Clinical evaluation of the effects of a single oral dose of gabapentin on fear-based aggressive behaviors in cats during veterinary examinations

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Introduction

During the last decade, many light handling techniques have been developed in attempts to improve cats' experience during veterinary visits and prevent sensitization that leads to a situational phobia associated with veterinary visits.[1,2] However, the approaches to feline veterinary care are far from being systematic and generalized for several reasons, including owners' negative perception of veterinary visits because of their cats' signs of stress in these situations.[1,3] For instance, a 2010 study[4] that included 100 healthy cats found that only a partial clinical examination could be performed for 20 cats, and examination could not be correctly performed for another 4 cats. Difficulty associated with veterinary visits can lead to a lack of compliance with recommended examination intervals and affect the quality of medical care of cats to the detriment of their health and welfare. Stressed cats can exhibit aggressive behaviors, signs of fear such as avoidance attempts, and physical manifestations of fear such as trembling, mydriasis, or paw sudation.[2,5]

Cats' aggressive reactions during physical examination can have various origins. Some cats have phobias toward unfamiliar people or things before the first veterinary visit, so that it becomes a negative experience despite careful and gentle handling attempts. Other cats are initially compliant but have a negative experience in the clinic setting such that subsequent visits elicit fearful responses. In both of these situations, a sensitization mechanism leads to increasingly negative experiences that reinforce the cat's negative reactions. This cycle often leads cats to have avoidance behaviors even before they are transported to the veterinary clinic. Breaking this cycle requires a combination of cat-friendly handling techniques[6,7] and medical treatments.[8] In this context, administration of anxiolytic agents or sedatives by the owner before anticipation of the veterinary visit begins may be a valuable option. Some over-the-counter products are available, such as synthetic pheromones[9] and the nutraceutical α-casozepine,[10] but even though these have been reported to decrease signs of stress during transportation and examination, cats' compliance during examinations is not improved by pheromone applications.[9,10] To our knowledge, the effects of α-casozepine on this variable have not been described in the veterinary literature. Several psychotropic drugs are suggested to improve

compliance, but their use may be problematic. Trazodone[11,12] is not presently available in France; oral transmucosal detomidine treatment[13] is not labeled for use in cats, and benzodiazepines[14] or neuroleptics[15] can have adverse consequences on the health of dogs and cats. Gabapentin is a second-generation antiepileptic drug. Although not presently labeled for use in veterinary patients in the US and France, it is used to treat some forms of anxiety disorders, social phobia, and alcohol dependence in human patients.[16,17,18] Moreover, some reports[19,20] mention gabapentin as a possible anxiolytic agent in rats, and 2 recent investigations[21,22] evaluated the use of gabapentin to attenuate signs of fear or stress in cats.

Despite its structural resemblance to the GABA neurotransmitter, gabapentin does not bind to GABA receptors; unlike benzodiazepines, it is not a GABA mimetic drug.[23] A more probable mechanism of action is specific binding to a α2δ1 calcium channel subunit present in the mammalian brain.[24,25] Through binding with this subunit, gabapentin inhibits calcium flux into nerve cells, which leads to reduced release of several monoamine neurotransmitters, including noradrenaline,[25,26] and decreased synaptic transmission of specific excitatory neurotransmitters such as glutamate.[26] In addition, gabapentin appears to increase GABA synthesis by a mechanism that remains unknown.[26,27]

In cats, gabapentin has good oral bioavailability (88.7%), with a time to maximum plasma concentration of 100 minutes and a terminal half-life of 177 minutes.[28,29] Its elimination is mainly renal.[29] Gabapentin is commonly used in feline medicine for its antiepileptic properties at a dose of 10 to 40 mg/cat, PO, every 8 to 12 hours,[30,31] but is also used as an antinociceptive agent at a dose of 5 to 20 mg/kg, PO, every 8 hours.[32,33,34,35] Recently, gabapentin has been evaluated as an anxiolytic at a dose of 50 or 100 mg/cat.[21,22] Two studies[21,22] investigated the effects of a single orally administered gabapentin treatment, compared with a placebo, on fear responses in cats. One study[21] investigated the use of a low or high dose of gabapentin (50 or 100 mg) in 53 confined community cats that were captured for a trap-neuter-return program and found that cats receiving gabapentin had lower stress scores than those that received the placebo, but the cats were not directly examined while awake. The other study[22] included 20 healthy pet cats that had a history of fractious behavior or signs of stress during veterinary examinations; these cats were administered assigned treatments (100 mg of gabapentin or a placebo) 90 minutes before scheduled veterinary appointments in a crossover-design study, and their behavior during transportation and veterinary examinations was observed. The cats' signs of stress were scored by owners through the use of questionnaires, and video recordings of the examinations were used for evaluation of the cats' compliance by a neutral observer. These assessments indicated that oral administration of 100 mg gabapentin 90 minutes before

