Urination	Defecation	Destruction	Vocalization	Salivation	Reaction to noises
Dogs with separation anxiety alone (n = 25)						
Always	4	4	8	58	21	4
Mostly	24	8	64	25	8	4
Consistently	16	24	8	8	8	0
Seldom	12	12	4	0	0	4
Never	44	52	16	8	63	88
Dogs with noise or thunderstorm phobia alone (n = 5)						
Always	0	0	0	0	0	100
Mostly	0	0	0	0	0	0
Consistently	0	0	0	0	0	0
Seldom	20	20	0	0	0	0
Never	80	80	100	100	100	0
Dogs with both (n = 21)						
Always	14	10	29	63	43	86
Mostly	10	5	38	0	5	5
Consistently	10	10	5	0	14	9
Seldom	18	24	19	16	0	0
Never	48	52	9	21	38	0

Always = 100% of the time. Mostly = More than 60% of the time. Consistently = 40 to 60% of the time. Seldom = Less than 20% of the time. Never = 0% of the time.

indicate that their dogs always destroyed, urinated, vocalized, or salivated than were owners of dogs that reacted less often in such situations. Dogs that had noise phobia in addition to separation anxiety had more severe signs (ie, higher frequency designations) for all of the nonspecific signs than did dogs that had separation anxiety alone (**Table 1**). Correlation analysis indicated that the following pairs of signs occurred together more frequently than would be expected: defecation and urination ($P < 0.001$), vocalization and destruction ($P = 0.012$), and salivation and vocalization ($P = 0.018$). On the other hand, the reaction to noise and vocalization occurred together less frequently than would be expected ($P = 0.005$).

Of the 141 dogs included in the second part of the study, 41 (20 males and 21 females) had separation anxiety alone, 1 (female) had thunderstorm phobia alone, 1 (female) had noise phobia alone, 7 (4 males and 3 females) had separation anxiety and thunderstorm phobia, 21 (15 males and 6 females) had separation anxiety and noise phobia, 10 (4 males and 6 females) had thunderstorm phobia and noise phobia, and 60 (38 males and 22 females) had all 3 conditions. Males and females did not differ significantly in regard to the relative frequencies of these conditions (Fisher exact test; $P = 0.22$); therefore, data for males and females were combined for all subsequent analyses.

For these dogs, the observed frequency of separation anxiety alone was significantly higher than expected if these conditions had been completely independent (likelihood ratio χ^2 test; $P < 0.05$; **Fig 1**). In addition, the observed frequencies of noise phobia alone, of separation anxiety in conjunction with thunderstorm phobia, and of separation anxiety in conjunction with noise phobia were all significantly lower than expected if these conditions had been completely independent. On the other hand, the frequency of all 3
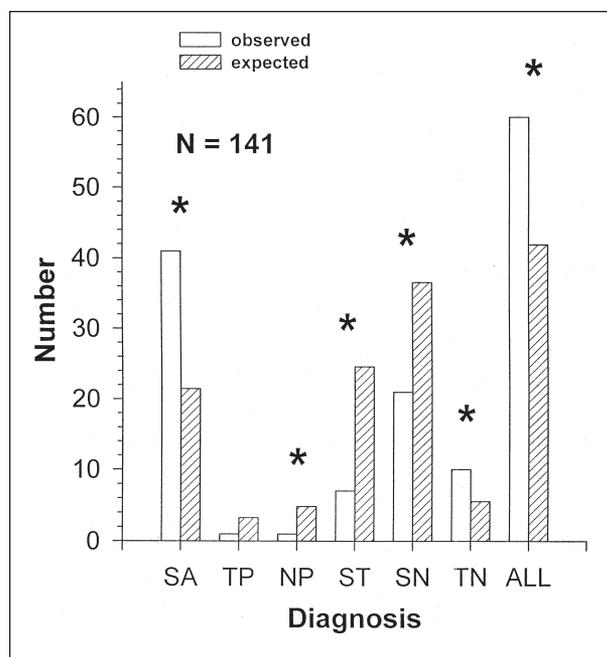

Figure 1—Observed and expected numbers of dogs with separation anxiety alone (SA), thunderstorm phobia alone (TP), noise phobia alone (NP), separation anxiety and thunderstorm phobia (ST), separation anxiety and noise phobia (SN), thunderstorm phobia and noise phobia (TN), or separation anxiety, thunderstorm phobia, and noise phobia (ALL) in a study of 141 dogs with behavioral disorders. The distribution of expected numbers was obtained by analyzing the results of 1,000 Monte Carlo simulations, assuming complete independence among SA, TP, and NP. *Observed frequency was significantly different ($P < 0.05$) from the expected frequency.

