



Smith, M. I., Mendl, M. T., & Murrell, J. C. (2022). Associations between osteoarthritis and duration and quality of night-time rest in dogs. *Applied Animal Behaviour Science*, *253*, [105661]. https://doi.org/10.1016/j.applanim.2022.105661

Publisher's PDF, also known as Version of record License (if available): CC BY Link to published version (if available): 10.1016/j.applanim.2022.105661

Link to publication record in Explore Bristol Research PDF-document

This is the final published version of the article (version of record). It first appeared online via Elsevier at https://doi.org/10.1016/j.applanim.2022.105661. Please refer to any applicable terms of use of the publisher.

University of Bristol - Explore Bristol Research General rights

This document is made available in accordance with publisher policies. Please cite only the published version using the reference above. Full terms of use are available: http://www.bristol.ac.uk/red/research-policy/pure/user-guides/ebr-terms/



Contents lists available at ScienceDirect

Applied Animal Behaviour Science



journal homepage: www.elsevier.com/locate/applanim

Associations between osteoarthritis and duration and quality of night-time rest in dogs

Melissa Smith, Michael Mendl^{*}, Joanna C. Murrell¹

Bristol Veterinary School, University of Bristol, Langford House, Langford BS40 5DU, UK

ARTICLE INFO	A B S T R A C T
<i>Keywords:</i> Actigraphy Chronic pain Dog Osteoarthritis Sleep	Human patients with chronic pain from osteoarthritis often report impaired sleep, but it is not yet known if sleep is also impaired in dogs with osteoarthritis. This study aimed to compare the night-time sleep behaviour of osteoarthritic (N = 20) and healthy control (N = 21) dogs over a 28-day period, using an actigraphic device (the FitBark activity monitor) and an owner questionnaire designed to measure sleep quality (the SNoRE). Acti- graphic data were aggregated to estimate the time each dog spent resting each night, and questionnaires were completed every 7 days. Data were analysed using robust mixed-effects linear regression. The presence of clinical signs of osteoarthritis had a significant effect on actigraphic recordings, with osteoarthritic dogs spending lower proportions of the night period resting (and therefore higher proportions of the night period active) compared to control dogs (z = 2.21; P = 0.0268). However, there was no significant difference between the SNoRE scores of osteoarthritis and control dogs (z = -1.01 , p = 0.312). The actigraphic findings of this study suggest that dogs with osteoarthritis may experience impaired sleep, which could have important welfare implications and merits further study

1. Introduction

Osteoarthritis is a common cause of chronic pain in humans (Arendt-Nielsen et al., 2010; Peat et al., 2001; Sofat et al., 2011), and human osteoarthritis patients often report sleep impairments (Power et al., 2005; Taylor-Gjevre et al., 2011; Wilcox et al., 2000). These disruptions to sleeping patterns are likely to be associated with the chronic pain of osteoarthritis, since chronic pain is a predictor of sleep problems in other human conditions (Drewes et al., 2000; Nicassio and Wallston, 1992; Riley et al., 2001). Sleep impairments themselves may exacerbate chronic pain (Affleck et al., 1996; Morin et al., 1998; Stone et al., 1997) and adversely affect cognition (Chee and Choo, 2004; Steenari et al., 2003). They therefore represent a significant threat to wellbeing.

Osteoarthritis also causes chronic pain in dogs (Brown et al., 2007, 2008; Conzemius et al., 2003; Hielm-Björkman et al., 2009; Hunt et al., 2018; Moreau et al., 2003; Wiseman et al., 2001), and canine osteoarthritis is thought to be highly prevalent (Anderson et al., 2018; Henrotin et al., 2005; Johnston, 1997). However, it is not known whether osteoarthritic dogs also experience sleep deficits. In a blinded placebo-controlled study, Knazovicky et al. (2015) found that

meloxicam analgesia caused significant improvements in scores on an owner questionnaire designed to measure sleep quality of dogs; the Sleep and Night-time Restlessness Evaluation (SNoRE) questionnaire. However, there were no significant differences in actigraphic measurements of night-time activity between meloxicam-treated and baseline or placebo-treated osteoarthritic dogs. This suggests that meloxicam treatment improves owner-reports of how well their osteoarthritic dog is sleeping, but does not alter night-time movement of the dogs. However Knazovicky et al. (2015) did not include a control group of healthy dogs, and therefore it is not known whether the observed effects of meloxicam analgesia on reported sleep in osteoarthritic dogs were due to a reversal of the effects of osteoarthritis on sleep or due to a non-specific effect of the analgesic, and hence whether osteoarthritis is indeed associated with impaired sleep in dogs.