transportation reduces signs of stress during transportation and physical examination. However, the authors acknowledged that the use of video recordings to evaluate cats' compliance may be more difficult than making a direct assessment while performing the examination.

The purpose of the study reported here was to build on results of the aforementioned study[22] that suggest compliance of cats with a history of signs of stress or fractious behavior during a veterinary examination improves after gabapentin administration. Our study design was similar but centered on a standardized examination protocol that included a manipulator-based evaluation, rather than evaluation of the cats' behavior by review of video recordings. We also aimed to investigate potential dose effects and adverse effects of orally administered gabapentin and to assess owner-determined ease of treatment administration at home.

Materials and Methods

Animals

Two groups of client-owned, healthy domestic cats were enrolled in the prospective study. One group consisted of cats with a history of ≥ 1 episode of fear-based aggressive behavior (FAB) during veterinary appointments. Fear-based aggressive behavior included growling and hissing, swatting, and successful or unsuccessful attempts to scratch or bite that necessitated physical (eg, use of protective puncture-resistant gloves, towel wrapping, or a restraint cage) or chemical (eg, inhalation anesthetics) means of restraint to protect the veterinarian. The other group comprised untreated control cats with no history of FAB toward the veterinarian.

Recruitment of cats with FAB for study participation was performed by means of a posting and by word of mouth at 3 veterinary clinics in France where the clinical investigator (MK) saw patients (clinics A, B, and C), with a goal of enrolling ≥ 20 cats. Interested owners were asked to provide their contact information to the veterinary staff and were subsequently contacted through e-mail or telephone by the clinical investigator. The study was then explained to the cats' owners, and instructions for the whole study were provided. All cat owners gave their informed consent for study participation, and the cat's eligibility was checked against the inclusion and exclusion criteria. Cats were included in the study if they were family pets ≥ 6 months of age that were deemed healthy, were not receiving medication other than vaccines and deworming treatments, and had required use of ≥ 1 of the aforementioned restraint methods for clinical examination in the previous 2 (or more) veterinary appointments. Cats were excluded if they were community cats, < 6 months of age, or receiving medical treatment for a disease or behavioral condition or had evidence of other health issues such as kidney disease. Cats that were deemed compliant during general physical examinations or had shown aggressive behavior toward the veterinarian on only 1 occasion were also excluded. The owners of cats > 10 years of age were not contacted if there was no record of a serum or plasma

biochemical analysis with normal results (values within the respective reference intervals or showing no clinically important changes) on file dated ≤ 12 months before the study, but no biochemical tests were performed specifically for study purposes.

Untreated control cats were enrolled in the study to help ensure that the standardized examination procedure did not present any particular difficulty for cats that did not typically show FAB during veterinary appointments. Recruitment of these cats was performed by the clinical investigator during an appointment for a routine physical examination at clinic C. During the visit, the owners gave informed consent for cats to be examined according to the standardized protocol used in the study. To be included in the study, these cats were required to be deemed healthy and receiving no medications other than vaccines and routine deworming treatments. In addition, only cats with no history of aggressive reactions toward the veterinarian or postures indicating fear during veterinary visits were eligible for inclusion in this group. The enrollment goal was the same as the goal for cats with FAB. Evaluation of the untreated control cats was completed prior to the main study that investigated the effects of gabapentin in cats with FAB.

All examinations were performed by the clinical investigator at the clinics where the cats were routinely seen for their veterinary care. The study protocol was performed in compliance with the French governmental guidelines for research on animals.[36]

Study design and procedures

The main study was designed as a double-blind, randomized, placebo-controlled, crossover clinical trial. Cats of the FAB group were randomly assigned to receive gabapentin or a placebo 2 hours prior to the first of 2 physical examination visits. All cats received the alternate treatment 2 hours prior to the second visit. Treatment order was determined by a random drawing performed by a veterinarian who had no other role in the study. Timing of the second visit was dependent on the owners' schedules, but the 2 examinations were ≥ 1 day apart. At each visit, a standardized clinical examination was performed to evaluate each cat's compliance during examination procedures as a means of assessing treatment effects.