conditions was significantly higher than expected if these conditions had been completely independent. Therefore, the null hypothesis that individual diag-
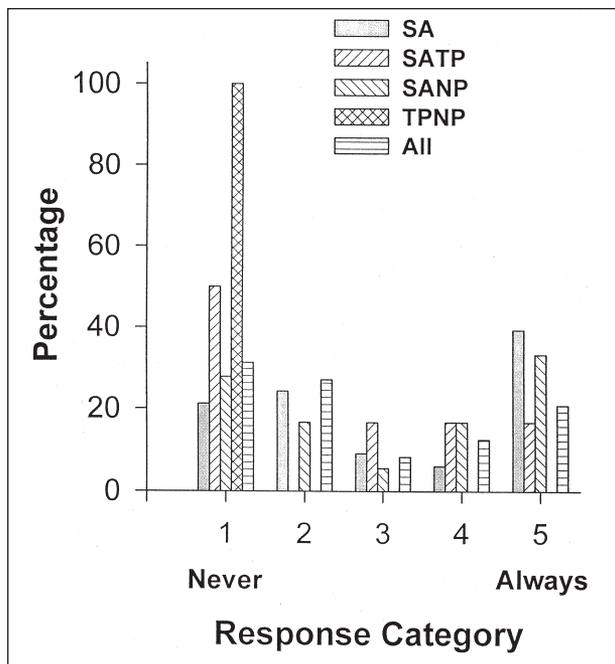
Figure 2—Frequency of vocalization during the owner's absence in dogs with separation anxiety alone (SA), separation anxiety and thunderstorm phobia (SATP), separation anxiety and noise phobia (SANP), thunderstorm phobia and noise phobia (TPNP), or separation anxiety, thunderstorm phobia, and noise phobia (All). Owner response categories were defined as never (1), > 0% but < 40% of the time (2), 40 to 60% of the time (3), > 60% but < 100% of the time (4), and 100% of the time (5). Frequency of the various owner response categories varied significantly among diagnostic disorders (CMH χ^2 test with 4 df; Q = 13.73; n = 114; P = 0.008).
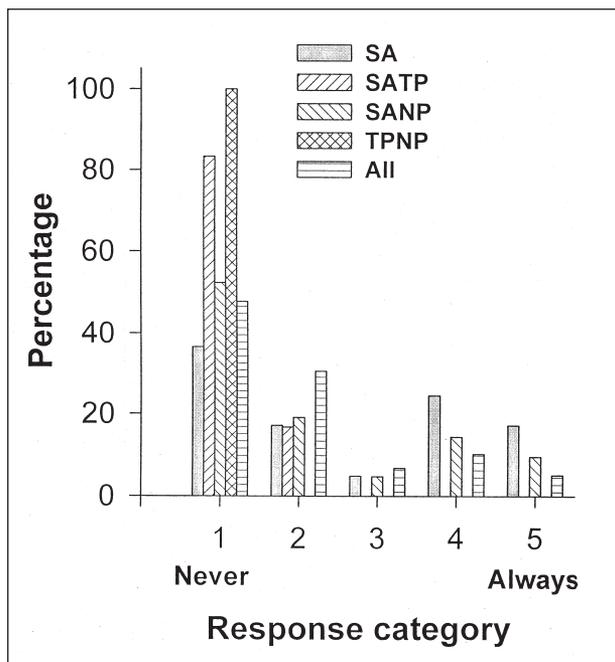

