Veterinary clinic visits can be stressful events for dogs and cats. Döring et al categorized 78.5% of dogs participating in their study as fearful, particularly on the examination table. Several studies have tried to identify this stress through behavioral and physiological responses, aiming to reduce the intensity of the negative experience on companion animals. Among several known reasons, stress affects the animal’s welfare and accuracy of the outcome of veterinary physical examinations and diagnostic tests, which may mislead the treatment plan of the patient. In addition, the stressed animal may react aggressively during the examination and treatment, which is also a major concern to companion animal owners and the veterinary team. Since many owners recognize their companion animal’s stress at the veterinary clinic, some may avoid bringing their pets regardless of their needs for the timely provision of preventative care and early diagnosis of diseases. The owners’ avoidance leads to a negative economic impact on the veterinary clinic as it results in a reduction in revenue. The stress response of companion animals can be evaluated by observing and measuring stress-related behaviors caused by fear and anxiety. It can also be measured by physiological variables such as cortisol concentrations, blood pressure, heart rate, and body temperature.

Several methods to alleviate animal stress in veterinary clinics have been proposed; however, research on the efficacy of these methods is limited. Studies show that environmental management such as

**OBJECTIVE**
To evaluate the effects of a single dose of orally administered gabapentin in alleviating stress at a veterinary visit in privately owned dogs.

**ANIMALS**
22 healthy client-owned dogs (1.5 to 8.5 years old) were enrolled in this study.

**PROCEDURES**
Each dog received a 50-mg/kg oral dose of either gabapentin or placebo 2 hours before the beginning of each visit protocol. The dog’s behavioral responses were coded from recorded video clips during a 5-minute-long standardized physical examination and pre- and post-physical examination phases. The veterinary technician separately rated each greeting behavior at each visit. Physiological variables during veterinary visits (ie, eye surface temperature and salivary cortisol concentrations) were also compared between the pre- and post-physical examination phases. The owner was queried 24 hours after a visit to determine the incidence of adverse events.

**RESULTS**
The greeting test score, eye surface temperature, and cortisol concentrations did not differ substantially between the gabapentin and placebo treatment groups. Lip licking frequency during the physical examination phase was significantly lower in the gabapentin treatment group than in the placebo group ($P = 0.001$). Lip licking frequency during the pre- and post-physical examination phases was also significantly lower in the gabapentin treatment group than in the placebo treatment group ($P = 0.004$). No serious adverse events were reported by the owners following gabapentin treatment.

**CLINICAL RELEVANCE**
Results showed that the 50-mg/kg dose of gabapentin was well tolerated without serious adverse effects in healthy dogs. Further studies are recommended of dogs with documented stress in response to a veterinary visit.
playing background music, having the dog wait outside and not in the waiting room of the clinic, examining the dog in an examination room and not a common treatment room, placing the owner and pet into the examination room instead of a waiting room, and having the owner present during the examination might be beneficial in reducing stress in dogs. Additionally, administration of nutraceutical products and the use of pheromone products might further reduce dogs’ stress in the veterinary clinic.

Another commonly used method is pharmaceutical intervention with several classes of drugs with a short latency to effect. The commonly recommended classes in recent reference textbooks and publications are benzodiazepines, sympatheticolytic agents, serotonin antagonists and reuptake inhibitors, and antiadrenergic agents. Benzodiazepines have antianxiety properties that bind to GABA receptors and facilitate GABA in the CNS. Their known side effects include paradoxical excitation and anxiety, and, although controversial, they might interfere with learning. In the sympatheticolytic agents class, there are 2 medications that are commonly used in behavior medicine: clonidine and dexmedetomidine, which work by blocking noradrenaline in the CNS. In a recent study, Hauser et al reported that dexmedetomidine oromucosal gel reduces stress-related behaviors in dogs during veterinary examinations. Serotonin antagonist and reuptake inhibitors block serotonin 2A and 2C receptors and inhibit serotonin reuptake, and trazodone is the only widely used medication in this class of behavioral medicine in companion animals. Trazodone reduces transport- and examination-related anxiety signs in cats and stress-related signs and behaviors in hospitalized dogs. Kim et al recently reported the effect of trazodone in dogs during veterinary visits. According to the study, it was effective in reducing the level of stress, which was measured by physiological and behavioral parameters.

