

# Link between gastric chronic diseases and anxiety in dogs

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**Abstract:** Anxiety in a population of dogs with chronic gastric disease was evaluated to determine whether there is a potential link between certain chronic gastric disorders and behavioural disorders. This preliminary study compared anxiety scores in a cohort of 20 dogs with chronic gastric disorders and a control group comprised of an equal number of healthy dogs. The control group included dogs without digestive disease, age-, breed-, and sex-matched with the ill dogs. Clinical, biochemical, and endoscopic exams were performed for each of the dogs with chronic gastric disease.

The Evaluation of Emotional Disorders in Dogs scale (EDED, or ETEC in French) is used to score anxiety in dogs.

The average age of the dogs included in the study was 5.7 years, and 75 % were male. Yorkshires, Labradors, and poodles were numerous in our study. Smaller breeds were better represented than large or average breeds, but the small sample size did not allow us to identify any significant difference. Small breeds were better represented than large and average-sized breeds. Smaller dogs often live in closer contact with their owners than do large dogs. It is possible that vomiting or dyspeptic episodes go unnoticed if a dog lives primarily outdoors. Yorkshire terriers, Poodles, and Labrador retrievers were the breeds that were most represented in our study (45%). However, when this distribution is compared to the distribution of breeds within the French canine population, it appears that these were the three most common breeds in France at the time of the study.

In the group of dogs with chronic gastric disease, 85 % had an EDED score between 17 and 35, three dogs scored less than 17, and no dogs scored over 35. Only one of the control dogs had an EDED score greater than 17, and could thus be classified as having anxiety. The ill animals primarily exhibited vomiting (75%). The average EDED score of dogs with dyspepsia was 23.2, compared to 19.6 for dogs who exhibited vomiting. The average EDED score in the ill dog group was 20.5, and the median was 20.5 with a variance of 21.8. For the control group, the average was 11.5, the median was 11, and the variance was 6.25. The Wilcoxon test yielded a p-value of 0.00023, indicating a very significant difference between the two groups. The animals with chronic gastric disease had significantly higher EDED scores than the control animals.

There was no significant difference between the scores obtained for the dogs with dyspepsia and those who exhibited vomiting.

The differential diagnosis for chronic gastric disease should include anxiety, and not only as an exclusion diagnosis. Scoring chronic and relapsing dogs on an EDED scale can save time. Treating anxiety improves the outcome of these dogs.

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## Introduction

Anxiety, in dogs, manifests as a collection of clinical signs and behavioural manifestations. Aggressiveness, destructive behaviour, wandering, running away, inhibition, and vocalising are the behaviours that are frequently associated with anxiety. The clinical signs reported in the literature include trembling, panting, urination, and defecation (Overall et al., 2001; Tiira, 2016).

The differential diagnosis of chronic gastric disease in dogs includes digestive and systematic causes. As multiple afferent nerves for the vomiting centre are located in the medulla oblongata, several conditions can account for this syndrome. Elwood et al. have carried out a systematic review of the causes of emesis in dogs. They include gastrointestinal disease conditions, especially gastric ulceration, pyloric stenosis, infection, inflammatory bowel diseases, gastric or intestinal neoplasia, obstructions or intestinal occlusions. Vomiting may also occur as a result of non-gastrointestinal abdominal disease conditions such as hepatobiliary or pancreatic disease. Finally, there are systemic disease conditions causing vomiting, which include metabolic, toxic or drug induced causes.

In human medicine, the link between anxiety and chronic gastric disease has been the subject of many studies. Out of 1641 patients with gastrointestinal complaints, Addolorato et al. (2008) found that 84.1 % (1379) presented in a state of anxiety. A prospective study of 4181 adults reported that individuals with gastritis exhibit significantly more anxiety than the rest of the population (Goodwin et al., 2013).