Figure 3—Frequency of destructive behavior during the owner's absence in dogs with various anxiety-related behavioral disorders. Frequency of the various owner response categories varied significantly among diagnostic disorders (CMH χ^2 test with 4 df; Q = 16.44; n = 136; P = 0.002). See Figure 2 for key.
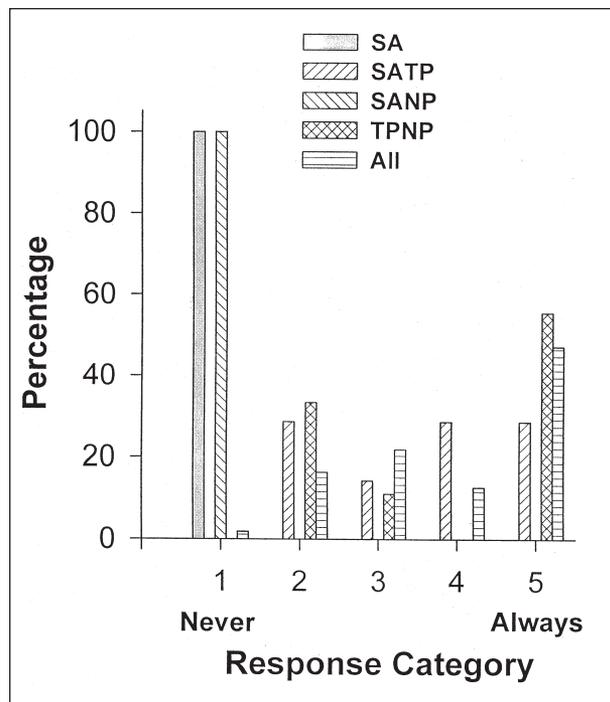

Figure 4—Frequency of reactions during thunderstorms in dogs with various anxiety-related behavioral disorders. Frequency of the various owner response categories varied significantly among diagnostic disorders (CMH χ^2 test with 4 df; Q = 91.63; n = 131; P = 0.001). See Figure 2 for key.

noses (separation anxiety alone, thunderstorm phobia alone, noise phobia alone, separation anxiety and thunderstorm phobia, separation anxiety and noise phobia, thunderstorm phobia and noise phobia, all 3 conditions) were independent was rejected (likelihood ratio χ^2 test; P < 0.001). The conditional probability that a dog with thunderstorm phobia would also have separation anxiety was 0.86, whereas the probability that a dog with separation anxiety would also have thunderstorm phobia was only 0.52. Similarly, the probability that a dog with noise phobia would also have separation anxiety was 0.88, whereas the probability that a dog with separation anxiety would also have noise phobia was only 0.63. Finally, the probability that a dog with noise phobia would also have thunderstorm phobia was 0.76, and the probability that a dog with thunderstorm phobia would also have noise phobia was 0.90.

Because only 1 dog had thunderstorm phobia alone and only 1 dog had noise phobia alone, these dogs were excluded from analyses of the association between nonspecific signs and individual diagnoses. For these analyses, CMH χ^2 tests were used to test whether owner responses to specific questions on the screening questionnaire were associated with the actual diagnosis. Results of the analyses of association indicated that frequency of vocalization during an actual absence of the owner (P = 0.008; **Fig 2**), frequency of destructive behavior during an actual absence of the owner (P = 0.002; **Fig 3**), frequency of reactions to thunderstorms (P = 0.001; **Fig 4**), and frequency of reactions to fireworks (P = 0.001; **Fig 5**) were not inde-
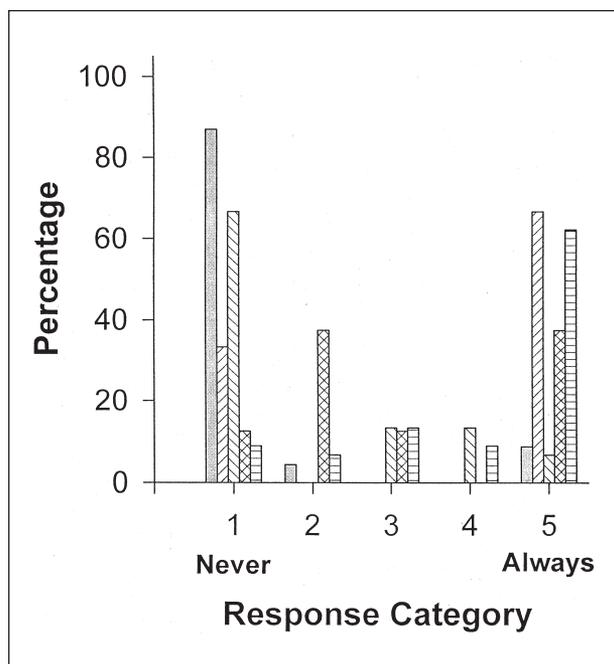
Figure 5—Frequency of reactions to fireworks in dogs with various anxiety-related behavioral disorders. Frequency of the various owner response categories varied significantly among diagnostic disorders (CMH χ^2 test with 4 df; Q = 40.60; n = 94; P = 0.001). See Figure 2 for key.

pendent of the actual diagnosis. In addition, P values for whether frequency of urination during an actual absence of the owner (P = 0.110; n = 132) and frequency of salivation during an actual absence of the owner (P = 0.085; n = 100) were independent of the actual diagnosis were close to the cutoff for significance. However, frequencies of vocalization, destructive behavior, urination, defecation, and salivation during virtual absences of the owner and frequency of defecation during an actual absence of the owner were not associated with the actual diagnosis. One clear pattern identified was that dogs with thunderstorm phobia in conjunction with noise phobia never vocalized, salivated, urinated, or engaged in destructive behavior during an actual absence of the owner.

