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RESEARCH

An evaluation of owner expectation on apparent treatment effect in a blinded comparison of 2 homeopathic remedies for firework noise sensitivity in dogs

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Abstract A blinded and randomized study was carried out to investigate whether dog owners would report different treatment effects depending on whether they knew they might be administering a placebo, versus if they knew they were definitely administering a homeopathic remedy. A secondary aim was to determine the consistency of owner reports of treatment effect across multiple trial periods. A total of 73 dogs with a stable, predictable, and easily assessable response to firework noises were enrolled and randomly allocated to receive 1 of the 2 homeopathic preparations along with a basic behavior modification program. Treatment A was a homeopathic treatment formulated for firework noise sensitivity that had previously been tested in a placebo-controlled study by the authors, and Treatment B was a different formulation for the same condition. The same allocated treatment was trialed on 2 occasions by all participants to allow assessment of owner-report reliability. It was found that knowledge of participating in a placebo-controlled trial had no effect on the owners' perception of treatment effect, and that their reports of effect were consistent across both trial periods. No specific effect of homeopathic treatment was found in this study; however, it was observed that the reported behavioral effects that followed each treatment were similar across the 2 firework periods, but that there was a consistently different pattern of behavioral effects reported between Treatment groups A and B. These results might be ascribed to either a treatment or population effect. We suggest that examination of the consistency of owner-reported effects within and between treatments may be used as part of the suite of methodologies available to investigate whether any specific effect can be ascribed to homeopathic interventions.
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Introduction

Sensitivity to loud noises, such as fireworks and thunderstorms, is a common concern reported by dog owners to veterinarians (Landsberg et al., 2003; Bamberger and Houpt, 2006; Sherman and Mills, 2008). When severe, the pet can demonstrate panic behavior, with potentially disastrous consequences to itself and to the owner or the owner's property. Additionally, the pet may become hypersensitized to noises other than those that caused the initial problem (Sherman and Mills, 2008). There is a need for studies that will allow veterinarians to make evidence-based decisions on the potential use of alternative therapies to address the problem of noise sensitivity in dogs.

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The use of owner ratings is common in studies related to the efficacy of treatment for behavioral problems of companion animal (Sheppard and Mills, 2003; Gaultier et al., 2005; Cottam and Dodman, 2009; Irimajiri et al., 2009), and have certain benefits to researchers. The researchers can produce a large amount of information in a short period and at a relatively low cost, which is advantageous when trying to generate adequate sample sizes for statistical power (Meagher, 2009). However, this method also has limitations related to the unknown reliability and validity of the responses provided. One factor that may affect an owner's reporting of treatment effect is the involvement of a placebo, resulting in a change in the placebo effect. The placebo effect is the measurable, observable, or felt improvement in health or behavior which is not attributable specifically to a treatment (McMillan, 1999). The effect is believed to be related to the expectations of the subject: those who believe a treatment will work report a stronger placebo effect than those who do not (see Bausell et al., 2005; Linde et al., 2007, for examples of this in acupuncture). The authors have previously reported a placebo effect of about 50% (Cracknell and Mills, 2008), emphasizing the importance of placebo controlled, double-blinded methodologies, especially when relying on owner reports of effect.

Homeopathy has been used in animals to treat a multitude of conditions (Saxton and Gregory, 2005); however, its use remains a controversial subject for many veterinarians and scientists despite studies claiming to demonstrate its effectiveness (Searcy et al., 1995; Guajardo-Bernal et al., 1996; Albrecht and Schutte, 1999). There are 2 main areas of contention among skeptics who feel that the laws of homeopathy conflict with those of conventional medicine, physics, and chemistry. First, conventional science cannot currently offer any mechanism to explain how ultra-dilute solutions (in which it is unlikely that there is a single molecule of the original solute) can produce a specific beneficial therapeutic effect. Second, there is an absence of sound scientific studies that can establish whether homeopathy actually produces a specific clinical benefit (Cucherat et al., 2000).

As a first step in assessing whether a treatment program including a homeopathic remedy could produce improvements in undesirable canine behaviors linked to firework noises, the authors recently undertook a placebo-controlled trial involving a homeopathic remedy (Cracknell and Mills, 2008). Both treatment groups (homeopathic and placebo) reported a significant level of behavioral change during the trial, and there was no evidence that the homeopathic remedy had a specific effect above that observed in the control group. It was also noted in this report that the percentage reported improvement in the severity of the dogs' response to firework noises in the homeopathic treatment group was substantially lower (38%) than had been suggested by analysis of previous field data supplied by the sponsor about the homeopathic remedy (Levine and Mills, unpublished data). These previous data suggested that a reported improvement rate of approximately 65% would be normal when the homeopathic remedy was used in the field. Although there are several possible explanations for the discrepancy between the original field data and the data observed in the placebo-controlled trial, one explanation that was thought to be relevant, and which deserved investigation was the consideration that dog owners may have been cautious when reporting improvement if they were aware that they were potentially giving their dog a placebo. This factor would not apply when the remedy was used in the field with no control.

