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Single oral dose of gabapentin reduces vigilance and increases play behavior without changing mobility in New Zealand white rabbits (*Oryctolagus cuniculus*)

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OBJECTIVE
To evaluate rabbit behavioral responses and activity after gabapentin administration.

METHODS
In this study, 5 intact female and 3 intact male New Zealand white rabbits aged 8 to 12 months were administered a single oral 25-mg/kg dose of gabapentin. This study was conducted from December 2020 to February 2021. Effects on individual behavior, posture, and motor activity were evaluated with ANY-maze software (video tracking system) and ethograms. Rabbits were assessed 2 hours after gabapentin administration. Rabbits were acclimated to the assessment pen for 3 days prior to testing, and baseline measurements (control) were assessed 1 day prior to the first gabapentin administration. Treatment was performed 3 times daily, with each rabbit given gabapentin once a day for morning, midday, and late afternoon doses. Treatments were repeated with a 1-week interval period in between until all rabbits had received dosing at all 3 time periods. Data were analyzed as continuous with a linear mixed model.

RESULTS
There was a significant increase in frolicking behavior and significant decrease in observing behavior between baseline and after gabapentin administration. There was no significant change in other rabbit behaviors, postures, or motor patterns.

CONCLUSIONS
Results indicated that oral gabapentin at 25 mg/kg increased play (frolicking) and decreased vigilance (observing) behaviors without significantly affecting motor patterns, suggesting that this dose reduced stress-associated behaviors without causing excessive sedation.

CLINICAL RELEVANCE
Oral gabapentin appears to reduce fear and anxiety in rabbits in a controlled environment. This shows promise for its ability to reduce stress with veterinary visits, transport, and other stressful events.

Keywords: behavior ethogram, gabapentin, *Oryctolagus cuniculus*, rabbit, stress

Gabapentin is a γ-aminobutyric acid analogue, binding with high affinity to the α2-delta subunit of voltage-activated Ca^{2+} channels.[1] Gabapentin has many different clinical uses, but most pertinent to this study is its anxiolytic properties in multiple species including humans, cats, dogs, and horses.[2–8] A single dose of gabapentin has been shown to reduce stress behaviors in both cats and dogs in a variety of settings.[4–8] The pharmacokinetics of gabapentin in rabbits (*Oryctolagus cuniculus*) were recently published, as well as a pharmacodynamic study demonstrating that gabapentin had an effect on reducing the rabbit stress response to humans.[9,10]

The domestic rabbit plays a dual role in veterinary medicine as both a popular companion species

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and a useful laboratory model.[11–13] Rabbits are a prey species, with associated high anxiety levels, and often demonstrate stress behaviors both in novel environments and in the presence of humans.[14–17] This stress response can have consequences varying from altering the physical examination to life-threatening illnesses like gastrointestinal stasis and instability under anesthesia.[16–20] This constitutes a major health and welfare issue, as car rides, veterinary hospitals, and handling as part of the physical examination are all likely to trigger this stress response.[18]

Ethograms are defined as a list of behaviors exhibited by a species using descriptive terms and phrases.[21–23] Ethograms have been developed to evaluate stress and pain in both rodents and rabbits, as well as assess the effects of enrichment on behavior in both laboratory and companion animals.[16–17,24–29]

An important aspect of the evaluation of drugs used to reduce stress is an evaluation of sedation, which can be assessed with multiple modalities including mobility. An increasingly utilized method of examining mobility in rodents and rabbits is the use of the ANY-maze behavioral tracking software (Stoetling Co). This software is commonly used in laboratory animal medicine for assessing locomotion and anxiety and has been used in rats, mice, and guinea pigs.[30–32] ANY-maze has not previously been utilized in published studies of rabbits, with searches on PubMed and Google Scholar for ANY-maze and rabbits yielding no results.

The first objective of this study was to evaluate rabbit behavioral responses after gabapentin administration to assess for changes in stress-related behaviors. The second objective was to demonstrate whether gabapentin had any significant effect on rabbit activity by assessing mobility. Finally, we wished to validate the ANY-Maze software in rabbits. The hypotheses of the study were that gabapentin would reduce stress-related behaviors, increase nonstress behaviors, and cause sedation as assessed by decreased mobility.