Discussion

The finding in the present study that separation anxiety alone occurred significantly more often than would be expected and that noise phobia alone occurred significantly less often than would be expected under random conditions supported the concept that although these conditions share some nonspecific signs, they are separate entities. The finding that separation anxiety in conjunction with thunderstorm phobia and separation anxiety in conjunction with noise phobia occurred significantly less often than would be expected were these conditions independent but that thunderstorm phobia in conjunction with noise phobia and all 3 conditions together (separation anxiety, noise phobia, and thunderstorm phobia) occurred significantly more often than would be expected were these conditions independent supports 2 important conclusions. First, this suggests that noise phobia and thun-

derstorm phobia are different from each other and affect the frequency and intensity of related behaviors in dogs with other conditions differently. Second, this suggests that the interaction of multiple pathologic responses to noise likely reflects an altered dysfunctional underlying neurochemical substrate or is the result of one. In previous studies,[15-17] the extent to which dynamic interactions among comorbid conditions shaped the expression of behavioral phenotypes was reflective of differential responses to psychotropic medications. The newer psychotropic medications such as tricyclic antidepressants, selective serotonin reuptake inhibitors, and monoamine oxidase inhibitors use the same second messenger systems and transcription pathways that are used to develop cellular memory or to learn something via mediation and induction of long-term potentiation in the CA1 region of the hippocampus.[18-20]

In the present study, owner responses to questions about the signs exhibited by their dogs and the frequency of those signs were not independent of the diagnosis (separation anxiety alone, thunderstorm phobia alone, noise phobia alone, separation anxiety and thunderstorm phobia, separation anxiety and noise phobia, thunderstorm phobia and noise phobia, and all 3 conditions together). Again, this finding supports the conclusion that the interaction of multiple pathologic responses to situations associated with distress (noise phobia, separation anxiety, thunderstorm phobia) may reflect an altered dysfunctional underlying neurochemical substrate or be the result of one and that the various phenotypes are a result of this dysfunction.[18-21]

The roles played by arousal and reactivity cannot be ignored if we are to understand dogs with anxiety-related conditions such as separation anxiety, noise phobia, and thunderstorm phobia. Some dogs respond more quickly or react more intensely to a given stimulus than do other dogs. At some level, this hyper-reactivity is probably truly pathologic and represents yet another phenotypic manifestation of some neurochemical variation associated with anxiety. If so, the more frequently the dog reacts to the anxiety-provoking stimulus, the worse and more rapid the response. At some point, any exposure can then result in a full-blown nongraduated anxious reaction in which true panic may be involved. Accordingly, anticipation and early treatment is critical for these individuals, again supporting the concept that behavioral phenotypes and underlying neurochemical responses are linked in a dynamic way. Early intervention can only be accomplished by understanding the spectrum of signs exhibited in related conditions.

Approximately 20 to 30% of human patients with major depressive disorder have panic attacks. The role of panic has only recently been investigated in dogs.[b,c,d] Panic attacks share many of the attributes of noise and thunderstorm phobia. In dogs with combinations of separation anxiety, thunderstorm phobia, and noise phobia, the signs of each appear worse and more intense than in dogs with only 1 of these conditions.[22] If such dogs follow the pattern common for humans with comorbid diseases, the comorbidity may result in

a longer persistence of clinical signs and a less favorable overall outcome.[23,24] In human medicine, childhood separation anxiety is seen as an important antecedent in adult panic disorder and is a common undercurrent in the dreams of human patients with panic disorders.[25] This suggests that in humans, as in pets, separation anxiety can occur apart from panic disorders and other phobia-related conditions, but in patients with 2 or more conditions, the interaction among these conditions is an important factor in the assessment and treatment. If the phobic reactions to noise and thunderstorms are related to panic in dogs, such interactions are important.