It was therefore decided to undertake another study retesting the remedy from the previous study, but without a placebo. Given the necessity of the placebo control in tests of treatment efficacy it was considered important to know whether the involvement of the placebo itself had an effect on the reported efficacy of an intervention. In addition, since this was part of a larger series of studies exploring the evidence for the specific efficacy of homeopathy in this context, the consistency of owner reporting across 2 firework periods was of interest. Therefore, this second study was conducted over 2 consecutive firework periods, with owners receiving the same allocated homeopathic remedy on both occasions (although they were unaware of this), so that the consistency of owner reports could be assessed across different firework periods.

Materials and methods

Ethical approval for this study was obtained from the University's ethics committee.

Recruitment of dogs

Dogs with a sensitivity to firework noises were recruited onto the study by means of notices in veterinary practices, advertisements in the national media, and from an established pool of participants who took part in the previous study by Cracknell and Mills (2008). Dogs had to meet a number of inclusion criteria to qualify for enrollment (Table 1). These related to selecting dogs with a stable, predictable, and easily assessable response to firework noises and excluding those that might confound any response to the homeopathic treatment.

Owners of dogs that satisfied all inclusion criteria were briefed in writing about the procedures involved in the study, and informed written consent was obtained from both the owners and their veterinary surgeon before the dog was enrolled into the trial. Newly recruited owners had to complete 2 questionnaires relating to their dog's fear of noises; a behavioral history questionnaire which provided both demographic data and a detailed evaluation of the dog's problem, and a baseline assessment questionnaire detailing the behaviors that the dog displayed in response to fireworks which included a rating of the severity of each behavior during the most recent firework exposures (without medication). This allowed elimination of differentials of

Table 1 Enrollment criteria for dogs accepted into the study

Dog is at least 6 months old.
Dog should not show aggression in any context prior to enrollment
Dogs should not be receiving any significant psychoactive medication.
Dog is not currently receiving any homeopathic treatments.
Dog is not exposed to strong odors in the home (e.g., essential oil aromatherapy, air fresheners, or camphor based products).
Dog's diet excludes coffee, garlic, mint and sweets.
The dog displays fear responses to specific, identifiable firework noises.
The fear responses should occur in the home.
The fear response must be reliably elicited by the naturally occurring noise stimulus
Fear should not have generalized to the extent that the eliciting cues are too numerous to be identifiable and the dog rarely appears relaxed.

noise fears, such as attention-seeking behaviors, and an assessment of the dog's baseline level of response. Owners who had previously completed trials with the authors had to complete another baseline assessment questionnaire, in case their dog's fear response had changed since the last trial.

Treatments and blinding process

Two homeopathic interventions were used in the study; Treatment A, which was a homeopathic formulation that had previously been used in the study by Cracknell and Mills (2008) and was based on phosphorus, rhododendron, borax, theridion, and chamomilla (6C and 30C in 20% alcohol), and Treatment B which was a patent pending proprietary blend complex homeopathic formulation in an identical bottle with integrated dropper. Treatment B was submitted for testing as an improved formulation of Treatment A. Both treatments were analyzed for volatiles by an independent laboratory technician using headspace gas chromatography/mass spectrometry and liquid–liquid extraction with hexane followed by gas chromatography/mass spectrometry. No compounds were found in either treatment beyond the ethanol base.

All owners were instructed that during firework exposures they should use the trial treatment first but, if they were not satisfied with the response, they could elect to use any other treatment of their choice. This decision to switch treatments was decided upon as one of the potential parameters for comparison between the 2 treatment groups, while helping to protect the welfare of the dogs in the trial.

The treatment blinding process was carried out by an independent university researcher who was responsible for allocating treatments but was not involved further in the study. This researcher was provided with 2 batches of preparation differing externally in their batch numbers and label color. The identity of the 2 batches was contained within a sealed envelope, and so the identity of each formulation remained blind to all researchers at this time. The external bottle labels were covered up with a blank sticky label (to hide the batch number and original label color) and an individual identifier number (unique 6-digit code system) for each participant was attached to their assigned bottle by the independent researcher. The independent researcher then sealed the bottle in an envelope that stated the name of the participant for whom the treatment was meant and recorded which of the 2 treatments were given to each participant in a spreadsheet to which only she had access. In this way only the independent researcher could determine to which batch the bottles belonged to. This controlled for any bias that could have occurred as a result of perceived batch effects as the study progressed. This procedure also ensured that no one associated directly with the project could determine either the specific identity (Treatment A or Treatment B) or batch identity of the bottles until all response data had been entered into the database. The extra level of blinding then allowed analysis of results by group without revealing the identity of Treatments A and B. Treatments were allocated depending on the previous treatment allocation in Cracknell and Mills (2008). A list containing the name of the participants and which treatment they had received in the previous study was provided to the independent researcher, on the basis of which she created her allocation so that half of the group that received the active homeopathic in the earlier study received the same homeopathic remedy (i.e., Treatment A) and half received Treatment B. Also, from the original placebo group, half received Treatment A and half received Treatment B. Any new participants were randomly allocated to one of the 2 treatment groups.