Capsules of gabapentin (100 mg) were supplied as a commercially available product and compounded at a pharmacy (Pharmacie Delpech) into 130-mg capsules that contained 100 mg of gabapentin and 30 mg of lactose powder (Zentivia Pharmaceuticals). To ensure blinding, placebo capsules were compounded at the same pharmacy from lactose powder, cornstarch, and talcum powder so that the shell and contents appeared identical to those of the gabapentin capsules. The capsules were labeled as drug A or B by the pharmacist and delivered to veterinary clinics A, B, and C. Neither the cats' owners nor the clinical investigator was aware of the order in which each cat received gabapentin and the placebo. The veterinarian who determined treatment order allocation provided the clinical

investigator with the treatments to be dispensed in assigned order for each cat and did not reveal the treatment order information until the analyses were complete.

Each cat's owner received 2 envelopes labeled with the number of the veterinary visit before which a predetermined number of the enclosed capsules was to be administered. One envelope contained 4 capsules of the gabapentin treatment, and the other envelope contained 4 capsules of the placebo. The owner was instructed to give 1 (for cats that weighed < 7 kg) or 2 (for cats that weighed ≥ 7 kg) capsules to the cat at home 2 hours prior to the scheduled visit. An excess number of capsules was provided in each envelope to ensure the assigned treatment could be given in the event that some were damaged at the time of administration. Owners were also instructed to keep a record of the ease of treatment administration and to assign a score for this (1 = very difficult administration requiring use of the extra capsules, 2 = difficult administration requiring several attempts, 3 = easy administration with a special treat or by placement directly into the cat's mouth, or 4 = very easy administration with regular food) as well as any potential adverse effects of the treatment. When adverse effects were observed, owners were asked to contact the clinical investigator via email and to follow up with another message indicating when these effects had resolved.

The standardized clinical examination for all cats in the study was a 9-step procedure **(**Appendix**)**, and compliance was scored from 0 to 9 according to the number of steps completed. Each step was deemed to require an increasing level of tolerance to handling or manipulation by the veterinarian. The examination was continued if the cat growled or hissed but was stopped if the cat attempted to scratch or bite. When the examination procedure was discontinued because of aggressive behavior, the cat's compliance score was calculated by subtracting 1 from the step in which the behavior occurred. During the examinations, the owner was present in the room but was asked not to speak or interact with the cat.

Statistical analysis

Associations between the administered treatment (placebo or gabapentin) and responses to veterinary examination (the main outcome variable) among cats of the FAB group were assessed by comparison of compliance scores between treatments (gabapentin and placebo) with a Wilcoxon signed rank test. The cats' compliance scores after each treatment were additionally compared with the compliance scores of cats in the untreated control group by use of a Mann-Whitney test.

Individual and mean compliance progression scores for cats of the FAB group were determined by subtracting their compliance score after placebo administration from their compliance score after gabapentin administration, such that a score of 9 represented maximum improvement and a score of −9 represented maximum worsening for this variable after treatment. Progression scores were also used as a secondary measure of the effect of gabapentin on the main outcome variable and to determine whether some of the test conditions were associated with this outcome. The potential

effects of treatment order (ie, gabapentin followed by placebo or placebo followed by gabapentin) and veterinary clinic (A, B, or C) were assessed by the statistical comparison of progression scores with a Mann-Whitney test and Kruskal-Wallis test, respectively. Spearman correlation analysis was used to investigate associations between compliance progression scores and the interval between the first and second veterinary visits or the dose of gabapentin on the basis of body weight.

The ease of gabapentin administration was analyzed by comparison between owner-assessed scores for placebo and gabapentin administration with a Wilcoxon signed rank test. Finally, the presence or absence of adverse effects reported by owners or observed by the clinical investigator was analyzed to determine an association with compliance progression scores (Mann-Whitney test) and with the dose of gabapentin on the basis of body weight (Student *t* test after confirming normal distributions with the Shapiro-Wilk test and *F* test for equality of variances).

All data were analyzed with 2-tailed tests. Analyses were performed with statistical software.[37] Values of $P < 0.05$ were considered significant.