In canine medicine, however, few studies have investigated the behavioural aspect of gastric illness. Some studies have explored the possible link between functional digestive disorders and anxiety. Dogs with chronic idiopathic large bowel disease (CILBD) of idiopathic origin exhibit significantly higher anxiety scores than control dogs (Reiwald et al., 2013). Another study showed that more than 9 % (8/85) of dogs with CILBD improved when treated with a psychotropic agent (Lecoindre & Gaschen, 2011). These studies addressed intestinal disorders. The work reported here involves solely functional disorders of gastric origin.

To determine whether there is a potential link between certain chronic gastric disorders and behavioural disorders in dogs, we chose to evaluate anxiety in a population of dogs with chronic gastric disease as compared to control dogs.

## Materials and Methods

This preliminary study compared anxiety scores in a cohort of 20 dogs with chronic gastric disorders and a control group comprised of an equal number of healthy dogs.

The inclusion criteria for the ill animals were as follows:

- a) History of chronic gastric disorders, accompanied by vomiting or dyspepsia, without associated diarrhoea (intermittent or chronic). Dyspepsia was defined by the postprandial appearance of signs of digestive discomfort. A dog was considered to have dyspepsia if one of the following three signs was present: gastric distension, abdominal pain, or gastroesophageal reflux;
- b) Absence of comorbidities, excluding any behavioural disorders;
- c) Complete biochemical assessment within normal limits;
- d) Absence of macroscopic lesions upon endoscopic examination;
- e) Absence of histological lesions on biopsies taken during the endoscopic examination;
- f) The presence of *Helicobacter* was not a criterion for exclusion;
- g) Ineffectiveness of treatments or diets in preventing recurrence;
- h) All selected animals were under medical treatment and/or are on a hyper-digestible diet;

The control group included dogs without digestive disease, age-, breed-, and sex-matched with the ill dogs. Each control dog was the same age as the corresponding ill dog, plus or minus 10 months. The control dog was required to be of the same breed, but did not necessarily need to be pedigreed. Each control was of the same sex and reproductive status (with respect to sterilisation).

Clinical, biochemical, and endoscopic exams were performed for each of the dogs with chronic gastric disease by the same veterinarian, who has a degree from the European College of Veterinary Internal Medicine (ECVIM-CA). The pathology tests were performed by the BIOMNIS laboratory. A clinical examination of each control dog was performed by its usual veterinarian.

The Evaluation of Emotional Disorders in Dogs scale (EDED, or ETEC in French) is used to score anxiety in dogs (Pageat, 1990; Reiwald, 2013). A table is completed for each dog based on an interview with the owners (Figure 1).

Figure 1. Evaluation of Emotional Disorders in Dogs (EDED) Scale

	Behaviors	Items	V1	V2	V3	V4
Self focused	Eating	Bulimia (3)				
		Anorexia:hyporexia (4)				
		Dysorexia (ranging from hyper to hypo) (5)				
		Normal appetite (1)				
		Bulimia with regurgitation and reingestion (3)				
	Drinking	Eudipsia (1)				
		Polydipsia (documented) (5)				
		Chews at water without swallowing (3)				
		Pushes the empty bowl around (2)				
	Somesthetic	Normal grooming behaviour (1)				
		Licking, chewing (4)				
		Stereotypical chewing, turning (5)				
	Sleep	Normal (or no change) (1)				
		Increase, hypersomnia (2)				
		Insomnia while sleeping (3)				
		Wakes soon after going to sleep, unsettled upon waking (5)				

Outward focused	Exploratory behaviors	Normal (1)				
		Simple inhibition (2)				
		Increased with hypervigilance (4)				
		Oral (5)				
		Frequent avoidance behaviours (3)				
	Aggression	Aggressiveness unchanged (with no relational problems) (1)				
		Aggression in response to irritation (3)				
		Aggression in response to fear (4)				
		Aggression in response to fear and irritation (5)				
	Social skills	Steals, does not release stolen items (5)				
		Bites without growling (4)				
		Absence of submission (2)				
		Lack of control when playing (2)				
		Unchanged (1)				
	Specific skills	Same response capacity (taking tiring into account) (1)				
		Random responses (3)				
		More responses (5)				
Physical examination	Normal (1)					
	Episodes of tachycardia/tachypnoea (2)					
	Diarrhoea, colic (2)					
	Dyspepsia (2)					
	Increased urine output (3)					
	Lick granuloma (4)					
	Obesity (4)					
	PUPD (4)					
Total score						