Treatment instructions

All cases were managed through the client's normal veterinary practice. Owners were provided with brief written instructions on how to manage their dog's response to firework noises behaviorally (Table 2) and their designated treatment bottle. Owners also received written instructions on how and when to dose their dog, and how many drops of treatment constituted 1 dose based on the weight of their dog. A total of 5 drops per 10 kg were used up to 20 kg and 15 drops for dogs over 20 kg.

Owners were instructed to give the treatment dosage onto any available mucous membrane, for example into the mouth or directly onto the gingiva. The dose was given once a day for the length of the trial. Owners were advised to give the dose in the afternoon, before the expected beginning of any firework events. During firework episodes, owners were then advised to give follow-up doses every 20 minutes until either the dog calmed down, or they decided to stop dosing because of a lack of effect.

For phase 1 of the trial, dosing with the treatment began approximately 2 weeks before it was predicted the 2006

Table 2 Behavioral advice for dogs with a fear of fireworks

Do not punish you dog when he is scared, it only confirms that there was something to be afraid of.
Do not fuss or try to reassure your dog when he is scared, as this rewards the behavior.
Ignore any fearful behavior that occurs for no good reason.
Make sure your dog is kept in a safe and secure environment at all times so that it does not bolt and escape if sudden noise occurs.
Try to move your dog to a blacked out room at sundown with toys for him and preferably things for you to do as well, so he is not abandoned in the room. Blacking out the room removes the potentially additional problems of flashing lights, etc.
Provide your pet with a safe and secure retreat, such as a cupboard under the stairs or wardrobe. Pack the area with old pillows and duvets to make it comfortable and muffle the noise around.
Ignore the noises yourself and try to engage your pet in some form of active game.
If you know of a dog that is not scared by the noises and which gets on with your own dog, then keeping the two together during the evenings may help. Playing with the nonfearful dog if your own dog becomes scared may help to encourage the fearful dog that all is not so bad after all.

November fireworks period would begin, and lasted for 4 weeks in total. Similarly for phase 2 of the trial, dosing began approximately 2 weeks before it was predicted the 2006/2007 New Year's firework period would begin, and lasted for 4 weeks.

Trial periods

The study took place over both of the main firework periods in the United Kingdom; November (Guy Fawkes Night) and New Year. Participants in the study were told that they would be allocated 1 of the 2 treatments at each period. All participants received the same treatment during both study periods, of which the authors were aware of at the beginning of the trial, but of which participants were unaware. By carrying out 2 identical trials, it would be possible to evaluate the consistency of the owner reports.

Monitoring of behavior and response to treatment

Assessment of the severity of a dog's response was based on the owners' perception of their dog's behavior, both before, during, and after they had completed the trial periods.

The baseline assessment was administered before the trial began and asked owners to rate the frequency (0, never; 1, rarely; 2, frequently; 3, always) and intensity (1, small amount; to 5, extensive amount) of each behavior that their dog displayed to fireworks, from a list of behaviors provided (Table 3). Aggression was included in this list as, although owners of dogs that showed aggression in response to fireworks were excluded from participation, it was possible that some dogs may have responded aggressively during treatment, for example when being restrained for dosing while scared. These perceptions of the dog's response were then converted into a severity score for each behavior by multiplying the frequency score with the intensity score. A total severity score was also calculated by summing the severity scores for each behavior the dog exhibited. This methodology for assessing the overall severity of a dog's response has been used in other studies of firework noise sensitivity in dogs (Levine et al., 2007; Cracknell and Mills, 2008), but varies from that used in reports of the treatment of other canine behavior problems. For instance, in placebo-controlled separation anxiety studies, improvement has been based on the binary outcome effect (improved or not) of owner assessments of severity (King et al., 2000; Simpson et al., 2007) rather than the magnitude of severity values.

Table 3 Behavioral signs analyzed in the baseline assessment

Running around
Drooling saliva
Hiding (e.g., under furniture, behind owner, etc.)
Destructiveness (e.g., furniture, doors, carpets, etc.)
Cowering (e.g., tucks tail flattens ears, etc.)
Restlessness/pacing
Aggression (e.g., growling, snapping, or biting)
Freezing to the spot
Vocalization (barking/whining/howling)
Panting
Elimination (vomiting, defecating, urinating, and/or diarrhea)
Owner-seeking behavior
Vigilance/scanning of the environment
Bolts
Exaggerated response when startled
Shaking or trembling
Self-harm

The owners were also asked to rate the global severity of their dog's response to fireworks (without any medication) on a scale from 1 to 10 (1, mild response; 10, most severe response imaginable). Although this global response score is quite subjective, it was thought important to include a rating of the owners' overall perception of how bad they believed their dog's problem to be, as there may have been factors other than the behaviors recorded that affected the owners' perception of the severity of their dog's problem.