Gabapentin, a member of the gabapentinoid medications, is an antiepileptic and analgesic drug in humans and animals. In humans, the anxiolytic effect is used to treat a variety of medical conditions of chronic and acute pain. It is also used to treat various psychiatric illnesses, such as anxiety disorders and bipolar disorders. Several studies have reported the clinical anxiolytic use of gabapentin in cats, and a recent double-blinded placebo-controlled crossover trial reported its effect on storm phobia in dogs; however, to our knowledge, no study has evaluated its efficacy in dogs as a pre–veterinary visit medication.

Although the underlying mechanisms of the anxiolytic properties of gabapentin remain unknown, previous studies suggest it has an inhibitory effect to α2β subunits of voltage-activated Ca2+ channels in neural tissues. Gabapentin’s chemical structure is similar to that of the GABA neurotransmitter, but it does not have a strong affinity for GABA receptors. While gabapentin is eliminated through urine in all tested species of mice, rats, dogs, monkeys, and humans, dogs are the only species with a high level of the metabolite N-methylgabapentin. Approximately 32% of a single 50-mg/kg dose of gabapentin is metabolized in dogs to N-methylgabapentin, which is not found in humans. N-methylgabapentin is excreted unchanged, and it is not known whether this metabolite has any clinical effect on dogs. Pharmacokinetic studies have reported that the half-life of gabapentin in dogs ranges from 2.2 to 3 hours for oral doses of 50 to 60 mg/kg and from 1.3 to 1.5 hours for oral doses of 10 to 20 mg/kg, respectively. Another recent study that used an orally administered 50-mg/kg dose of gabapentin 2 hours before the induction of anesthesia reported that gabapentin significantly prevented the increase in intraocular pressure associated with tracheal intubation in dogs anesthetized with propofol. On the basis of this available information, we selected the dose and administration timing of gabapentin in our study design.

The goal of this study was to evaluate the effects of a single dose of orally administered gabapentin (50 mg/kg) in alleviating stress during a veterinary visit in privately owned dogs. We hypothesized that dogs administered gabapentin orally at a dose of 50 mg/kg would have fewer stress responses, as measured by behavioral and physiological parameters, compared to dogs administered the placebo.

Materials and Methods

Animals

Dogs were recruited for the study between April 2019 and March 2020 through emails and flyers at Purdue University Veterinary Hospital. The inclusion criteria were as follows: any breed, intact or neutered of either sex, weighing between 10 and 40 kg, aged between 1.5 and 12 years, clinically healthy as defined by a CBC and biochemistry panel within 2 months prior to enrollment, and a participant travel time to the hospital of under 40 minutes. The exclusion criteria were as follows: dogs receiving treatment with any medication other than internal and external parasite preventatives and dogs with a known history of aggressive behavior (from growling to actual biting) toward people. The Consolidated Standards of Reporting Trials chart is shown (Figure 1). The study was approved by the Purdue University Institutional Animal Care and Use Committee (protocol No. 1811001825), and all owners read and signed an informed consent form prior to participation in the study.

Procedures

This was a double-blinded, randomized, placebo-controlled crossover study with a 2-week washout interval. The testing procedures were carried out by 2 people: 1 male investigator in the role of the veterinarian (OOS) and 1 female veterinary technician (MSC) in her role. The study was conducted in 2 windowless adjacent rooms located at the Purdue University Veterinary Hos-
pital; the first room served as a waiting room and the second as an examination room. The room was thoroughly cleaned before and after each visit. The participants had never visited these rooms at any time before the study visits. For the purpose of the study design, the Purdue Veterinary College Pharmacy compounded both placebo and active ingredients into a common size and color of capsule, providing the opportunity for a double-blinded study. Each owner received 2 vials: one labeled drug A and the other labeled drug B. Drug A was the placebo, and drug B was the gabapentin. A randomization chart was utilized to determine which drug, A or B, was dispensed for the first visit and which was dispensed for the second visit. The parameters of the randomization chart included drugs A and B, visits 1 and 2, and patient weight classes of < 20 kg and > 20 kg. Green and white No. 1 capsules were hand packed to provide a calculated dose in milligrams of gabapentin US Pharmacopeia (USP) powder (pure Active Pharmaceutical Ingredient [API] obtained from the Professional Compounding Centers of America) plus lactose USP such that the final weight of the capsule would be 400 mg plus the weight of the empty capsule for drug B, and 400 mg lactose was hand packed for drug A. Each hand-packed capsule was individually weighed for accuracy. Keeping drug A and drug B even in weight contributed to the double blindness of the study. A green and white No. 1 capsule was found to be able to contain a maximum of 400 mg of gabapentin. This formed the basis for determining the number of capsules needed to provide 50-mg/kg dosing. Each vial was labeled by the pharmacy with which visit the drug was to be administered. The study team and the participants’ owners were blinded to the contents.