The aim of this study was to explore whether dogs with clinical signs of osteoarthritis also display impaired sleep compared to healthy control dogs. Polysomnography can distinguish true sleep and wakefulness periods as well as different sleep stages and has been developed for use in dogs by Kis et al. (2014), initially in a canine sleep laboratory with researchers on hand to place electrodes, but more recently in dog owners'

* Corresponding author.

https://doi.org/10.1016/j.applanim.2022.105661

Received 4 February 2022; Received in revised form 13 May 2022; Accepted 25 May 2022 Available online 27 May 2022

0168-1591/© 2022 The Authors. Published by Elsevier B.V. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

E-mail address: mike.mendl@bris.ac.uk (M. Mendl).

¹ Present address: Highcroft Veterinary Referrals, 615 Wells Rd, Whitchurch, Bristol BS14 9BE, UK.

homes allowing in situ night-time recordings of up to 3 h duration (Reicher et al., 2021). Given the aim of recording sleep over a 28-day period, it was considered unlikely that sufficient owner compliance including regular and correct placement of electrodes could be achieved each night across the study period in owners' homes. Therefore, polysomnography was considered infeasible for this study and, instead, sleep behaviour was assessed by measuring the proportion of the night-time period spent resting using an actigraphic device; the FitBarkTM activity monitor system.

In humans, actigraphy generally has agreement rates with polysomnography of approximately 80%. However, its sensitivity is considerably higher than its specificity, which can lead to poorer agreement rates in populations where participants spend lower proportions of the night period sleeping (Sadeh, 2011). Nevertheless, it has accurately discriminated human participants with sleep impairments from control participants in a range of studies (extensively reviewed by Sadeh, 2011), indicating that actigraphic measurements are a useful proxy measure of sleep in these populations. Although actigraphy in companion dogs has not yet been systematically validated against polysomnography, its promise in human sleep studies and its ability to remotely monitor dog activity in owners' homes over several weeks, made it the most appropriate technique for objective monitoring of dog sleep in this study.

We used the FitBark actigraphy system (Knazovicky et al., 2015 used Actical Activity monitors) as it has been specifically designed for dogs, is significantly more affordable than most competitors, allowing the purchase of one device per participating dog, is very easy for owners to use and synchronise, and allows data to be uploaded remotely from the device via Bluetooth. Consequently, it was unnecessary to perform repeated visits to the owner's home to download data. Whilst the FitBark has not been fully validated in the peer-reviewed literature, it has been used in previous studies to investigate the effects of a nutraceutical product on activity levels (Di Cerbo et al., 2017) and the effect of dogs' activity and rest patterns on those of their owners (Patel et al., 2017).

Alongside actigraphic measures of sleep quality, we assessed sleep quality using the SNoRE questionnaire developed by Knazovicky et al. (2015). We hypothesised that dogs with osteoarthritis would show decreased sleep quality (increased SNoRE scores) relative to control dogs, and would also show significantly decreased proportions of the night period spent resting.

2. Methods

Ethical approval for animal use and human (owner) participation was obtained from the University of Bristol Animal Welfare and Ethical Review Body (VIN/17/005) and University of Bristol Faculty of Health Sciences Research Ethics Committee (Application Ref: 31623) respectively.

2.1. Animals

Forty-one dogs were recruited via a social media campaign (using a combination of the study's Facebook Page https://www.facebook.co m/dog.arthritis and posts on dog-related groups and pages based in South West England) as well as poster and leaflet placement within veterinary clinics in Bristol and North Somerset. Inclusion criteria required dogs to be between 5 and 11 years of age and weigh less than 12 kg, to be free from signs of age-related cognitive decline and pain conditions other than osteoarthritis, and to have no signs or history of health conditions that could cause study participation to impair their health or welfare. Dogs receiving analgesic medication were not excluded, the numbers of dogs receiving analgesia and the types and frequency of analgesic treatment are shown in Table 1. Dogs were assigned to groups (osteoarthritis (n = 20) or control (n = 21)) based on clinical examination by a veterinary surgeon (MS) using a standardised clinical checklist and a verbal history take from the owner about any

Table 1

Signalments of recruited dogs in each group.