Methods

Animals

Five female and 3 male New Zealand white rabbits aged 8 to 12 months and weighing 3 to 4.5 kg were utilized for this study. The number of 8 rabbits was selected on the basis of available funding. Rabbits were purchased from a commercial vendor (Western Oregon Rabbit Co). All rabbits were considered healthy on the basis of results of a physical examination. Rabbits were singly housed in standard laboratory rabbit caging systems (Allentown Inc) maintained in a climate-controlled room with a 12:12-hour light cycle and temperatures ranging from 20 to 23 °C. They received ad libitum municipal tap water via a water bottle, ad libitum pelleted diet (Teklad 2031 High Fiber Rabbit Diet; Envigo Inc) in a pellet hopper, and a handful of loose orchard grass hay (Standlee Hay Company Inc) provided once daily. The study was approved by the institution's animal care and use committee.

Acclimation

All rabbits were housed in the facility for a minimum of 1 month and maximum of 6 months prior to testing. All rabbits were placed into the behavior assessment pen twice daily for 3 consecutive days immediately before baseline data collection. Pen dimensions were 1.2 X 1.2 m, with a nonslip floor. The pen walls were made of transparent plastic and were approximately 0.9 m high **(Figure 1)**. Rabbits were placed into the pen between 07:00 and 11:00 for a minimum of 30 minutes, returned to their home enclosure, and then the process was repeated between 14:00 and 17:00.

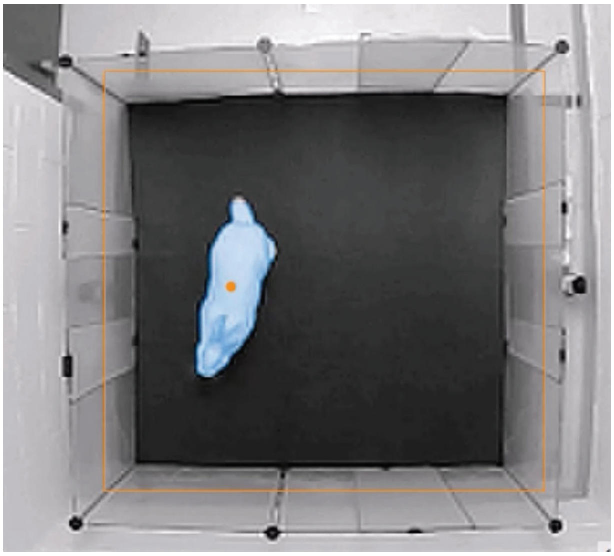

Figure 1—Behavior assessment pen setup for ANY-Maze and behavioral ethogram testing in 8 New Zealand white rabbits to assess rabbit behavior before and after gabapentin administration. Pen dimensions were 1.2 X 1.2 m, with a nonslip floor. The pen walls were made of transparent plastic and approximately 0.9 m high. Rabbits were placed into the pen for 30 minutes twice a day in the 3 days leading up to the testing period for acclimation. Rabbits were then placed inside the pen for 10-minute testing intervals 2 hours after randomized gabapentin administration.

Data collection

Data collection took place over a 3-month period between December 2020 and February 2021. Rabbits were assessed with a randomized, blinded, crossover study design that simulated morning, midday, and late afternoon veterinary appointments. There is evidence that time of day influences rabbit behavior, and this method was used to remove time of day as a confounding factor.[24,27] All rabbits were tested at each time point during their treatment period and randomly assigned a dosing time for each day with an online randomizer (www.randomizer.org). Each treatment day was performed 3 times, with a week interval period in between, allowing for each rabbit to be administered gabapentin for a morning, midday, and late afternoon dose **(Figure 2)**. Morning drug administration occurred at 07:00, midday at 11:00, and late afternoon at 15:00. The testing timeline can be visualized in **Figure 3**.

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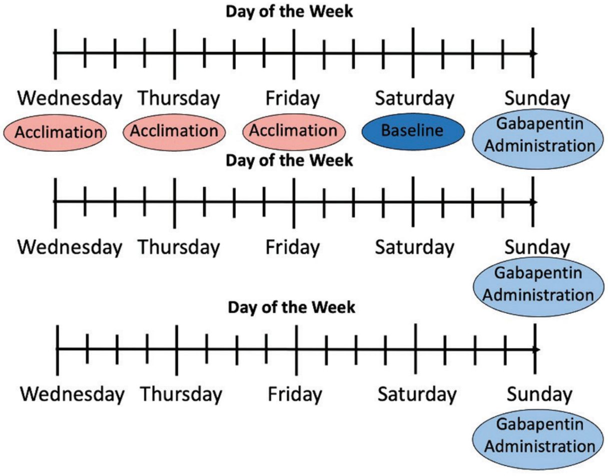