As shown (Figure 2), each visit in both treatments consisted of 3 phases carried out in a sequence of procedures, which were video recorded for later analysis. The capsules were given to the dogs by their respective owners at home 2 hours before the beginning of each visit.

Preexamination (9-minute duration)—Upon arrival, the owner and their dog were escorted to the study waiting room where the dog was tethered to the wall by the owner with a 3-m lightweight nylon leash, which allowed the dog to roam freely in the room. A water bowl and blanket were provided in the room for the dog, and the owner was seated in a chair while ignoring the dog. At the end of the 9-minute preexamination phase, the veterinary technician entered the room and conducted a greeting test, which was followed by measuring the eye surface temperature. The veterinarian then entered the room to collect a saliva sample with the assistance of the owner. The details of each procedure (eg, greeting test and eye surface temperature measurement) are described in the following section.

Physical examination (5-minute duration)—The owner and the dog were escorted to the examination room, and the owner placed the dog on the examination table, which was located in the middle of the room. All dogs were positioned with their head facing the main video camera and a second camera for backup. The veterinarian stood on the right side of the dog and the owner stood on the left while the veterinary technician sat quietly on a chair out of sight. The owner was instructed to ignore the dog.

Figure 1—Consolidated Standards of Reporting Trials chart for the double-blinded, placebo-controlled study reported here on the effects of a single dose of orally administered gabapentin in 22 client-owned dogs during a veterinary visit.

Figure 2—Veterinary visit timeline for the 22 dogs of this report.
but to prevent the dog from jumping off the table if the dog tried.

A 5-minute-long standardized physical examination was performed in the order of 1 to 7 by the veterinarian (Appendix 1). If the dog showed any aggressive behavior, the examination was aborted and the dog was removed from the study. After completion of the physical examination, the patients were returned to the waiting room.

**Postexamination (9-minute duration)—**The owners were given the same instructions as those in the pre-examination phase. At the end of the 9-minute postexamination phase, the owner and the dog returned to the study waiting room and the dog was tethered by the owner with the same long leash. Then, the greeting test and eye surface temperature were measured by the veterinary technician, and the postexamination saliva sample was collected by the veterinarian in the same manner as in the preexamination phase.

**Greeting test—**A modification of the greeting test from Lind et al2 was scored by a veterinary technician at the end of the pre- and postexamination phases. The veterinary technician opened the door and kneeled at the entrance. If the dog approached, three 5-second-long pettings were given to the dog on its chest, 5 seconds apart. If the dog did not approach the technician, she calmly approached the dog from its right side, knelt 0.9 m away, then attempted to pet the dog. A standardized score between 1 and 5 was recorded, with 1 indicating that the dog rejected or avoided the greeting and 5 indicating that the dog showed intense greeting behaviors. Dogs that did not approach the technician but stayed next to or under their owner’s chair were automatically scored 1.

**Infrared thermography—**Remote eye surface temperature images were taken by use of a portable infrared thermography (IRT) camera (RAZ-IR NANO; SPI Corp.). The images were taken by the veterinary technician following the description in a previous study.57 The maximum eye surface temperature was chosen as the IRT target on the basis of information derived from previous studies.2,10,57,58 Our pilot study during physical examination with the owner’s presence showed the significant correlation between the rectal and IRT temperatures. The maximum left eye surface temperature (°C) was measured and determined within a circular area traced around the eye by use of thermal imaging analysis software (Guide InAnalyser; Wuhan Guide Infrared Co Ltd).59

**Salivary cortisol concentrations—**Saliva samples were collected with a SalivaBio children’s swab (Salimetrics LLC), and the time interval between collection of the 2 samples was 10 to 15 minutes, as recommended in a previous study.60 The owners were requested to gently hold the dog’s body to allow collection of the saliva, and the saliva flow was stimulated by presenting the smell of treats. Each saliva collection was performed within 2 minutes to minimize the influence of the sample collection on cortisol concentrations.2,61

The samples were frozen at –80 °C until testing in the internal laboratory by use of a salivary cortisol ELISA kit (Salimetrics LLC).