Results

Cats

In total, 55 cats were enrolled in the study; 44, 5, and 6 cats were patients of clinics A, B, and C, respectively. The FAB group included 26 cats (15 females and 11 neutered; mean ± SD age, 5.6 ± 3.8 years [range, 1 to 14 years]). The mean ± SD body weight for these cats was 4.8 ± 1.8 kg (range, 2.8 to 12.0 kg). The mean ± SD dose of gabapentin was 24 ± 5.6 mg/kg (range, 17 to 36 mg/kg). Thirteen cats in the FAB group received gabapentin for visit 1 and the placebo for visit 2, and the remaining 13 cats received the treatments in the opposite order. The mean ± SD interval between the 2 physical examination visits was 15.6 ± 15.9 days (range, 1 to 66 days).

The untreated control group comprised 29 cats (13 females and 16 neutered males). The mean ± SD age of these cats was 8.0 ± 4.3 years (range, 2 to 16 years).

Effects of gabapentin on FAB

The compliance scores of cats in the FAB group after administration of gabapentin (median, 9; range, 0 to 9) were significantly ($P < 0.001$) greater than compliance scores for the same cats after administration of the placebo (median, 0.5; range, 0 to 7). Moreover, compliance scores of FAB-group cats after receiving the placebo were significantly ($P < 0.001$ lower than the compliance scores of untreated control group cats (median, 9; range, 6 to 9), but compliance scores did not differ significantly ($P = 0.226$) between these 2 groups after FAB-group cats received gabapentin **(**Figure 1**)**.