Variable	Control Group	Osteoarthritis Group	
Sex			
Female (neutered)	6	12	
Male (neutered)	15	8	
Breed Class:			
Gundog	10	10	
Crossbred	4	3	
Hound	1	0	
Pastoral	1	4	
Terrier	2	1	
Utility	1	0	
Working	2	2	
Analgesia provision			
No	20	10	
Yes	1	10	
Analgesia frequency			
None	20	10	
Occasional	1	3	
Daily	0	7	
Analgesia type			
None	20	10	
Nonsteroidal analgesia only	1	7	
Other analgesics provided ^a	0	3	
Season of data collection			
Summer (May-August 2017)	12	13	
Winter (November-February 2017)	9	7	
Continuous variables			
Age (years)	$\textbf{7.86} \pm \textbf{0.50}$	$\textbf{7.80} \pm \textbf{0.77}$	
Body Condition Score	$\textbf{4.67} \pm \textbf{0.42}$	5.50 ± 0.62	

Data are expressed as counts for each categorical variable level and as means with 95% confidence intervals for each continuous variable.

^a Of the three dogs that received "other analgesics", one received tramadol in addition to nonsteroidal analgesia, one received gabapentin and paracetamol in addition to nonsteroidal analgesia, and one received tramadol only.

signs of osteoarthritis (stiffness, pain, slowing down during walks, difficulty jumping or climbing; see Table S1 in Supplementary Material). Signalments of the dogs recruited are shown in Table 1. Participating owners received a £ 10 gift card (John Lewis Partnership, London, UK) following completion of the study. Sample size was based on that previously used in a similar study by Knazovicky et al. (2015) which investigated the effects of NSAID-treated and placebo-treated osteoarthritic dogs on night-time accelerometry and SNoRE scores in a cross-over design (N = 19).

2.2. Apparatus

The FitBark system (FitBark Inc., Kansas City, MO) consisted of an electronic activity monitor (electronic accelerometry device, 3.9 cm * 2.8 cm*1.2 cm) attached to each dog's collar, a smartphone app allowing owners to upload their dog's data, and an online database from which each dog's data were downloaded.

2.3. Procedure

A clinical examination including an orthopaedic examination of all appendicular joints was performed to assign the dogs to the osteoarthritic or healthy control group. A clinical history was also taken from the owner to determine any signs of osteoarthritis or potential signs of other health problems. Since a single researcher was responsible for clinical examinations and data analysis, it was not possible to blind analysis with respect to group. Body condition score (BCS) was measured on a scale from 1 to 9 (WSAVA Nutritional Assessment Guidelines Task Force Members, 2011).

Owners received an instruction sheet detailing how to use and charge the FitBark activity monitor and smartphone app, as well as four identical sets of questionnaires. Each of these contained the SNoRE as well as two previously-validated clinical questionnaires designed to assess the severity of pain in dogs; the Helsinki Chronic Pain Index (HCPI), which has a single outcome score (chronic pain score (range 0–44): Hielm-Björkman et al., 2009) and the Canine Brief Pain Inventory (CBPI), which has two validated outcome scores (CBPI Severity score (range 0–10) and CBPI Interference score (range 0–10)) as well as a single-question quality of life (CBPI QOL (range 0–4)) score (Brown et al., 2007).