**Behavior recording and analysis—**The behaviors of the dogs were recorded during all 3 phases of both treatment sessions. In the waiting room, the recording was performed with a wall-mounted video camera at a height of 3 m, oriented toward the dog’s body. The location of the camera and its lens angle covered the entire area within the dog’s reach. A backup video camera was located on the floor, directly below the wall-mounted video camera. In the examination room, 2 cameras were placed 1 m apart from each other. Each camera was able to capture the dog’s face and the side of its body relative to its location. For the analysis, the recordings from the camera located at an angle to the right of the dog were primarily used, while the second camera served as a backup.

All recorded behaviors, on the basis of ethograms adapted from Csoltova et al2 and Beerda et al62 (Appendices 2 and 3), were coded as either a state (duration in seconds) or an event (frequency) with BORIS software.62

The room was divided with adhesive tape by means of taping the floor into 6 equally sized squares. Zones A and B were on the side of the room where the owner was sitting and the tether was connected. Zones E and F were the furthest from the owner and were adjacent to the entry door to the examination room. Zones C and D were located in the middle of the room. For the statistical calculation, the durations the dog spent in zones A and B, zones C and D, and zones E and F were combined, as they represented the same distance from the owner.

Interrater reliability was assessed by use of 2 independent coders for random samples of the recorded videos (10%) using the Cohen κ test. The results were κ = 0.73, with P < 0.001, which was considered a substantially good level of agreement.

**Adverse events—**The owners were contacted via email 24 hours after each visit and were asked to describe any physical or behavioral abnormalities if they occurred, as well as the time of onset and duration of these abnormalities.

**Statistical analysis—**A Shapiro-Wilk test was used to assess the normality of all collected numerical study data. Summary statistics were expressed as mean ± SD (parametric) or median with range (nonparametric). The mean change (post-physical examination) in continuous variables, such as eye surface temperature, cortisol concentrations, and the duration of the behavior variables, was compared between the 2 treatment groups by use of a mixed-effects (repeated-measures) linear model, with the patient as a random effect and the treatment group and treatment order as fixed effects. The change (post-physical examination) in nonparametric variables—for example, the greeting test score—was compared between the 2 treatment groups by use of a mixed-effects proportional odds (ordinal logistic) model, with the patient as a random effect and the treatment group as a fixed effect. All analyses were performed with standard software (SAS Institute Inc) and 2-tailed tests; statistical significance was set at P < 0.05.
Results

Participants

Twenty-two dogs participated in the study and completed 2 treatment visits (placebo and gabapentin). Their mean age was 49.6 ± 23.1 months, and mean weight was 22.9 ± 5.7 kg. There were 10 males (45.5%), of which only 1 was intact, and 12 females (54.5%), of which 3 were intact. There were 8 mixed breeds, 3 Australian Shepherds, 2 Golden Retrievers, and 2 Labrador Retrievers, and the remaining 7 dogs were from 7 different breeds (Boxer, Greyhound, Shetland Sheepdog, German Shepherd Dog, American Staffordshire Terrier, English Bulldog, and Beagle). Eleven dogs received gabapentin, and 11 received the placebo at the initial visit. The χ² test comparison for the initial treatment groups did not differ in age, weight, or sex (P > 0.505). The treatment order was not a significant fixed effect in any of the analyses.

Greeting test score

Statistical analyses were performed by use of data from all 22 participants. The 11 dogs in the gabapentin treatment and 11 dogs in the placebo treatment showed no change in the greeting test score between the pre- and post–physical examination phases. The results are presented as the median range of the score change between the pre– and post–physical examination.