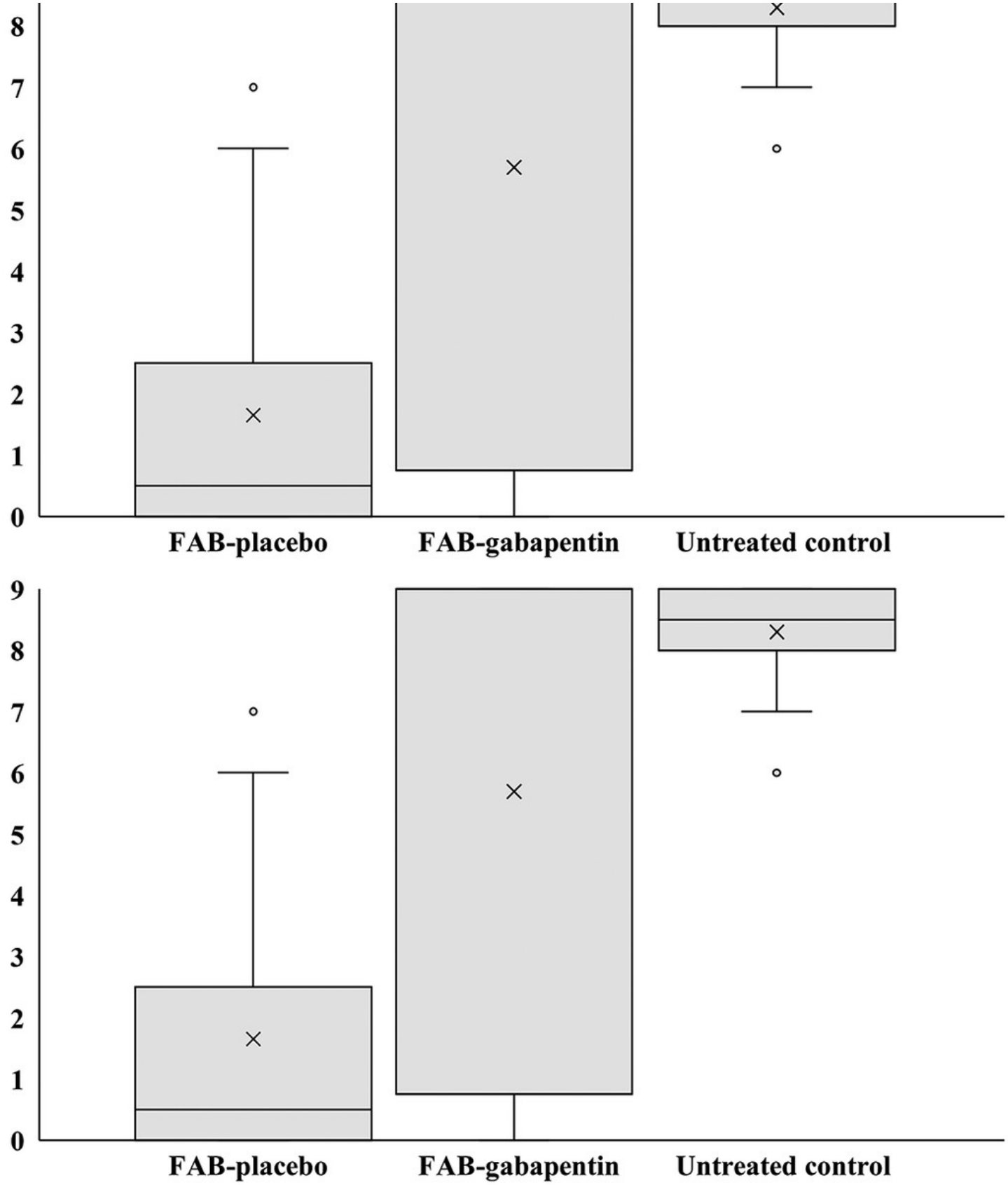

Figure 1

Box-and-whisker plots of compliance scores during a standardized veterinary examination for cats that had a history of fear-based aggressive behavior (FAB) during veterinary visits (n = 26) and for untreated control cats that did not have a history of FAB (29). Results for the FAB group are shown

after oral administration of gabapentin (100 mg, compounded into capsules with 30 mg of lactose powder) or an identical-appearing placebo by the owner at home 2 hours before the examination; cats that weighed < 7 and ≥ 7 kg received 1 or 2 capsules, respectively, for 1 randomly assigned treatment 2 hours prior to the first of 2 veterinary visits and received the alternate treatment prior to the second visit 1 to 66 days later. Boxes represent the interquartile (25th to 75th percentile) ranges, horizontal lines within the boxes represent medians, X marks indicate means, whiskers indicate the minimum and maximum values (excluding outliers), and circles outside of boxes indicate outliers. The median value for the FAB-gabapentin group coincided with the upper limit of the interquartile range. ***See*** Appendix for scoring information.

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Figure 1

Box-and-whisker plots of compliance scores during a standardized veterinary examination for cats that had a history of fear-based aggressive behavior (FAB) during veterinary visits (n = 26) and for untreated control cats that did not have a history of FAB (29). Results for the FAB group are shown after oral administration of gabapentin (100 mg, compounded into capsules with 30 mg of lactose powder) or an identical-appearing placebo by the owner at home 2 hours before the examination; cats that weighed < 7 and ≥ 7 kg received 1 or 2 capsules, respectively, for 1 randomly assigned treatment 2 hours prior to the first of 2 veterinary visits and received the alternate treatment prior to the second visit 1 to 66 days later. Boxes represent the interquartile (25th to 75th percentile) ranges, horizontal lines within the boxes represent medians, X marks indicate means, whiskers indicate the minimum and maximum values (excluding outliers), and circles outside of boxes indicate outliers. The median value for the FAB-gabapentin group coincided with the upper limit of the interquartile range. ***See*** Appendix for scoring information.

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Compliance progression scores for cats of the FAB group were ≥ 1 (n = 20) or 0 (6), with a median value of 3.5 (range, 0 to 9). Thus, signs of FAB were decreased in 20 of 26 (77%) cats and unchanged in 6 (23%) after gabapentin administration. Comparison of results according to treatment order (ie, gabapentin followed by placebo or vice versa) revealed no significant (P = 0.920) difference in progression scores for cats that received gabapentin prior to visit 1 (median, 4; range, 0 to 9) and those that received gabapentin prior to visit 2 (median, 3; range, 0 to 9). There was also no significant

(P = 0.255) difference in progression scores among clinics A (median, 5; range, 0 to 9), B (median, 7; range, 0 to 9) and C (median, 1; range, 0 to 7). Compliance progression scores were not significantly correlated with the interval between examination visits (r_S = −0.064; P = 0.755) or the administered dose of gabapentin (r_S = 0.117; P = 0.566).

Ease of administration of the treatments

The administration scores for the placebo and gabapentin capsules each had a median value of 3 and range of 1 to 4. These results could not be statistically compared because of the very small number of nonzero differences between data pairs (n = 1).