All of the interviews were conducted by the same veterinarian, who is experienced in behavioural evaluation and trained in administering the questionnaire. The interview includes a series of 42 questions. Each response is assigned a score, and the cumulative score for all of the questions is the EDED score for the dog. For each question in the behavioural part of the questionnaire, only one answer is possible, whereas for questions regarding physical behaviour, multiple responses can be checked. The total score can range from 9 to 44. A dog is considered to have anxiety if its score is greater than or equal to 17 and less than or equal to 35 (Table 1).

Table 1. Behavioral status as a function of EDED score

EDED Score	9 to 12	13 to 16	17 to 35	36 to 44
Status	Normal	Phobic	Anxious	Mood disorder

The results obtained for each group were compared using Student test and Wilcoxon test.

The Wilcoxon test determines whether the difference observed between the means for two samples can be attributed to a systematic cause, or whether it is due to random fluctuation. It is suitable for studies involving small sample sizes, for quantitative paired data when there is a difference in variation in the two populations studied. In this study, it was used to compare the means of the EDED scores in the ill and control groups. The Student test compares measurements of a variable taken from two independent samples of different sizes. It is suitable for comparison of average EDED scores of dogs suffering from dyspepsia and dogs suffering from vomiting. The statistical calculations were performed using R software. Probability values less than 0.05 were considered as significant.

The examinations were performed in accordance with the animals and people present. The examinations were conducted in a manner designed to prevent the risk of pain and injury to the individuals and the animals included in the study.

## Results

The average age of the dogs included in the study was 5.7 years, and 75 % were male (15/20) (Figure 2).

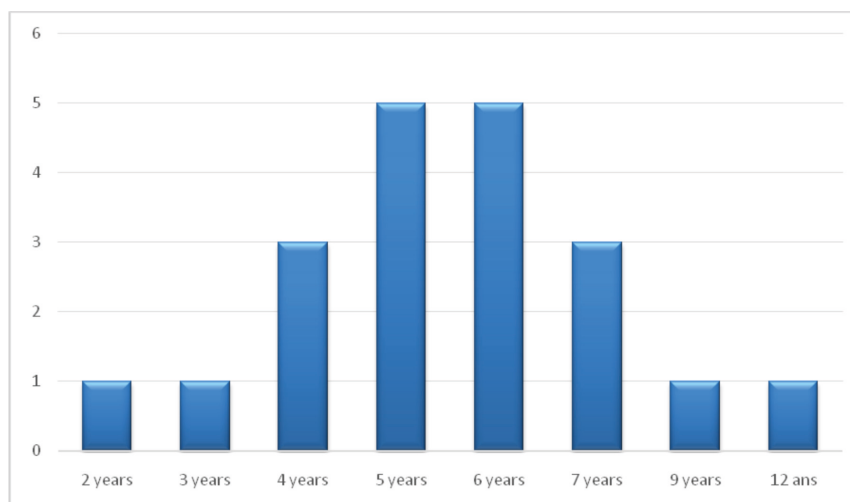


Figure 2. Age distribution of the ill population.

Yorkshires, Labradors, and poodles were numerous in our study. Smaller breeds were better represented than large or average breeds, but the small sample size did not allow us to identify any significant difference.

In the group of dogs with chronic gastric disease, 85 % (17/20) had an EDED score between 17 and 35 (inclusive), three dogs scored less than 17, and no dogs scored over 35. Only one of the control dogs (5 %, 1/20) had an EDED score great than 17, and could thus be classified as having anxiety (Table 2 and Figure 3).

Table 2. EDED results in ill dogs and their matched controls.