Changes in the scores of pre– and post–physical examination phases did not significantly differ between the gabapentin (0 [-1 to 2]) and placebo treatments (0 [-4 to 1]; P = 0.181). The score of the pre–physical examination phase did not significantly differ between the first visit (5 [1 to 5]) and the second visit (5 [1 to 5]; P = 0.484).

Infrared thermography

Data were only analyzed for images that were clear and had 2 time points at each visit. Sixteen participants were included in the analysis. Eye surface temperature changes between the pre- and post–physical examination phases did not significantly differ between gabapentin (0.28 ± 1.67 °C) and placebo (0.16 ± 1.62 °C; P = 0.894). Also, eye surface temperature in the pre–physical examination phase did not significantly differ between gabapentin (38.11 ± 1.41 °C) and placebo (39.74 ± 6.30 °C; P = 0.441), or in the post–physical examination phase between gabapentin (38.39 ± 1.50 °C) and placebo (39.90 ± 6.30 °C; P = 0.479).

Salivary cortisol concentrations

Five participants were excluded due to lack of adequate sample volume; hence, the remaining 17 participants were included in the analysis. Cortisol concentration changes between pre– and post–physical examination phases did not significantly differ between gabapentin (0.94 ± 4.18 µg/dL) and placebo (0.10 ± 0.47 µg/dL; P = 0.388).

Behavioral data

Videos were recorded for all 22 participants, but due to technical errors in the pre–physical examination phase during one of the visits of 1 participant, data were analyzed for 22 participants for the physical examination phase but for 21 participants for the pre– and post–physical examination phases.

Among all the anxiety-related behavioral variables that were measured during the physical examination phase, only the mean frequency of lip licking significantly differed between the treatment groups (P = 0.001). The frequency of lip licking in the participants that were administered a placebo (15.0 ± 14.7 times) was greater than in those administered gabapentin (9.8 ± 10.1 times). The duration and frequencies of all other measured behaviors were not significantly different (Table 1).

Table 1—Behavioral results for the dogs of this study.

<table>
<thead>
<tr>
<th>During physical examination phase</th>
<th>Placebo (Mean ± SD)</th>
<th>Gabapentin (Mean ± SD)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shake off</td>
<td>0 ± 0 times</td>
<td>0 ± 0.2 times</td>
<td>&gt; 0.198</td>
</tr>
<tr>
<td>Jump off</td>
<td>0.4 ± 0.9 times</td>
<td>0.8 ± 1.3 times</td>
<td>&gt; 0.198</td>
</tr>
<tr>
<td>Whine</td>
<td>0.4 ± 1.2 times</td>
<td>0.3 ± 0.9 times</td>
<td>&gt; 0.198</td>
</tr>
<tr>
<td>Growl</td>
<td>0.1 ± 0.4 times</td>
<td>0 ± 0 times</td>
<td>&gt; 0.198</td>
</tr>
<tr>
<td>Yawn</td>
<td>0.7 ± 0.8 times</td>
<td>1.1 ± 1.2 times</td>
<td>0.079</td>
</tr>
<tr>
<td>Lip licking</td>
<td>15.0 ± 14.7 times</td>
<td>9.8 ± 10.1 times</td>
<td>0.001</td>
</tr>
<tr>
<td>Pant</td>
<td>1.5 ± 1.4 min</td>
<td>1.4 ± 1.5 min</td>
<td>&gt; 0.198</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>During pre– and post–physical examination phase</th>
<th>Placebo (Mean ± SD)</th>
<th>Gabapentin (Mean ± SD)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yawn</td>
<td>2.14 ± 2.29 times</td>
<td>1.48 ± 1.63 times</td>
<td>0.099</td>
</tr>
<tr>
<td>Whine</td>
<td>12.10 ± 25.74 times</td>
<td>9.43 ± 14.88 times</td>
<td>0.529</td>
</tr>
<tr>
<td>Lip licking</td>
<td>16.5 ± 20.2 times</td>
<td>8.6 ± 12.4 times</td>
<td>0.004</td>
</tr>
<tr>
<td>Sit</td>
<td>0.80 ± 0.95 min</td>
<td>0.17 ± 0.32 min</td>
<td>0.008</td>
</tr>
<tr>
<td>Lying in sternal recumbency</td>
<td>9.55 ± 5.81 min</td>
<td>9.77 ± 5.08 min</td>
<td>0.686</td>
</tr>
<tr>
<td>Lying in lateral recumbency</td>
<td>0.77 ± 2.33 min</td>
<td>0.85 ± 2.04 min</td>
<td>0.845</td>
</tr>
<tr>
<td>Standing</td>
<td>6.83 ± 5.45 min</td>
<td>7.20 ± 4.99 min</td>
<td>0.210</td>
</tr>
<tr>
<td>Occupying zones A and B</td>
<td>10.59 ± 6.12 min</td>
<td>11.35 ± 5.59 min</td>
<td>0.406</td>
</tr>
<tr>
<td>Occupying zones C and D</td>
<td>5.01 ± 5.06 min</td>
<td>4.38 ± 4.27 min</td>
<td>0.519</td>
</tr>
<tr>
<td>Occupying zones E and F</td>
<td>2.03 ± 3.98 min</td>
<td>2.04 ± 2.67 min</td>
<td>0.985</td>
</tr>
<tr>
<td>Sniff</td>
<td>1.99 ± 1.46 min</td>
<td>2.38 ± 0.95 min</td>
<td>0.233</td>
</tr>
<tr>
<td>Pant</td>
<td>4.02 ± 4.38 min</td>
<td>3.86 ± 4.49 min</td>
<td>0.845</td>
</tr>
</tbody>
</table>
The duration or frequencies of the location, posture, and anxiety-related behaviors during the pre- and post-physical examination phases were summed to express the overall experience of the veterinary visit. Changes in the means, which mainly represented the effect of the physical examination phase, were also examined. The 2 behavioral variables were significantly different between the treatment groups. The total duration of the sitting posture in the waiting room (ie, the sum of the pre- and post-physical examination phases) was 0.17 ± 0.32 minutes for the gabapentin treatment group; this was significantly different from that of the placebo treatment group, which was 0.80 ± 0.95 minutes (P = 0.008). The total frequency of lip licking in the waiting room (ie, the sum of the pre- and post-physical examination phases) for the gabapentin treatment group was 8.6 ± 12.4 times; this was significantly different from that of the placebo treatment group, which was 16.5 ± 20.2 times (P = 0.004). The durations and frequencies of all other measured behaviors were not significantly different (Table 1).