The CBPI and HCPI questionnaires were selected for this study over alternative questionnaires relating to chronic pain in dogs for two main reasons. Firstly, they were used by Knazovicky et al. (2015), allowing findings from this study to be easily compared with theirs. Furthermore, both questionnaires have been extensively validated. Both were formulated via discussion between veterinary professionals and dog owners followed by removal of questions with low inter-item correlations or no difference between osteoarthritic and control dogs, giving good face and content validity (Brown et al., 2007; Hielm-Björkman et al., 2003). They also have good criterion validity, being correlated with existing measures of lameness and quality of life (Brown et al., 2007, 2009; Hielm-Björkman et al., 2009), and construct validity, with PCA being performed to identify constructs measured and significant differences in scores between healthy and osteoarthritic dogs (Brown et al., 2007, 2009; Hielm-Björkman et al., 2003). They also have high internal consistency and repeatability scores (Brown et al., 2009; Hielm Björkman et al., 2009) and have shown significant responsiveness to carprofen analgesia (Brown et al., 2008; Hielm-Björkman et al., 2009). The main drawback of the HCPI is that the English translation has not itself been validated and the translation from Finnish is slightly stilted, which may affect owners' responses. This is not an issue for the CBPI which was originally written and validated in English.

Each set of questionnaires was marked with the day of the study that they were to be completed (7, 14, 21 and 28), where the system was initially set up on day 0. Owners also received a sleep diary sheet in which they recorded the times at which they went to bed at night and got up in the morning each day over the course of the 28-day study period. Owners were able to record on the sheet any events that may have affected the dog's activity or rest on a particular day.

2.4. Data preparation

Dogs wore the activity monitors 24 h per day except when they needed charging which was always done during daytime hours. Raw activity results for each minute from the 28-day study period were downloaded from the FitBark website's online database for each dog. These consisted of the date and time of each recording along with a recorded activity value. Proprietary algorithms provided by FitBark were used to determine whether the dog was in a state of "rest", "activity" or "play" (high-intensity activity) for each minute recorded. Because this study focused predominantly on the distinction between rest and activity, and because it was difficult to determine what "play" recordings truly represented, "play" and "activity" were combined into a single category such that for each minute a dog was either at "rest" or "activity".

The true night-time period was calculated for each dog as the period between one hour after the owner's reported mean bedtime and one hour before the owner's mean getting up time, following Knazovicky et al. (2015). The range was 296–461 min. For each minute of data recorded for each dog, the following values were entered: The day (0–28) and week (1–4) of the recording, whether the recording was made during the daytime or night-time period, and whether the dog was resting or active (according to the algorithm provided). From this the proportion of the night-time period that was spent resting was calculated for each day of the study for each dog. Questionnaire scores (SNoRE, HCPI and CBPI) were calculated for each week for each dog from owner questionnaire responses. SNoRE and HCPI scores were calculated as the sum of all individual question scores for each dog in each week. CBPI Pain Severity Score was calculated as the mean of individual question scores for CBPI questions 1–4, and CBPI Pain Interference Score was calculated as the mean of individual question scores for CBPI questions 5–10 for each dog in each week.

2.5. Statistical analysis

Differences in age, body condition score and questionnaire scores (HCPI Score, CBPI Severity Score, CBPI Interference Score and CBPI Quality of Life (QOL) score) between groups were investigated using Mann-Whitney U-tests. Holm-Bonferroni corrections (Holm, 1979) to the p-value thresholds for significance (α) were performed to account for multiple testing.

Due to non-normality of residuals and a large number of outliers, both outcomes (proportion of night-time period spent resting and SNoRE score) were analysed via robust mixed effects linear models, using the "rlmer()" function from the "robustlmm" package (Koller, 2016) in R (R Core Team, 2014). This is a modified version of the "lmer()" function from the package "lme4" (Bates et al., 2015), which increases robustness to non-normality and the presence of outliers at the expense of decreased asymptotic efficiency (Koller, 2016) (a measure of model quality related to the variance associated with parameter estimation) (Everitt and Skrondal, 2002; pp. 24 and 149).

Univariable models are commonly performed to select factors for inclusion in a final model (for example: Alves et al., 2002; Bogaert et al., 2005; Kooby et al., 2003). Because in this study, the interaction of each factor with group was as important as the main effects, and adding only the main effects to each initial model may cause the omission of a factor with a significant interaction with group from the final model, each initial model included not only the factor of interest but also group and the interaction between each factor and group as fixed effects (see Tables S2 and S3 in Supplementary Material). "Dog" and "week" were included as random effects. Initial models were performed for two outcome variables; proportion of the night spent resting and SNoRE score.