Name	Breed	Age	Sex	Sign	Score	Control
Jack	Airedale	5 years	male	dyspepsia	14	13
Hoppy	Griffon	9 years	male	vomiting	18	16
Sunny	WHWT	4 years	male	vomiting	19	12
Jazz	Yorkshire	7 years	male	vomiting	21	10
Minnie	Jack Russell	6 years	female	dyspepsia	30	9
Kenji	Labrador	6 years	male	vomiting	18	10
John	Poodle	7 years	male	dyspepsia	28	9
Guismo	Shih Tzu	5 years	male	vomiting	20	9
Olaf	Boxer	3 years	male	dyspepsia	23	14
Janie	Shih Tzu	6 years	female	vomiting	13	13
Newton	Shetland	4 years	male	vomiting	20	9
Nouki	WHWT	4 years	male	vomiting	18	10
Floyd	Labrador	5 years	male	vomiting	22	15
Gribouille	Yorkshire	12 years	male	vomiting	21	11
Lili	Yorkshire	7 years	female	vomiting	11	17
Noupy	Boxer	5 years	male	dyspepsia	21	12
Miss	Labrador	5 years	female	vomiting	20	9
Margot	Poodle	6 years	female	vomiting	26	12
Mozart	Poodle	6 years	male	vomiting	23	9
Moustique	Yorkshire	2 years	male	vomiting	24	11

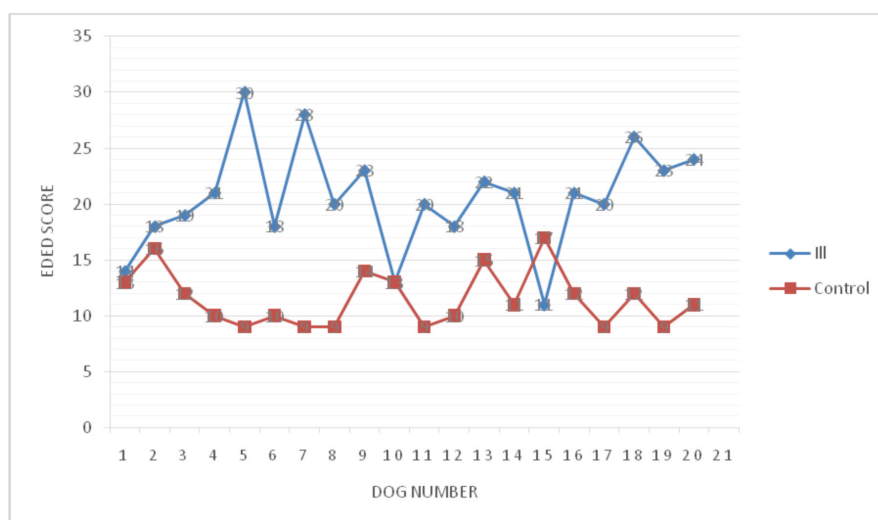


Figure 3. Distribution of EDED scores of the ill dogs and their matched controls

The ill animals primarily exhibited vomiting (75 %, 15/20). The average EDED score of dogs with dyspepsia was 23.2, compared to 19.6 for dogs who exhibited vomiting. The average EDED score in the ill dog group was 20.5, and the median was 20.5 with a variance of 21.8. For the control group, the average was 11.5, the median was 11, and the variance was 6.25. The Wilcoxon test yielded a p-value of 0.00023, indicating a very significant difference between the two groups. The animals with chronic gastric disease had significantly higher EDED scores than the control animals.

There was no significant difference between the scores obtained for the dogs with dyspepsia and those who exhibited vomiting (Student test, p-value = 0.28).

## Discussion

The presence of *Helicobacter* in the stomach of ill dogs was not used as a criterion for exclusion in this study. In humans, there is an infectious aetiology for ulcers and the associated dyspepsia. *Helicobacter* is identified in 30 % of healthy individuals and in 90 % of patients with gastric ulcers (Heams, 1996). Anxiety is one factor that can promote the proliferation of *Helicobacter pylori* in the stomach (Andreica-Sandica et al., 2011; Cader et al., 2015).