Adverse events

While no adverse symptoms were reported by the owners in the placebo treatment group, mild sedation was reported in 7 dogs from the gabapentin treatment group (50 mg/kg). The onset of sedation commenced between 2.5 and 3.5 hours after administration and resolved within 1.5 to 4 hours. One of the dogs vomited once 15 minutes after gabapentin administration. Another dog had mild ataxia 4 hours after administration of gabapentin that lasted for 3 hours, and a third dog had increased activity 7 hours after gabapentin administration that lasted for 3 hours. None of the owners requested withdrawal from the study.

Discussion

The goal of this study was to evaluate the effects of a single dose of orally administered gabapentin on alleviating stress, as measured by behavioral and physiological variables at a veterinary visit in dogs. No significant differences in physiological variables were found (salivary cortisol concentrations and eye surface temperature) between the placebo and gabapentin treatments. However, a significant reduction in the behavior variable of lip licking frequency was observed in the gabapentin treatment group during the physical examination phase and the total frequency in the pre- and post-physical examination phases, supporting our hypothesis. Lip licking is considered to be a sign of anxiety in dogs, and its frequency increases in response to different stressful stimuli, such as sound blasts, short electric shocks, restraint, negative facial expressions of people, and veterinary examinations. Several factors could be attributed to the insufficient stimulus intensity. Previous studies have shown that salivary cortisol concentrations in dogs are not affected by stressful stimuli in the presence of their owners or caretakers. Recent studies have shown that the presence of owners during the veterinary examination is associated with fewer stress signs and lower physiological signs. The results also showed that other factors, such as the location and environment of the examination room, could impact the level of stress response.

Despite several variable measurements of behavior and physiological responses in this study, significant differences were only observed in limited variables. These results may have been affected by the selection criteria of the participants. Since veterinary visits are stressful events for the majority of dogs, our inclusion criteria did not limit dogs that were known to be stressed during a veterinary visit. However, if we had recruited only stress-affected dogs, the result might have indicated notable differences between the placebo and gabapentin treatment groups.