During the trial owners were asked to keep a daily diary recording the number of doses of treatment given each day, whether the dog had experienced fireworks that day, whether the dog had experienced anything else that it usually reacted fearfully toward, and whether they had noticed any side effects. If the dog experienced a fireworks event, the owner

was to complete a separate "real exposure questionnaire" detailing the intensity and duration of the firework exposure, whether the behavioral advice given had been undertaken, and whether any other treatments had been given to the dog. Owners were also asked to rate their dog's response compared with the response that they would have expected with no treatment on a 5-point scale (1, much better than expected; 2, a bit better than expected; 3, same as expected; 4, a bit worse than expected; 5, much worse than expected).

After each phase of the trial, the owners were contacted to complete an exit interview. At this time, the owners were asked to re-rate the frequency (0, never; 1, rarely; 2, frequently; 3, always) and intensity (1, small amount; to 5, extensive amount) of each behavior that their dog displayed to fireworks during the treatment period, and final severity scores were calculated as before. They were also asked to re-rate the global severity of their dog's response to firework noises (while using their assigned treatment), this time on a scale from 0 to 10 (0, no response to fireworks; 1, mild response; 10, most severe response imaginable).

Statistical analysis

After all data had been entered into the spreadsheet, the first level of unblinding occurred to allow the segregation of subjects into 2 groups (A and B), using the code provided by the independent researcher. Behaviors that were shown by fewer than 5 dogs were excluded from statistical analysis. Similarly, if any dog did not show one or more of the behavioral signs (listed in Table 3) both before and after treatment (i.e., that dog did not show the behavior at any point before, during or after the trial), then that dog was excluded from the analysis of those particular behavioral signs.

As the data were not normally distributed, nonparametric tests were used in the analysis using Minitab 13 (Minitab Inc., State College, PA). The sex and breed distributions of the treatment groups were compared using chi-squared tests, and the ages of the dogs in both treatment groups were compared using a Mann–Whitney *U* test.

To compare the reported change in the severity of the dogs' behavioral response to firework noises (both overall and in the specific behavioral signs), and the owner-rated global scores of their dogs' response to fireworks noises between the treatment groups, a Mann–Whitney *U* test was used. Wilcoxon matched-pairs tests were used to analyze the same factors between the 2 firework periods, and between this study and the previous placebo-controlled study (Cracknell and Mills, 2008). To determine the consistency of the owner-reported change in the individual behavioral signs, between the treatment groups and between the firework periods, a Spearman's correlation was carried out. Comparisons were made between the response profiles for the individual treatments on the 2 occasions by correlating the median-reported change in each sign; that is, the following 6 correlations were made; Treatment A November vs. Treatment A New Year, Treatment A November vs. Treatment B November, Treatment A New Year vs. Treatment B November, Treatment B New Year vs. Treatment A November, Treatment B New Year vs. Treatment A New Year, and Treatment B New Year vs. Treatment B November.

Because Treatment A had previously been used in a placebo-controlled study by the authors with some of the same dog owners (n = 11), further analysis of the data from these subjects was undertaken to determine whether there was a greater reported response to Treatment A in this study, when owners were told that 2 active preparations were being used, compared with when Treatment A was previously used against an inactive placebo. A Wilcoxon matched-pairs test was used to determine any significant differences in response to treatment on the 2 occasions.

Results

Demographic data

A total of 73 dogs took part in both phases of the study. After unblinding, 37 dogs were found to be in Treatment group A, and 36 in Treatment group B. Both treatment groups appeared to be well matched, with no significant difference in the age of dogs ($U = 1325.5$, $P = 0.95$, Treatment group A [A]: median = 6 years, range = 1-13 years; Treatment group B [B]: median = 6 years, range = 1-13 years), or the breed groups with the 3 most commonly represented United Kingdom Kennel Club groups in both treatment groups being gundog, pastoral, and terrier breeds (chi-square on gundog, pastoral, terrier, and other breed groups = 1.114, 3 *df*, $P = 0.77$). However, there was a difference between the 2 groups regarding the sex distribution of the dogs (A: 6 male, 31 female; B: 19 male, 17 female; $\chi^2 = 10.832$, 1 *df*, $P = 0.001$). A comparison was made between the males and females in relation to the amount of change in the total severity of behavioral signs; however, no significant difference could be found at either fireworks period (November: male median = −38, female median = −26, $U = 946$, $P = 0.76$; New Year: male median = −30.5, female median = −25, $U = 831.5$, $P = 0.5$), suggesting that non-matching on this criterion was not a problem. During both phases of the trial, no owners opted to use any other form of treatment or discontinued using the treatment provided.