Figure 2—Timeline of acclimation and testing used in 8 New Zealand white rabbits to assess rabbit behavior before and after gabapentin administration. Rabbits were first acclimated to the environment for 3 days before the study began. Baselines were collected the day before gabapentin was first administered. Rabbits were administered 1 dose per day and were allocated the time of day that they were given gabapentin in a randomized fashion. Each rabbit was dosed a total of 3 times in a crossover design to ensure that they got a dose at each time point, with a week interval between doses.

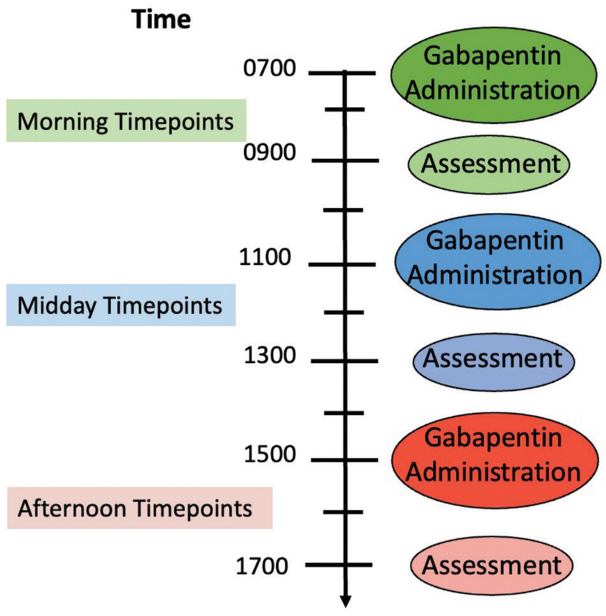

Figure 3—Daily testing timeline used in 8 New Zealand white rabbits to assess rabbit behavior before and after gabapentin administration. To examine the effects of gabapentin, rabbits were given a single oral dose of gabapentin at 25 mg/kg (compounded to 100 mg/mL, approx 1 mL given to each rabbit). Weaver et al[24] had shown that rabbit behavior was influenced by the time of day, and therefore 3 different times of day were elected to assess the rabbits. Rabbits were dosed once per day at either the morning, midday, or afternoon time point, which is outlined on the figure. Rabbits were assessed 2 hours after administration of gabapentin. For assessment, each rabbit was placed into a 1.2 X 1.2-m pen with cameras on either side and above the pen to record.

Rabbits were administered gabapentin at 25 mg/kg PO via syringe. No placebo was administered. The dose of gabapentin was selected from a previous pharmacokinetic study of rabbits.[9] Gabapentin oral suspension (100 mg/mL) was prepared according to USP standards for use in this study.[33–36] Gabapentin USP powder (Medisca Inc) was mixed with equal amounts of a flavored suspending vehicle (Ora-Blend; Perrigo Co) to form a base suspension. The gabapentin powder was added to the base suspension in increasing amounts and then added quantum sufficit to achieve the desired volume. The final concentration strength of the gabapentin suspension was 100 mg/mL. The final product was stored in an amber-colored bottle to protect it from light, stored at 4°C during the study, and followed the beyond-use date guidelines of the USP.

Physiologic parameters and additional behavior assessments (human intruder test and tractability) were measured at 1-, 2-, and 4-hour time points after drug administration; findings from these assessments are published elsewhere.[10] The ANY-maze and behavioral assessments were conducted 2 hours after gabapentin administration. Baselines of all assessments were conducted following the same timeline the day before the first dosing so that rabbits could act as their own controls. The same blinded observer recorded all behavioral assessments for all rabbits. All rabbits were tested at each time point, regardless of whether they were administered gabapentin, to keep the observer blinded. Two handlers were utilized for the duration of the study and were not blinded to the treatments.