This difference is not seen in dogs. Even though *Helicobacter* bacteria are present in dog stomachs, there is no significant difference in the rate of colonisation between dogs with gastrointestinal disease and healthy dogs (Lecoindre, 2001). Multiple species of *Helicobacter* are present in dogs, including *H. felis*, *H. bizzozeronii*, and *H. salomoni*. They have not been shown to be pathogenic in dogs. Experimental infection is accompanied by gastritis and an immune response with no associated clinical signs (Lecoindre et al., 1997).

The average age of the dogs in this study was 5.7 years. The chronic gastric disorders responded well to symptomatic treatment. These complaints do not increase the mortality risk for the animal. Considering the difficulty of motivating dog owners to bring them in for this type of examination, it is likely that the average age of the dogs in this study was higher than the average age at which these symptoms appear. Conversely, this type of examination requires a general anaesthetic. Owners of older dogs may prefer to treat them without a specific diagnosis instead of subjecting them to the risk of general anaesthesia. These factors could explain the Gaussian distribution of the study population (Figure 2).

In our study of 20 dogs, 15 were males and 5 were female, yielding a 75% male population. One study performed during the same time period involved 489 dogs who were brought to 6 different veterinary practices for vaccination and reported that 55% of the dogs were male (intact and sterilised), whereas 45% were female (intact and sterilised) (Beaumont, 2002). The sex ratio was the opposite for dogs presenting with CILBD, with females representing more than 56 % (30/53) of the affected dogs (Reiwald, 2013). Our results suggest that males are overrepresented in our “ill” population. A larger study is needed to confirm this hypothesis.

Small breeds were better represented than large and average-sized breeds. Smaller dogs often live in closer contact with their owners than do large dogs. It is possible that vomiting or dyspeptic episodes go unnoticed if a dog lives primarily outdoors. Yorkshire terriers, poodles, and Labrador retrievers were the breeds that were most represented in our study (45 %, 9/20). However, when this distribution is compared to the distribution of breeds within the French canine population, it appears that these were the three most common breeds in France at the time of the study. Yorkshires, Labradors, and Poodles were therefore highly represented in our study because they are very common in the French dog population (distribution based on a study by Facco/Sofres, unpublished results).

The statistically significant difference ( $p$ -value < 0.05) between the average EDED scores of the two populations allows us to conclude that anxiety is a possible aetiology of chronic gastric diseases.

The pathophysiology of chronic gastric disorders resulting from anxiety remains largely uncharacterised. However, experimental work has demonstrated a link between acoustic stress and changes in gastrointestinal motility in dogs (Gué, 1989). Dogs were fitted with headphones that played music with a high sound intensity. This stimulus induced objective stress, as demonstrated by an accelerated heart rate and an increase in plasma cortisol levels. In fasting dogs, experiencing acoustic stress for one hour results in inhibition of gastric motility (though intestinal motor function is not affected). During the postprandial phase, applying acoustic stress for two hours also causes gastric disturbances, as demonstrated by delayed gastric evacuation of the solid phase of a meal, associated with an increase in plasma levels of digestive hormones (gastrin, somatostatin, and pancreatic polypeptide). Stimulation of the secretion of digestive hormones is prolonged beyond the duration of the stress event, suggesting that this effect is mediated by factors other than solely activation of the corticotropic axis. Prolonged postprandial motor activity at the gastric and intestinal level, leading to both delayed gastric evacuation and hypersecretion of digestive hormones, has also been observed in dogs.

The neurotransmitters and nerve pathways involved in the genesis of gastric disorders linked to stress have been the subject of previous study (Gué, 1989). The pneumogastric nerves may be involved in motility disorders. In addition, corticotropin releasing hormone (CRH) could help initiate or mediate gastrointestinal perturbations induced by stress. It could act through the supraspinal structures that regulated gastrointestinal motility, and not through the hypothalamic-pituitary-adrenal axis. However, this work did not focus on digestive disorders linked to acute stress. Chronic gastric disorders arising from anxiety could occur due to other pathophysiologic mechanisms. Multiple studies conducted in rats and mice seem to indicate that chronic stress could lead to intestinal inflammation, associated with the mobilisation of mast cells and accumulated secretion of CRH and acetylcholine. This inflammation could induce an increase in intestinal permeability (Glaser & Kiekolt-Glaser, 2005; Qiu et al., 1999; Velin et al., 2004).