In a study of cats, Hudec and Griffin speculated that the lack of significant effects of gabapentin on cortisol and glucose concentrations can be explained by its sedative effects being responsible for its stress-alleviating effects rather than its hypothalamic-pituitary-adrenal axis effects. If this was the case in dogs, the anxiolytic effects of gabapentin may not be indicated by cortisol concentrations. Since only mild sedation was observed by a few owners in this study, we could not confirm this possibility, and further research is needed to investigate the association between the observed behavioral efficacy and physiological variables in dogs treated with gabapentin.

Additionally, if we had monitored more physiological variables that reflect the sympathetic-adrenal-medullary reactivity in addition to eye surface temperature, the results might have been different. Sympathetic-adrenal-medullary reactivity is known to be faster. Through its effect on the adrenal medulla and the autonomic nervous system, catecholamine release leads to vasoconstriction in minute blood.
vessels. Other parameters, such as heart rate, heart rate variability, respiratory rate, and glycolysis rate, may reflect sympathetic-adrenal-medullary reactivity, and all of these physiological changes are part of the body’s preparation for the fight or flight response.50

The primary symptoms of gabapentin overdose in dogs, as reported by the American Society for the Prevention of Cruelty to Animals Poison Control Center, are ataxia, lethargy, and vomiting.50 In this study, there were some adverse symptoms reported in the gabapentin group that received a 50-mg/kg dose; however, none of them were severe to the point of withdrawal of the subject from the study. Although the owners perceived these signs to be insignificant, we confirmed that all symptoms resolved within a few hours after onset.

The gabapentin used in this study was compounded from USP-grade bulk substance, gabapentin USP API obtained from Professional Compounding Centers of America, a licensed vendor that subjects the gabapentin product to at least 4 rounds of testing to verify and validate identity and purity and provides a certificate of analysis for the quality of the product. Since the study required an individual body weight for each study dog that could not be provided by the commercial product, Purdue Veterinary College Pharmacy needed to assure the final potency of the compound. The most reliable method to accomplish this was to use gabapentin USP API instead of commercial gabapentin capsules. That being said, it needs to be determined that our results are consistent with those of studies that used commercial gabapentin products. Whenever possible in a clinical setting, commercially prepared products are preferred. With gabapentin, multiple dosage strengths are commercially available, and combinations of these strengths can easily accommodate a wide range of doses in clinical cases.

Results of this study indicated a significant decrease in stress signs (eg, a reduction in the frequency of lip licking during a physical examination and in the total frequency of lip licking in the pre- and post-physical examination phases) in dogs administered gabapentin compared to those administered a placebo. Our study showed the 50-mg/kg dose was well tolerated without serious adverse effects in healthy dogs. Since no other variable was significantly different between the 2 treatments, further studies should confirm the effect of gabapentin as a potential preappointment medication. Conducting a further study of dogs with documented stress to a veterinary visit is recommended.

Acknowledgments

This project was supported by Fear Free Veterinary College Research Grants and the Purdue University-Veterinary Clinical Sciences Graduate Competitive Research Fund. The authors declare that there were no financial or professional conflicts of interest. The authors thank Melinda Sue Cotton for her invaluable help in the data collection and Lacey Rae Schram for assistance with analyzing the videos and assisting with the cortisol assays. The authors also thank the Purdue Veterinary College Pharmacy department for making and blinding the treatment capsules.

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Continued on next page.
Appendix 1
Standardized physical examination.
1. Three gentle strokes from the neck to the base of the tail.
2. A hand placed over the inner right thigh pulse point for 30 s.
3. A stethoscope placed against each side of the chest for 30 s.
4. Gentle abdominal palpation for 30 s.
5. Paws lifted and examined for 5 s in the order of right and then left hind limb, followed by right and then left forelimb.
6. Right, then left ear flaps lifted for 5 s each.
7. Rectal thermometer placed in position until sound indicated the completion of the measurement.

Appendix 2
Ethogram during the pre- and post-physical examination phases.