Behavioral assessment

Behavioral assessment was performed with the use of both ANY-maze testing and ethogram evaluation. The ANY-maze evaluated mobility parameters, and the ethogram was utilized to record behavior. Subjective observations (visual observances) were also recorded. The ethogram was implemented via a computerized monitoring software, Zoomonitor (version 4.1; Lincoln Park Zoo). Rabbits were alone in the room during testing times and monitored live via 2 video cameras (Nest; Google) that were set up on either side of the behavior assessment pen facing each other. One camera was primarily utilized, and the other was used as a backup in case of technological issues. There was an additional camera above the pen for an overhead view. Each behavioral assessment lasted 10 minutes, with the first 30 seconds removed from analysis to allow time for handlers to exit the room. Behavioral assessments were conducted at the peak drug concentration, which was determined by a previous pharmacokinetic study[9] and corresponded to 09:00, 13:00, and 17:00.

The ethogram was developed with reference to Weaver et al,[24] Krall et al,[16] and Leach et al[25] and was tailored to focus on behaviors that were relevant to the stress response. Therefore, it is better described as a partial ethogram, as it does not include every single rabbit behavior, but it is referred to as an ethogram for the rest of the manuscript for simplicity. Focal scan sampling was used to record state behavior or activity (exploring, grooming, resting, observing, nonvisible) and posture (sitting, lying down, moving,

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sprawled, standing) at 15-second intervals. All occurrences of the following behavioral events (frolicking, rearing, and thumping) were recorded through focal continuous sampling. All behaviors are further defined in **Table 1**. This ethogram was validated with intraobserver and interobserver testing.

For ANY-maze testing, each rabbit was placed into the behavior assessment pen, with a camera above the pen providing video for the program to assess. This test evaluated the rabbit's mobility parameters (distance traveled; mean, minimum, and maximum speed; time mobile vs immobile; and number of mobile vs immobile episodes). Descriptions of each parameter can be found in **Table 2**. The test was started immediately to maximize the ANY-maze's ability to track the animal (based on motion); however, no motion analysis was collected during the first 30 seconds to remove any bias in the rabbits' behavior in response to humans. Parameters were then analyzed and calculated with the ANY-maze program.

Statistical analysis

Baselines, which served as controls, were collected the day prior to the first day of testing and compared to the rabbits' behavior 2 hours after gabapentin administration. All time budgets, instantaneous behaviors, and mobility parameters were analyzed as continuous data, with mean and 95% confidence limits. All continuous data were evaluated for normality assumption with a Shapiro-Wilk test. If normality was not met, log transformation was performed prior to analysis and median and range were reported. Linear mixed models were used to compare continuous data between baseline and time points after gabapentin administration. The analysis was adjusted for the subject as random effect. The least-square means and 95% confidence limits were reported. All analyses were performed with SAS (version 9.4; SAS Institute Inc). A P value ≤ .05 was set as the criterion to determine statistical significance.

Table 1—Partial ethogram used in 8 New Zealand white rabbits to assess rabbit behavior before and after gabapentin administration.

Activity: focal sampling every 15 seconds	
Grooming	Rabbit uses its paw or mouth to groom any part of its body in a calm manner. Scratching is included in this category.
Exploring	Rabbit actively moving around the enclosure, sniffing or chewing, digging, shaking, rearing, frolicking, standing on 4 legs, or taking a single step forward without ambulation.
Resting	Rabbit sitting still, lying down, potentially sleeping, but not moving around or grooming.
Observing	Rabbit has a tense posture and is actively vigilant, either immobile or looking around.
Nonvisible	If the observer cannot confidently determine the behavior of the rabbit (ie, in a camera blind spot).
Posture: focal sampling every 15 seconds	
Sitting	Rabbit is fully balanced on pelvic limbs, forelimbs, or both. Can have forelimbs in flexion or extension, pelvic limbs in flexion
Lying down	Rabbit lying with pelvic limbs tucked under the rump and forelimbs extended horizontally in front of the body.
Moving	Rabbit actively moving around the enclosure or is taking a single step forward without ambulation.
Sprawled	Rabbit reclined in half-lateral recumbency; pelvic limbs, forelimbs, or both are extended horizontally. Pelvic limbs can be extended behind the animal or to the side.
Standing	Rabbit is standing on all 4 limbs.
Instantaneous: marked as occurred	
Rearing	Rabbit up on pelvic limbs, neither forelimb is touching the ground, supported or unsupported.
Thumping	An alarm behavior in which the pelvic feet are stamped on the floor.
Frolicking	Rabbit hops or jumps rapidly and flings pelvic limbs from one side to the other.