In the present study, the probability that a dog with noise phobia would also have separation anxiety was high (0.88) and approximately the same as the probability that a dog with thunderstorm phobia would also have separation anxiety (0.86). However, the probability that a dog with separation anxiety would also have noise phobia (0.63) was higher than the probability that a dog with separation anxiety would also have thunderstorm phobia (0.52). These data, combined with the finding that the probability a dog would have noise phobia given that it had thunderstorm phobia (0.90) was not equivalent to the converse (0.76), support the hypothesis that neurochemical responses to noise are different from those to thunderstorms. The unpredictability and uncertainty associated with thunderstorms may have a role in shaping the neurochemical and behavioral responses to these anxiety-provoking situations, suggesting areas for future exploration of anxiety-related responses in dogs.

Results of this study suggest that the probability of having noise phobia in conjunction with separation anxiety was higher than would be expected if these 2 conditions were not associated. This strongly suggests that adverse reactivity to noises in general may predispose dogs to separation anxiety and that unless veterinarians carefully question clients about their pets' behavior, both of these conditions could remain undiagnosed. The extent to which early fearful behaviors contribute to the development of separation anxiety is unknown. Overly fearful human youngsters are at risk for later emotional distress, including anxiety and depression, suggesting that such associations should be investigated in veterinary behavioral medicine.

The specific neuroanatomy of anxiety-related responses involves the **locus ceruleus (LC)**, the principal noradrenergic nucleus in the brain and a region rich in serotonergic nuclei. Dysregulation of the LC appears to lead to panic and phobias in humans.[26] The LC directly supplies the limbic system and sends efferent neurons to Barrington's plexus in the intestines, accounting for many of the gastrointestinal signs in affected dogs. Human patients with true panic and phobic responses are more sensitive to pharmacologic stimulation and suppression of the LC than are healthy control patients.[26-28] These same neuroanatomic regions are implicated in patients with panic disorders.[29] In patients with panic, parahippocampal blood flow (a marker of neuronal activity), blood volume, and oxygen metabolism, determined by means of positive-emission tomography, are asymmetric during nonpan-

ic conditions,[30] possibly because of an increase in norepinephrine output by the LC that, in turn, stimulates parahippocampal over-responsiveness. The effects of altering the underlying neurochemical response of a substrate associated with affect and learning has profound implications for outcome and severity of signs in human patients with comorbid panic disorders,[30-36] and a common genetic predisposition for such neurochemical responses has been implicated as a mechanism for their cooccurrence.[37-38] Our data support the concept that such phenomena are operating in dogs with separation anxiety in conjunction with thunderstorm or noise phobia. The extent to which reactions to noise may predispose dogs to other anxiety-related conditions, whether the interaction of nonspecific signs and individual conditions may have time penetrance, and whether the longer a dog has been affected with 1 condition may increase its risk for a more complex form of that condition or for other anxiety-related conditions can best be addressed in prospective studies.

Finally, any time a dog exhibits destruction, elimination, vocalization, salivation, pacing, or withdrawal only during virtual absences of its owner, regardless of the age of the dog, the veterinarian should ascertain the pattern of the behaviors and decide whether they meet the criteria for a diagnosis of separation anxiety. Questions about these behaviors should be a routine part of the history-taking process during all examinations, as separation anxiety is among the most common problem in dogs and is often missed during its early stages. Early intervention is important. Separation anxiety can be successfully treated but can also lead to euthanasia or relinquishment of the dog if left untreated.[3,39,40] Because rescued and re-homed animals are particularly at risk for separation anxiety, compared with other dogs, early intervention may stop the problem from progressing and break the relinquishment cycle.[40,e] Furthermore, in our experience, dogs with a history of separation anxiety that has resolved are at risk for more severe signs if the condition should recur.

[a]Copies of the questionnaire are available from the corresponding author on request.

[b]Overall KL. Assessment of potential canine models for panic: results of the lactate sensitivity test comparing dogs with separation anxiety and those with idiopathic fear (abstr), in *Proceedings*. Am Vet Soc Anim Behav Annu Meet 1999;4.

[c]Overall KL, Dunham AE, Acland G. Assessment of potential canine models for panic: results of the lactate sensitivity test comparing dogs with separation anxiety and those with idiopathic fear (abstr), in *Proceedings*. 2nd World Meet Ethol 1999;8–17.

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[e]Overall KL. Demographic factors don't distinguish dogs with separation anxiety (oral presentation). Novartis roundtable on separation anxiety, 1997.

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