Adverse effects of the treatments

Whereas no cats had possible adverse effects identified after administration of the placebo, adverse effects attributable to gabapentin treatment were reported by the cats' owners, observed by the clinical investigator, or both for 11 of 26 (42%) cats, with a range of 1 to 3 adverse effects/individual. The most common of these signs was drowsiness (9/11 cats), followed by myorelaxation (6), ataxia (3), prolapse of the gland of the third eyelid (2), and vomiting (1). All observed adverse effects had resolved ≤ 10 hours after they were first noted. Comparison of gabapentin doses on the basis of body weight between cats of the FAB group that did (n = 11) and did not (15) have adverse effects attributable to the treatment revealed no significant (P = 0.35) difference (mean ± SD dose, 25.0 ± 6.23 mg/kg and 22.8 ± 5.19 mg/kg, respectively). Comparison of compliance progression scores between cats of the FAB group that did (median score, 7; range, 0 to 9) and did not (median score, 1; range, 0 to 8) have adverse effects revealed that the scores were significantly (P = 0.003) greater for cats with adverse effects.

Discussion

Results of the study reported here suggested that a single 100- or 200-mg oral dose of gabapentin (17 to 36 mg/kg) administered by owners 2 hours before a veterinary visit can improve the compliance of healthy cats with a history of FAB during a physical examination. The improvement in compliance scores for cats in the FAB group was not associated with various testing conditions such as the treatment order (placebo prior to the first visit and gabapentin prior to the second, or vice versa), interval between treatments, or clinic where the cat was examined.

The amount of improvement observed with gabapentin treatment was highly variable among individual cats, ranging from no change at all to a maximum improvement (ability to complete the entire standardized examination without the cat attempting to scratch or bite). However, no cat was less compliant during the veterinary examination after gabapentin treatment than after the placebo,

and most (20/26 [77%]) of the cats had some degree of improvement. Moreover, the gabapentin treatment resulted in an overall degree of compliance among cats with FAB that did not differ from the findings for untreated control cats with no history of FAB.

Our experimental protocol addressed some of the limitations described in the report by van Haaften et al[22] by use of a more standardized examination procedure with a manipulator-based evaluation of the cats' compliance during veterinary examinations. However, the present study also had shortcomings. Even though we devised our standardized procedure with the objective of moving sequentially from the least invasive to most invasive aspects of the physical examination, some bias was introduced by the protocol. Although, in our experience, measurement of rectal temperature is generally less tolerated by cats than examination of the skin, each cat has an individual tolerance level to each type of contact or manipulation required during an examination. It should be noted that some cats' general tolerance will decrease over time, and at some point, they may have a reaction independent of the nature of the manipulation because their coping capacity is overwhelmed. Finally, examination of the cats on a table required that the investigator remove each cat gently but manually from its carrier.

To assess the tolerability of the standardized examination procedures described in this report, we first used the protocol for examination of 29 untreated healthy control cats with no history of FAB (neither aggressive reactions nor postures indicating fear) during veterinary visits. The control cats' compliance scores during this preliminary assessment were high, supporting the hypothesis that the 9-step examination procedure should be well tolerated by healthy cats without FAB.

The nature of the data prevented statistical evaluation of owner-reported ease of administration scores, as the scores for gabapentin and placebo capsule administration were identical for 25 of the 26 cats. However, the median score for both gabapentin and the placebo was 3 on a scale of 1 (very difficult) to 4 (very easy administration with regular food). This corroborated the observation by van Haaften et al[22] that gabapentin (also in capsules) was easy to administer. This is an important consideration because it can be difficult to medicate cats, and this difficulty can negatively impact treatment compliance. Ease of treatment administration at home and improved ability to perform examinations in a single visit could allow more systematic veterinary care of cats, and we consider that some cats may possibly benefit from such treatment in a preventive manner to help avoid sensitization to veterinary visits, instead of resorting to medication after FAB has developed and the patient's welfare during veterinary visits is already impaired. In our study, we evaluated effects of a single preappointment gabapentin treatment in cats known to have overt signs of aggression, which is usually attributable to fear, because if these cats were more compliant after receiving the medication, we could hypothesize that cats having signs of fear without aggression would also benefit from such treatment.