Developed with reference to Weaver et al,[24] Krall et al,[16] and Leach et al.[25] It was adapted to focus on behaviors that are relevant to the rabbit stress response. The activity and posture of the rabbit were focally sampled with a scan every 15 seconds, and instantaneous behaviors were marked as they occurred (continuously sampling).

Table 2—ANY-Maze mobility parameters assessed in eight New Zealand white rabbits to assess mobility in rabbits before and after gabapentin administration.

Parameter	Description
Distance (m)	Reports the total distance that the animal traveled during the test.
Mean speed (m/s)	Reports the average speed of the animal during a test.
Max speed (m/s)	Reports the maximum speed of the animal.
Time mobile (s)	Reports the amount of time the animal was mobile during the test.*
Time immobile (s)	Reports the amount of time the animal was immobile during the test.
Mobile episodes	Reports the number of times the animal was mobile during the test.
Immobile episodes	Reports the number of times the animal was immobile during the test.

Distance, mean and maximum speed, time mobile, time immobile, and the number of mobile versus immobile episodes were compared before and after gabapentin was administered. All parameters were measured and calculated with the ANY-maze program, which uses a camera to track motion of the rabbit to assess these values. Definitions were taken directly from the ANY-maze manual.[46]

*Forward motion, not vertical motion.

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Results

Data were analyzed initially with time of day as a factor, which yielded no significant results ($P > .05$). Thus, it was determined that the time of day was not a significant factor, and the data were pooled for analysis.

There were no adverse effects observed in any rabbits after gabapentin administration. Three rabbits had minor medical conditions during the study period, including a mild forelimb lameness, mild gastrointestinal hypomotility, and discolored urine. These conditions self-resolved within a few days and did not appear to be directly related to the study. There was 1 rabbit that repeatedly broke out of the pen during assessments, and the tests had to be paused and restarted.

There was no significant difference between baseline and after gabapentin administration in distance traveled ($P = .33$; 95% CI, 0.84 to 1.70), mean speed ($P = .33$; 95% CI, 0.83 to 1.70), or maximum speed ($P = .43$; 95% CI, 0.93 to 1.19). There was no significant difference in the time rabbits were mobile ($P = .41$; 95% CI, 0.82 to 1.64) or immobile ($P = .36$; 95% CI, 0.97 to 1.01), or the number of mobile ($P = .17$; 95% CI, 0.93 to 1.46) and immobile ($P = .17$; 95% CI, 0.93 to 1.46) episodes between baseline and after gabapentin administration. Detailed results for mobility are presented in **Table 3**.

There was a significant increase in the mean number of occurrences of frolicking between baseline and treatment with gabapentin ($P = .0001$; 95% CI, 1.76 to 4.99). There was a significant decrease in the percent of time spent observing ($P = .049$; 95% CI, –0.099 to –0.00019) between baseline and after gabapentin administration. There was no significant difference in all other activity parameters (exploring [$P = .68$; 95% CI, –0.058 to 0.089], grooming [$P = .68$; 95% CI, 0.70 to 1.73], being nonvisible [$P = .76$; 95% CI, 0.40 to 1.95], and resting [$P = 0.36$; 95% CI, 0.39 to 1.42]). There was no difference in rabbit posture (percent time spent standing [$P = .90$; 95% CI, 0.63 to 1.51], sitting [$P = .56$; 95% CI, –0.054 to 0.099], lying down [$P = .47$; 95% CI, 0.72 to 1.99], moving [$P = .84$; 95% CI, 0.67 to 1.38], or being nonvisible [$P = .60$; 95% CI, 0.36 to 1.81]) after gabapentin administration. There was no significant difference in the number of rears between baseline and with gabapentin ($P = .52$; 95% CI, 0.75 to 1.76). Sprawling could not be analyzed due to infrequent occurrence. Thumping could not be accurately assessed, as the sound on the videos was intermittent, and was therefore not analyzed. Detailed behavior results are presented in **Table 4**.

Table 3—ANY-maze mobility results in 8 New Zealand white rabbits at baseline and after gabapentin administration.