<table>
<thead>
<tr>
<th>Posture</th>
<th>Behavior description</th>
<th>Measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sit</td>
<td>Dog sits on hindquarters with front legs used as support for &gt; 2 s</td>
<td>Duration</td>
</tr>
<tr>
<td>Lie: sternal recumbency</td>
<td>Dog lies with sternum touching the ground and hind legs on either side of the body, with head on the floor or not on the floor for &gt; 2 s</td>
<td>Duration</td>
</tr>
<tr>
<td>Lie: lateral recumbency</td>
<td>Side of dog touching the floor completely for &gt; 2 s</td>
<td>Duration</td>
</tr>
<tr>
<td>Stand</td>
<td>Dog is upright on all 4 legs for &gt; 2 s</td>
<td>Duration</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Location in room</th>
<th>Behavior description</th>
<th>Measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zone A</td>
<td>Dog’s front half of body (past both front legs) in the left-hand corner of the room furthest from the camera for &gt; 2 s</td>
<td>Duration</td>
</tr>
<tr>
<td>Zone B</td>
<td>Dog’s front half of body (past both front legs) in the right-hand corner of the room furthest from the camera for &gt; 2 s</td>
<td>Duration</td>
</tr>
<tr>
<td>Zone C</td>
<td>Dog’s front half of body (past both front legs) in the left-hand middle zone of the room (midway between the camera and the wall on the opposite side) for &gt; 2 s</td>
<td>Duration</td>
</tr>
<tr>
<td>Zone D</td>
<td>Dog’s front half of body (past both front legs) in the right-hand middle zone of the room (midway between the camera and the wall on the opposite side) for &gt; 2 s</td>
<td>Duration</td>
</tr>
<tr>
<td>Zone E</td>
<td>Dog’s front half of body (past both front legs) in the left-hand corner of the room closest to the camera for &gt; 2 s</td>
<td>Duration</td>
</tr>
<tr>
<td>Zone F</td>
<td>Dog’s front half of body (past both front legs) in the right-hand corner of the room closest to the camera for &gt; 2 s</td>
<td>Duration</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Body language/activity</th>
<th>Behavior description</th>
<th>Measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yawn</td>
<td>Dog involuntarily takes a breath through a wide-open mouth</td>
<td>Frequency</td>
</tr>
<tr>
<td>Sniff</td>
<td>Nose to ground/object/air and sides of body are moving rapidly in and out for &gt; 2 s</td>
<td>Duration</td>
</tr>
<tr>
<td>Pant</td>
<td>Dog’s mouth is open and dog takes rapid breaths for &gt; 2 s</td>
<td>Duration</td>
</tr>
<tr>
<td>Lip licking</td>
<td>Dog’s tongue curls up to touch the outer side of the lip or nose</td>
<td>Frequency</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Vocalization</th>
<th>Behavior description</th>
<th>Measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whine</td>
<td>Dog generates whining sound (episode starts/ends when there is a ≥ 5-s interval between vocalization)</td>
<td>Frequency</td>
</tr>
</tbody>
</table>

Appendix 3
Ethogram during the physical examination phase.

<table>
<thead>
<tr>
<th>Body language/activity</th>
<th>Behavior description</th>
<th>Measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shake off</td>
<td>Dog rotates head and body rapidly for ≤ 3 s</td>
<td>Frequency</td>
</tr>
<tr>
<td>Yawn</td>
<td>Dog involuntarily takes a breath through a wide-open mouth</td>
<td>Frequency</td>
</tr>
<tr>
<td>Jump off</td>
<td>Dog tries to jump off or escape from the examination table</td>
<td>Frequency</td>
</tr>
<tr>
<td>Pant</td>
<td>Dog’s mouth is open and dog takes rapid breaths for &gt; 2 s</td>
<td>Frequency</td>
</tr>
<tr>
<td>Lip licking</td>
<td>Dog’s tongue curls up to touch the outer side of the lip or nose</td>
<td>Frequency</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Vocalization</th>
<th>Behavior description</th>
<th>Measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whine</td>
<td>Dog generates whining sound (episode starts/ends when there is a ≥ 5-s interval between vocalization)</td>
<td>Frequency</td>
</tr>
<tr>
<td>Growl</td>
<td>Dog generates growling sound (episode starts/ends when there is a ≥ 5-s interval between vocalization)</td>
<td>Frequency</td>
</tr>
</tbody>
</table>