Comparison of treatment groups

Comparison of treatment groups during November firework period

Overall, 64% (47/73) of owners reported some degree of change in their dog's behavioral response to fireworks during treatment (i.e., a rating of "a bit better than expected" or "very much better than expected" on the "real exposure questionnaire"). In Treatment group A, significantly fewer

Table 4 Median change in severity score of individual behavioral signs from baseline to final assessment for both trial periods

	November trial period				New Year trial period			
	Treatment group A		Treatment group B		Treatment group A		Treatment group B	
Behavioral sign	Decrease in score	*W*, *P* value	Decrease in score	*W*, *P* value	Decrease in score	*W*, *P* value	Decrease in score	*W*, *P* value
Running around	1	42*	2	26.5**	1	15**	2	6**
Drooling saliva	1	68.5	1	0**	1	31.5*	1	0**
Hiding	0	14.5**	3	18**	0	3**	3	23**
Destructiveness	1.5	7	2	0**	2	0*	2.5	0*
Cowering	3	2.5**	3	18**	3	3.5**	6	16.5**
Restlessness/pacing	1.5	62**	1	0	2	22**	3	6.5**
Freezing to the spot	2	10*	2	4**	2	5*	2	4.5**
Vocalization	1	10.5*	5	3**	2	2.5*	6	2.5*
Panting	2	26.5**	3	16**	2.5	11.5**	3	18**
Elimination	3.5	0*	3.5	0*	4	0	4	0*
Owner-seeking	0	87*	1	52.5*	1	82*	1	31**
Vigilance	2.5	34**	1	33**	2.5	13.5**	1	13.5**
Bolts	1	8**	1	5**	2	3**	4	0**
Exaggerated startle	2	34.5**	3	11.5**	2	12.5**	4	11.5**
Shaking	1	33**	3	27.5**	1	15.5**	3	27**

W is the Wilcoxon matched-pairs statistic.
*Represents $P < 0.05$.
**Represents $P < 0.001$.

owners reported some level of behavioral change during the real firework exposures compared with owners in Treatment group B ($\chi^2 = 5.557$, $df = 1$, $P = 0.018$, A: 51% or 19/37; B: 78% or 28/36).

There was no significant difference between the total severity scores for the 2 treatment groups at baseline (A: median = 82, B: median = 79.5, $U = 1{,}311$, $P = 0.82$). Both treatment groups reported a significant decrease in the total severity of the behavioral signs shown from baseline to final assessment (A: median = −25.5, $W = 92$, $P < 0.0001$; B: median = −33, $W = 9$, $P < 0.0001$). However, at the final assessment there was no significant difference between the 2 treatment groups in either the units of decrease reported in the total severity score (A: median = −17, B: median = −27, $U = 1{,}193$, $P = 0.13$), or the percentage reported decrease in the total severity score (A: median= −28%, B: median = −43%, $U = 1545$, $P = 0.15$).

Likewise, there was no difference between the groups in the owners' ratings of their dogs' global response score at the start of the study (A: median = 9, B: median = 9, $U = 1682$, $P = 0.85$), and the change in the owner ratings of their dogs' global response score before and after treatment was also not significantly different between the 2 treatment groups (A: median = −2, B: median = −3, $U = 1576$, $P = 0.23$). For analyzing change in specific behavioral signs, aggression and self-harm were excluded from analysis in both treatment groups, and in both firework periods, as aggression was exhibited by none of the dogs (as at the beginning of the study) and self-harm was exhibited by only 3 dogs.

At the final assessment, it was found that in Treatment group A, 13 of the 15 remaining behavioral signs of fear had significantly decreased, whereas in Treatment group B 14 of the 15 remaining behaviors had significantly decreased (Table 4). However, a comparison of the change in severity scores of each behavioral sign between each treatment group showed no significant differences between the groups, except for "barking/whining/howling" which had decreased significantly more in Treatment group B (A: median = −1, B: median = −5, $U = 384$, $P = 0.02$).

Comparison of treatment groups during New Year firework period

Overall, 68% (50/73) of owners reported some degree of change in their dog's behavioral response to fireworks during treatment. In Treatment group A, significantly fewer owners reported some level of behavioral change during the real firework exposures, compared with owners in Treatment group B ($\chi^2 = 4.789$, $df = 1$, $P = 0.029$; A: 57% or 21/37, B: 81% or 29/36).

Similar to that in the November firework period, both treatment groups reported a significant decrease in the total severity of the behavioral signs shown from baseline to final assessment (A: median = −26.5, $W = 33$, $P \leq 0.0001$; B: median = −32.5, $W = 11$, $P < 0.0001$). At the final assessment, there was no significant difference between the 2 treatment groups in either the reported units of decrease in the total severity score (A: median = −26.5, B: median = −32.5, $U = 1501$, $P = 0.25$), or the percentage reported decrease in the total severity score (A: median = −29%, B: median = −48%, $U = 1464$, $P = 0.14$).

There was also no difference between the groups in the owners' ratings of their dogs' global response score at the

start of the study (A: median = 9, B: median = 9, $U = 1682$, $P = 0.85$), and the change in the owner ratings of their dogs' global response score before and after treatment was also not significantly different between the 2 treatment groups (A: median = −2, B: median = −3, $U = 1576$, $P = 0.23$).