	Baseline			After gabapentin administration				
Test parameter	**Median**	**Min**	**Max**	**Median**	**Min**	**Max**	**95% CI**	***P* value**
Distance (m)	11.48	0.29	28.72	10.48	0.59	55.38	0.84–1.7	.33
Mean speed (m/s)	0.020	0.0053	0.050	0.018	0.0010	0.097	0.83–1.70	.33
Max speed (m/s)	0.87	0.44	1.53	0.92	0.30	2.09	0.93–1.19	.43
Time mobile (s)	35.85	0.40	101.40	32.25	2.10	111.80	0.82–1.64	.41
Time immobile (s)	534.20	468.60	569.60	537.75	458.20	567.90	0.97–1.01	.36
Mobile episodes	31.50	3.00	68.00	32.50	7.00	72.00	0.93–1.46	.17
Immobile episodes	32.00	3.00	68.00	32.50	7.00	72.00	0.93–1.46	.17

Lack of significant difference in any parameter was interpreted as gabapentin having no influence on rabbit mobility. *P* values listed are for a linear mixed model that compared baseline parameters to after gabapentin administration. Medians are reported, as the data did not meet the criteria for normality. A P value ≤ .05 was set as the criterion to determine statistical significance.

Table 4—Partial ethogram results in 8 New Zealand white rabbits at baseline and after gabapentin administration.

	Baseline				After gabapentin administration					
Test parameter	**Mean**	**Median**	**Range**	**SD**	**Mean**	**Median**	**Range**	**SD**	**95% CI**	***P* value**
Activity time budget (%)										
Exploring	0.30	—	—	0.17	0.31	—	—	0.18	−0.058 to 0.089	.68
Grooming	—	0.18	0.00 to 0.38	—	—	0.08	0.32 to 0.65	—	0.70 to 1.73	.68
Nonvisible	—	0.00	0.00 to 0.19	—	—	0.00	0.00 to 0.16	—	0.40 to 1.95	.76
Observing	0.38	—	—	0.14	0.33	—	—	0.14	−0.099 to 0.0019	.049*
Resting	—	0.054	0.00 to 0.57	—	—	0.081	0.00 to 0.84	—	0.39 to 1.42	.36
Posture time budget (%)										
Lying down	—	0.00	0.00 to 0.51	—	—	0.00	0.00 to 0.76	—	0.72 to 1.99	.47
Moving	—	0.14	0.027 to 0.41	—	—	0.16	0.00 to 0.41	—	0.67 to 1.38	.84
Nonvisible	—	0.00	0.00 to 0.19	—	—	0.025	0.00 to 0.16	—	0.36 to 1.81	.60
Sitting	0.55	—	—	0.19	0.57	—	—	0.23	−0.054 to 0.099	.56
Standing	—	0.14	0.00 to 0.43	—	—	0.16	0.00 to 0.38		0.63 to 1.51	.90
Instantaneous behaviors										
Frolicking	—	0.00	0.00 to 12	—	—	6.50	0.00 to 26	—	1.76 to 4.99	.0001*
Rearing	—	9.00	0.00 to 38	—	—	10.00	0.00 to 57	—	0.75 to 1.76	.52

Frolicking, exploring, grooming, and resting were considered nonstress behaviors, and observing, rearing, and thumping were considered stress behaviors. Posture was evaluated to further analyze generic behaviors, such as exploring and resting. The *P* values listed are for a linear mixed model that compared baseline parameters to after gabapentin administration. A P value ≤ .05 was set as the criterion to determine statistical significance. Means and SDs are reported if normality was met, and median and range are reported if normality was not met.

*Statistically significant.

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Discussion

The results of this study indicate that gabapentin, when administered as a single 25-mg/kg oral dose, may have some stress-reducing effects on rabbit behavior. This was suggested by the increase in frolicking behavior and decrease in observing behavior. We defined frolicking as a behavior colloquially referred to as "binkying," in which rabbits run and leap into the air, kicking their pelvic feet, or leap off the ground with all 4 feet. It is an indication of excitement or play.[37,38] Increases in play behavior indicate a decrease in stress response, as fear and stress typically repress these behaviors.[27] Hansen and Berthelson[27] discussed this behavior as similar to bucking in cows and horses, suggesting a low level of timidity. The behavior "observing" is an analog for vigilance behavior and included both freezing and scanning behaviors. Rabbits, as a prey species, tend to freeze and listen in response to any sort of danger, as well as pause and scan an area when threatened.[27,39,40–42] The combined findings of increased play and decreased vigilance suggest that gabapentin had an effect to reduce this stress response in rabbits.