Unlike the results reported by van Haaften et al[22] that suggest the effects of gabapentin on stress in cats are dose dependent, compliance scores of cats with FAB were not found to be correlated with the dose per kilogram of body weight in our study. The mechanism of action of gabapentin is complex and not completely elucidated, and we speculate that there could be an on-off threshold that varies among individual cats. This hypothesis could be explained by the existence of cat populations that possess different amounts or types of α2δ1 subunits. Consequently, it could be interesting to perform a similar investigation with a protocol in which cats that do not respond to the initial dose of gabapentin undergo repeated examination after receiving different doses at suitable intervals. Pharmacologic data also suggest that the peak plasma concentration of gabapentin after oral administration is widely variable among individual cats.[29]

In addition, the degree of sensitization of the cat to veterinary examination could have influenced the response to gabapentin administration in our study. The severity or type of stress response might influence the mechanisms of action of gabapentin at a molecular level. This should be investigated in future research by scoring the initial level of cats' aversion to veterinary care and tracking its source, if known, before starting the protocol.

Moreover, the long-term effects of gabapentin used to palliate FAB or other signs of fear associated with veterinary visits in cats should be further investigated. It should be considered that an improvement in a cat's compliance with the treatment does not necessarily indicate that the cat is not experiencing fear. It may be beneficial to investigate the effects of behavioral desensitization combined with gabapentin versus a placebo treatment in cats that have signs of fear associated with veterinary visits.

Our study results provided complementary information regarding the adverse effects attributed to a single dose of gabapentin in cats. These were not associated with the administered dose and were common, affecting 11 of 26 (42%) study cats that received the treatment. Several affected cats had > 1 sign. The most commonly reported adverse effects were drowsiness, myorelaxation, and ataxia, and owners reported that all adverse effects completely resolved ≤ 10 hours after they were first observed. This was considered compatible with an episodic use of gabapentin for veterinary visits. Surprisingly, the presence of adverse effects was associated with greater compliance progression scores in our study, although several cats had improved compliance with gabapentin treatment while showing no adverse effects. Another study would be needed to confirm this finding, but several hypotheses may be advanced as possible explanations. First, adverse effects such as drowsiness could have been responsible for the improved compliance, but this would not explain why some cats had improvement without showing adverse effects. Second, noradrenergic responses could compete at a molecular level with gabapentin in cats with substantial stress, so that both the positive and adverse effects of the drug are masked; however, when gabapentin effects outcompete the stress responses, the adverse

effects also become apparent.

Unlike van Haaften et al,[22] we did not test the possible effects of gabapentin on the signs of stress in cats associated with being placed in their carriers or transported to the veterinary clinic. However, many owners of cats in the present study mentioned that their cats had a calmer attitude in these 2 situations. This should be the subject of a future study because it has been shown that carrier training of cats to increase their level of comfort with confinement and being taken by car to the clinic can decrease signs of stress during transportation and during the veterinary visit.[38]

Results of the study reported here supported that gabapentin administered orally to cats at a mean dose of 24 mg/kg 2 hours before a veterinary visit results in improved compliance during physical examination. Moreover, most owners indicated that the capsules were easy to administer and that adverse effects resolved within 10 hours when they occurred. However, administration of these doses of gabapentin should be considered carefully for patients with kidney disease. From a welfare perspective, there is still an opportunity for educating veterinarians and owners to employ all appropriate methods available to help alleviate anxiety and fear associated with veterinary visits for cats. Such methods can include gentle handling and carrier training, but these techniques cannot always be successfully implemented without medication.

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Appendix

Description of a standardized clinical examination and corresponding compliance scores for cats enrolled in a study to evaluate the effects of a single oral dose of gabapentin on fear-based aggressive behaviors in cats during veterinary examinations.

Step	Description
0	None
1	Removal of the cat from its carrier
2	Step 1 plus cardiorespiratory auscultation
3	Step 2 plus abdominal palpation
4	Step 3 plus weight measurement
5	Step 4 plus intraoral examination
6	Step 5 plus ocular examination
7	Step 6 plus examination of ears
8	Step 7 plus measurement of rectal temperature
9	Step 8 plus return of the cat to its carrier

Each step was performed by 1 veterinarian (MK) in the described sequence. The examination was stopped if the cat attempted to scratch or bite the investigator. Hissing or growling was not a cause to discontinue the examination. The compliance score for each cat was recorded as the last step of the examination that was completed; when the procedure was discontinued because of aggressive behavior, the cat's compliance score was calculated by subtracting 1 from the step in which the behavior occurred.