At the final assessment, 14 of the 15 behavioral signs that were analyzed had significantly decreased in Treatment group A, whereas in Treatment group B all 15 behaviors had significantly decreased (Table 4). Concerning the amount of reported change between treatment groups in the severity scores of each behavioral sign, there were no differences between the groups, except for "exaggerated startle" which had decreased significantly more in treatment group B (A: median = −2, B: median = −4, $U = 1053$, $P = 0.04$).

Consistency of owner reports across November and New Year firework periods

Consistency of changes in overall severity of response between November and New Year

To determine whether the owners' reports of treatment effect were consistent across both firework periods studied, a within-subjects analysis was performed. Overall, there was no significant difference between the 2 firework periods with regard to either the units of decrease reported in the total severity score (November: median = −26, New Year: median = −30, $W = 690.5$, $P = 0.29$), or the percentage decrease reported in the total severity score (November: median = −39%, New Year: median = −42%, $W = 772$, $P = 0.11$). Likewise, there was no difference between the 2 firework periods in the change in the owner ratings of their dogs' global response score before and after treatment (November: median = −2, New Year: median = −2, $W = 102$, $P = 0.79$).

Within each treatment group, there was no significant difference between the 2 firework periods in either the units of decrease reported in the total severity score (November A: median = −17, New Year A: median = −26, $W = 190.5$, $P = 0.42$; November B: median = −27, New Year B: median = −31.5, $W = 165$, $P = 0.46$), the percentage decrease reported in the total severity score (November A: median = −18, New Year A: median = −21, $W = 231$, $P = 0.07$; November B: median = −45, New Year B: median = −47, $W = 167$, $P = 0.6$), or the change in the owner ratings of their dogs' global response score before and after treatment (November A: median = −2, New Year A: median = −2, $W = 13.5$, $P = 0.56$; November B: median = −3, New Year B: median = −3, $W = 46.5$, $P = 0.24$).

Consistency of changes in individual behavioral signs between November and New Year

Figure 1 shows the owner-reported change in the individual behavioral signs from baseline, for both firework periods. There was no significant difference found in the owners' rating of change of any of the 15 behavioral signs examined between firework periods (Table 4). Although there was a significant level of change in all signs during both firework periods, a comparison of the change in severity scores of each behavioral sign between each firework period showed no differences. There was also no difference between firework periods in any of the 15 examined behavioral signs when comparing the 2 treatment groups individually (Table 4).

Significant correlations were found for the response profile of individual treatments on both occasions (i.e., November A vs. New Year A: $r = 0.943$, $P < 0.0001$; November B vs. New Year B: $r = 0.977$, $P < 0.0001$). However, the correlation of the response profiles between the 2 treatments was not found to be significant for any other combination of treatment group or firework period (November A vs. November B: $r = 0.395$, $P = 0.145$, New Year A vs. November B: $r = 0.462$, $P = 0.083$; November A vs. New Year B: $r = 0.399$, $P = 0.140$; New Year A vs. New Year B: $r = 0.465$, $P = 0.081$). These results are reflected in Figure 1, suggesting that the behavioral effects reported by the 2 treatment groups were not identical.

Consistency of treatment effects in current study compared with placebo-controlled study

Of the 11 owners who participated in both the current study and the previous placebo-controlled study by the authors (and received Treatment A on both occasions), it was established that there was no difference between the total severity scores reported at baseline in either study (placebo study median = 78, current study median = 77, $W = 2.5$, $P = 0.59$). There was also no significant difference in the reported decrease in total severity score from baseline to final assessment (placebo study median = −31, current study median = −24, $W = 14$, $P = 1$).

Comparison of the reported change in the individual behavioral signs found no difference in either the baseline scores reported by the owners at the beginning of either study or the reported decrease in the severity of the signs at the final assessment of either study.

When considering all participants that had received Treatment A in either or both of the previous and current studies, no significant difference was found in the overall percentage change reported (placebo study median = −38%, current study median = −21%, $U = 1508$, $P = 0.19$).

Discussion

Similarity of treatment effect in reference study compared with placebo-controlled study

The primary aim of this study was to investigate the potential influence of owners knowing that they may be administering a placebo, versus knowing that they are definitely administering a treatment, on their reports of