If anxiety can cause chronic gastric disease, it is also possible that the causality could be reversed in some circumstances. Female rats are prone to developing signs of anxiety after iatrogenic gastritis (Luo, 2013). In addition, some behavioural problems, such as excessive licking of surfaces, are associated with gastrointestinal disorders in dogs, without, however, being associated with anxiety (Bécuwe-Bonnet et al., 2012).

There was no significant difference between the EDED scores of dogs with dyspepsia and dogs



exhibiting vomiting. This supports the homogeneity of the ill dog group based on the criteria investigated. Vomiting and dyspepsia represent two potential clinical manifestations of canine anxiety. Behavioural problems can therefore be included in the differential diagnosis for chronic gastric disorders, when accompanied by vomiting or dyspepsia.

## Conclusion

The differential diagnosis for chronic gastric disease should include anxiety, and not only as an exclusion diagnosis. Scoring chronic and relapsing dogs on an EDED scale can save time. Treating anxiety improves the outcome of these dogs. Vomiting and dyspepsia are clinical signs indicating anxiety as a behavioural pathology. These results should be corroborated in larger studies to confirm that a causal link exists between anxiety and chronic gastric disease in dogs.

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## Il legame tra malattia gastrica cronica ed ansia nel cane

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### Sintesi

È stata valutata l'ansia in una popolazione di cani con malattie gastriche croniche per determinare se esiste un legame tra alcuni disturbi gastrici e problemi comportamentali.

In questo studio preliminare sono stati confrontati i punteggi per l'ansia di un gruppo di 20 cani con disturbi gastrici cronici con quelli di un gruppo, costituito da un egual numero di cani sani. Il gruppo di controllo era composto da cani senza disturbi digestivi, abbinati per età, razza e sesso con i cani ammalati su cui sono stati effettuati esami clinici, biochimici ed endoscopici.

Per valutare l'ansia del cane è stato utilizzato la scala EDED (Evaluation of Emotional Disorders in Dogs).

L'età media dei cani inclusi nello studio era di 5,7 anni ed il 75% erano maschi. Yorkshire, Labrador e Barboni erano le razze più rappresentate (45% nel presente studio), come pure altre razze di piccola taglia; il ridotto numero dei soggetti inclusi nello studio non ha permesso di rilevare incidenze delle patologie statisticamente rilevanti. Bisogna però considerare che le razze di taglia piccola vivono spesso in contatto più stretto con la persona rispetto a razze di dimensioni maggiori e quindi i loro disturbi gastrici sono notati con maggior facilità.

Nel gruppo di cani con affezioni gastriche, l'85% aveva un EDED score compreso tra 17 e 35, tre cani uno score inferiore a 17 e nessun soggetto un punteggio superiore a 35.

Nel gruppo di controllo, un cane aveva uno score EDED superiore a 17 e potrebbe quindi essere classificato come ansioso.

Gli animali malati presentavano soprattutto vomito (75%). Lo score EDED medio dei cani con dispepsia era di 23,2, mentre quello dei cani che presentavano vomito era di 19,6.

Lo score EDED medio del gruppo dei cani malati era di 20,5, statisticamente maggiore ( $p=0,00023$ ) rispetto a quello dei controlli (11,5).

Non vi erano invece differenze statisticamente significative tra lo score ottenuto dai cani con dispepsia, rispetto a quelli che manifestavano vomito.

In conclusione, la diagnosi differenziale di disturbi gastrici dovrebbe includere anche l'ansia tra le possibili cause. Applicare la scala EDED può permettere una rapida individuazione di questo stato, permettendo l'instaurazione di una terapia idonea.