Exploring was defined and analyzed in the same way as suggested in the study by Coda et al,[26] which expressed it as actively exploring the environment through motion, sniffing, chewing, standing, digging, rearing, and frolicking. Coda et al[26] analyzed exploring as an increase in curiosity/stimulation and therefore an increase in animal welfare. Exploring did not change when gabapentin was introduced and could be inferred as a lack of effect on rabbit stress response, or a limit to its effects. However, with the limited sample size and small area of the behavior assessment pen, it is possible that if more rabbits were assessed and/or a larger space were used, differences may have been appreciated.

Intimately tied to exploring is assessment of mobility, which can be analyzed in different ways. One interpretation is that it is an indication of stress, or searching for a way out.[27,39] Another interpretation, however, is that it is a sign of boldness and curiosity, and it may be considered as a sign of decreased stress. This study used the latter interpretation for rabbits since they are a prey species whose instinctual response to danger is to remain still; therefore, exploring and increases in mobility would indicate boldness and reduced stress.[39] Most importantly, a decrease in mobility may be associated with sedation, which is a side effect of gabapentin.[8] Given that one goal of this study was to help veterinarians be able to better assess rabbit behavior and illness, a drug that causes sedation and may mask signs of illness would not be ideal. However, on the basis of results of this study, when tracked with the ANY-Maze software, there was no significant difference in mobility in the rabbits with the administration of gabapentin, suggesting that this dose does not cause the confounding factor of excessive sedation. This is further supported by a lack of change in resting behavior, which would likely increase if there was a strong effect of sedation.

Grooming is a challenging behavior to analyze, as it can be interpreted in multiple ways. One interpretation is that it is a display of natural behavior, making up approximately 2% of a rabbit's daily activity period.[27] Therefore, an increase in grooming may be a sign of decreased stress, as an increase in display of natural behavior is interpreted this way when assessing animal welfare.[43] Another interpretation is that grooming is a response to a moderately stressful event, such as transport or a novel environment, and an increase in grooming behavior may be a stress response.[27,42] Grooming can also develop into an abnormal repetitive behavior, indicating stress or boredom in many animals, including rabbits.[26,37,44,45] Given that this behavior can be analyzed in several ways—and that it was performed in a laboratory setting, which may have been prone to stereotypy—this confounds the interpretation and makes it difficult to draw a firm conclusion from its lack of change after gabapentin administration.

Rearing is another behavior that is difficult to decipher, as it may be either a vigilance behavior (scanning for predators) or a curiosity/exploring behavior, and has been analyzed with both frameworks previously in mice tested in an open field.[30] Meijsser et al[39] determined that rearing in rabbits is a measure of boldness, as it increased with the number of times that rabbits encountered the open field test. In this study, rearing was interpreted with the use of this definition. Its lack of change was interpreted similarly to exploring, as the results may change if tested using a larger sample size.

There were several limitations in this study, with the first being the small sample size used. A larger sample size may have increased the statistical power of the study, reduced the impact of uncontrollable variables, and demonstrated a more consistent response. A second limitation was that no placebo was administered. Because of this, the rabbits underwent extra handling to receive the drug, which could have influenced the rabbits' response; however, the fact that rabbits were assessed 2 hours after this handling event should have allowed for ample time to recover. Lastly, the ethogram used was not specifically validated for this study but was adapted from multiple previously published studies. There are, however, no specifically validated scales for fear or stress in rabbits, and this ethogram was validated with intraobserver variability testing.

As for future directions, this study serves as a foundation upon which more studies can and should be built. Further areas of exploration could include testing of how gabapentin can help with stress reduction when administered prior to transport and veterinary visits, similar to the van Haaften[6] study in cats, as these are times with the highest stress and therefore highest risk for rabbits. Another area to explore would be testing of higher doses to see whether stronger effects could be elicited. This would be especially important for those more anxious or fractious individuals that likely require higher doses to see an effect.

In conclusion, this study found that a single oral dose of gabapentin at 25 mg/kg reduced

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some indicators of rabbit stress, as evidenced by a reduction in vigilance behavior (observing) and an increase in play behavior (frolicking) without observable sedation. Given that exploratory behaviors (explore, rear) remained unchanged, gabapentin's effects may be limited, warranting further investigation. Given the results, gabapentin should be considered as a method to help rabbits facing stressors in their own home. Further investigation should be done as to whether this could also be efficacious in more stressful events like veterinary visits and travel.

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Disclosures

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