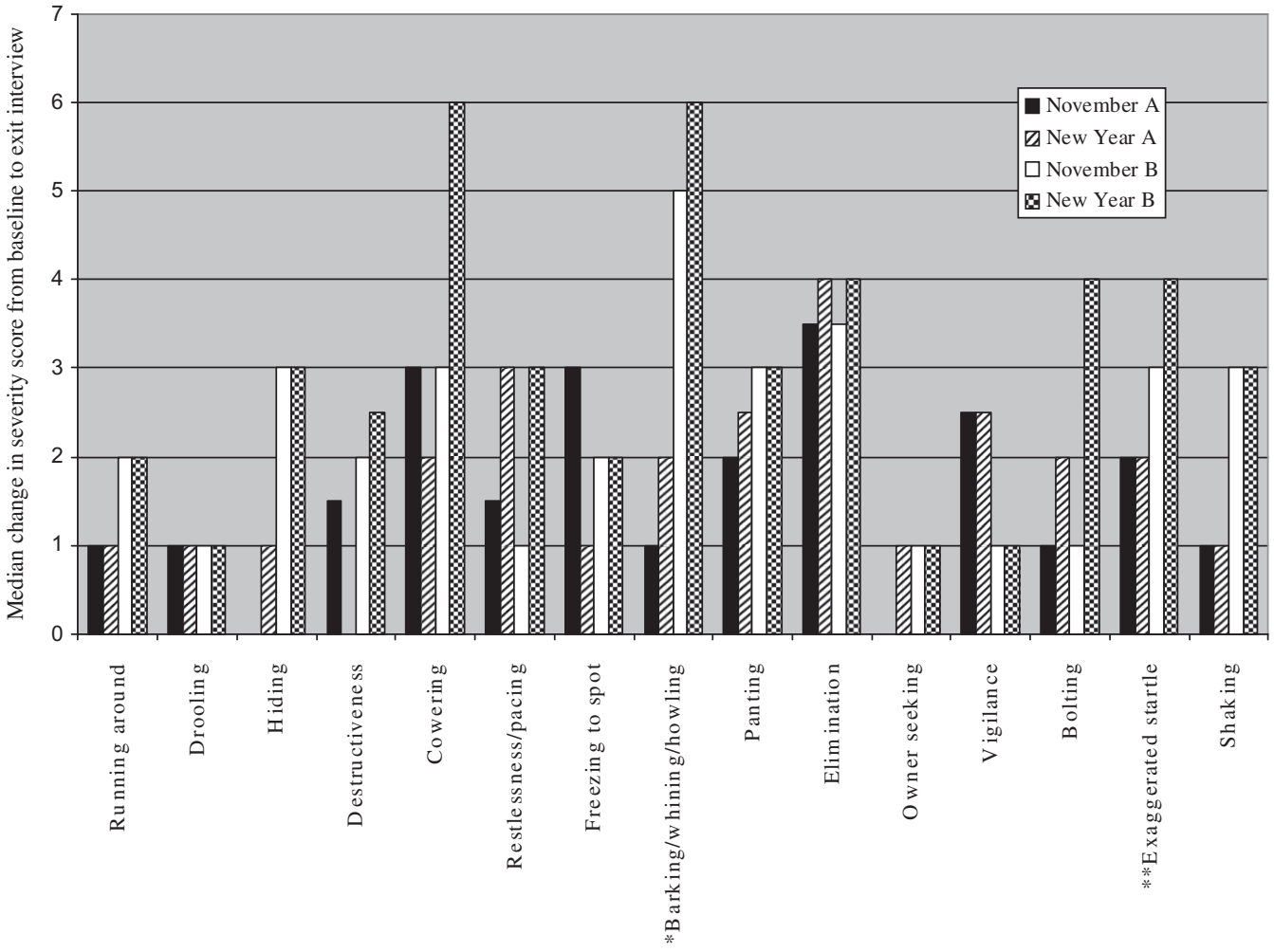

Figure 1 Median change in severity of behavioral signs as rated by dog owners, for both treatment groups at both firework periods (*significant difference between treatment groups at November, **significant difference between treatment groups at New Year).

treatment effect. Because treatment group A used the same homeopathic remedy and protocol as that trialed in an earlier placebo-controlled study by the authors (Cracknell and Mills, 2008), it was possible to make some comparisons between the reported changes associated with the remedy on the 2 occasions. A within-subjects comparison of the reported effects from 11 owners who participated in both studies was undertaken and revealed no significant differences in any of the measures taken between the 2 studies. This suggests a consistent reported response to the treatment programs described in this current study and the previous one, with an overall reported improvement rate of 21% in this study and 38% in the placebo-controlled study.

These results show that the knowledge of participating in a placebo-controlled trial did not appear to affect the owners' reports of behavioral change after treatment. Therefore, the authors reject the hypothesis that the overall improvement rate from Treatment A was lower than expected during the previous placebo-controlled study because owners were cautious when reporting any level of improvement as they were aware that they were potentially giving their dog a placebo. The difference as compared with the original field data (Levine and Mills, unpublished data) may therefore arise from the difference in sampling and quality of data provided from the field which would seem to overestimate the effect compared with the more carefully managed and controlled studies.

The consistency of the possible placebo effect in this study should not be interpreted as support for the exclusion of a placebo control when evaluating the efficacy of homeopathic or other treatments. However, in homeopathy there is an issue with finding a suitable placebo, given that it has been suggested that the alcohol in the placebo-control used in the authors' previous study may have had homeopathic potency. Given that both treatments were based on 20% alcohol, it is possible that any reported effect was due to a nonspecific change brought about by the effects of alcohol consumption. However, the authors are unaware of any research on the effect of such low doses of alcohol on the behavior of dogs, and believe the volume involved on each occasion, and the timing of the dosing in relation to any reported effects, make this unlikely.

Similarity of owner reports across 2 firework periods

Secondary aims of the current study were to assess the consistency of owner reports of treatment effect across firework periods, and to compare the consistency of owner reported effects within and between treatment groups.

Similar results were obtained at both the November and New Year firework periods, with no significant difference within groups being found between the 2 periods for any measure. This suggests that each time period is similar and might serve as useful replicates for future trials.

First, given that there was no difference in the treatment effects reported by a small sample of owners who participated in this study and the previous placebo controlled study, and second that owners had no way of knowing that they had administered the same treatment during each period, it would seem that owner reports of change appear to be consistent across multiple trials. This suggests that owner reports can be a reliable method of gathering large amounts of data about a problem in a relatively short time, although the objective validity of their observations has not been tested. As the amount of change reported is dependent on the owner's perception of the problem, a within-subjects design would need to be used to control for any differences between different owners when attempting to establish whether any intervention has a consistent effect on a given population. Alternatively, if between-subjects comparison is necessary it should be checked that the baseline data are not significantly different between the groups.

An ideal way to control for the differences in perception between owners would be to video tape the dogs' responses during a firework exposure before and after treatment, and have a single blinded researcher rate all dogs to ensure they are rated by the same standards. This was not feasible in the current study because of logistical constraints; however, if consistently significant differences were found between treatments this might be the next step of analysis so as to ensure the results are based on objective change.

Comparison of treatment groups

The demographic data suggest that the 2 treatment groups were well matched for age and breed. A significant difference was found between the sex distributions of the 2 treatment groups; however, no effect of sex on treatment outcome was found.

Few significant differences were found between the 2 treatment groups; however, where differences were identified (in the number of owners reporting some degree of change in their dog's response, and in the change reported in the behavioral signs "vocalization" during the November fireworks period and "exaggerated startle" during the New Year period), they were in favor of Treatment group B. This might be interpreted as an indication that there was a real treatment-related difference; however, this cannot be concluded from the results of this study given the possibility of a type I error (i.e., detecting a significant difference when none exists) given the number of comparisons made. This risk increases with the number of statistical tests that are undertaken, and no statistical correction was applied to account for this given the relatively low power of the study. Caution is also required in the interpretation of these results because of the high level of placebo effect found in the authors' previous study (50%).

Because the principles of homeopathy do not follow the "normal" dose-response principles of conventional medicine, the effect of dosing on the behavioral changes reported by owners was not investigated in this study. It is however noted that there was a significant difference in the amount of change reported in the behavioral sign "exaggerated startle" during the second treatment period but not the first, which might indicate a cumulative effect of treatment. However, this is thought unlikely given that the effect was only found for 1 measure, and also given that for a cumulative effect of dosing to be present there would need to be evidence of an effect of treatment, which has not been demonstrated by the authors to date.

The behavioral effects reported for each treatment on the 2 occasions of their use were found to be consistently similar, but the effects reported between treatment groups were found to be consistently different (Figure 1). This suggests that the 2 treatments were associated with different reported behavioral changes, and that these owner-reported behavioral changes were consistent across both firework periods, possibly indicating that the 2 treatments were not identical. However, it is also possible that this difference was due to a cohort effect, that is, owners in one group tending to report differently to the other. Because the same populations were trialing the same treatment on both occasions, any difference may look like a treatments effect, when in fact it is because of bias in the individuals reporting their observations. If the populations had swapped treatments for the New Year firework period, this effect would have been controlled. Treatment groups were not swapped as the consistency of owner reporting was a higher priority for this study. The possibility of such owner effects would need to be taken into account in any future study by using a cross-over design.

In terms of investigating whether the use of homeopathy has a specific measurable effect on sound sensitivity, this study presents a potential alternative methodology. If it could be demonstrated, with suitable controls and in multiple populations, that 2 physically identical but homeopathically distinct preparations consistently show greater within-treatment reliability than between-treatment reliability, suggesting that there was some specificity in their effects. Although this approach would not be sufficient for determining the clinical effect of a homeopathic treatment (where a placebo-controlled, double-blind protocol would be required), it would assist as an initial step.

Conclusion

The results of this study showed that the use of a placebo-controlled protocol had no effect on owner reports of perceived treatment effect and that owners were able to consistently report these treatment effects across multiple firework periods. In terms of the perceived effects of the homeopathic treatments, no evidence of a specific treatment effect of homeopathy was found in the current study. It was, however, observed that the reported changes that followed each treatment were similar across the 2 fireworks periods, but there was a consistently different pattern of reported behavioral changes between the treatment groups, suggesting perhaps that the effects of the treatments were not identical. Additional study is needed to address the potential confounds in this study and determine whether the possible effects detected in this study are real.

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