All fixed effects where p < 0.1 in initial models were selected for addition to the final model for each outcome variable, as using a stricter threshold of p < 0.05 often leads to omission of factors that would be significant in the final model (Bursac et al., 2008). Where multiple continuous variables were to be added to the final model, Pearson correlation tests were performed to assess whether these were significantly (p < 0.05) correlated with each other prior to inclusion. If so, the variable with the lowest p-value in the initial model was selected for addition to the final model, and the factors it significantly correlated with were omitted, in order to reduce the risk of collinearity (Dormann et al., 2013).

Although the focus of this study was on sleep-related behaviour at night, we also investigated whether control and osteoarthritic dogs differed in the proportions of time that they spent resting during the day (i.e. all times not in the night period), and whether this was correlated with night-time resting behaviour.

Results are given as test statistics with degrees of freedom (where appropriate), p-values, and α -values where these have been adjusted to account for multiple testing. R values are included for correlational tests.

3. Results

3.1. Signalments and questionnaire scores

The signalments of recruited dogs are summarised in Table 1. Osteoarthritic dogs had significantly higher HCPI, CBPI Severity and CBPI Interference scores than control dogs, but no differences were detected for age, body condition score or CBPI QOL score (Table 2; Fig. 1).

3.2. Proportion of night period spent resting

Results of initial screening models are shown in Table S2 (see

M. Smith et al.

Table 2

 $Comparisons \ between \ osteo arthritis \ and \ control \ groups \ for \ clinical \ questionnaire \ outcome \ scores \ and \ signalment \ variables \ (age \ and \ body \ condition \ score), with \ Holm-Bonferroni-adjusted \ \alpha-values.$

Variable	Mann-Whitney U-Statistic	p-value	p-value rank	Holm-Bonferroni α -value	Significant following Bonferroni-Holm correction?
CBPI Interference score	34	5.07 * 10 ⁻⁶	1	0.00833	Yes
CBPI Severity score	42.5	$1.12 * 10^{-5}$	2	0.01	Yes
HCPI score	60	9.45 * 10 ⁻⁵	3	0.0125	Yes
Body Condition Score	132	0.03255	4	0.0167	No
CBPI QOL score	247	0.04302	5	_	No
Age	206.5	0.9359	6	-	No



Fig. 1. Box plots showing the differences in questionnaire outcome scores between groups. Asterisks indicate a significant difference (p < 0.05) between groups. Boxplots show medians with interquartile ranges. Whiskers represent the highest and lowest values within 1.5 interquartile ranges of the upper or lower quartile. Outliers beyond this range are represented with points.

Supplementary Material). Since only Group was significant at the p < 0.1 threshold, the final model contained only Group as a fixed effect. The results of the final model are shown in Table 3. Dogs with chronic pain from osteoarthritis spent significantly (p < 0.05) lower proportions of the night period resting compared to healthy control dogs, as shown in Fig. 2.

3.3. Relationship between night-time and daytime resting behaviour

Proportion of the daytime spent resting did not differ between control and osteoarthritic dogs ($\beta=-0.00457\pm0.00308,\ z=0.55,\ p=0.550).$ A weak positive (Spearman) correlation was found between average proportion of time spent resting during the day and night (rho=0.391, p=0.04), suggesting that some dogs are more generally active than others.

3.4. SNoRE score

Independent variables that had a significant effect on SNoRE score in initial models (p < 0.1) were HCPI score, CBPI Severity score, CBPI Interference score, CBPI QOL score and the interaction between group

Table 3

Results of final model for which the outcome was proportion of the night period spent resting.

		95% confidence limits				
Variable	Beta estimate	Lower	Upper	z-value	p-value	
Group						
Control	Ref.					
Osteoarthritis	0.9760	0.9540	0.9970	2.2140	0.0268	

Ref. = reference category. P-values indicating significance at $\alpha=0.1$ are shown in bold.



Fig. 2. The proportion of the night-time period spent resting for osteoarthritic and healthy control dogs. Asterisks indicate a significant difference (p < 0.05) between groups. Values are shown as means with 95% confidence intervals. Crosses indicate mean values for each individual dog (with horizontal jitter applied for improved visualisation of individual points).

and HCPI score, as shown in Table S3 (see Supplementary Material). However, all of these variables were significantly correlated, as shown in Table S4 (see Supplementary Material). Therefore, HCPI score was selected for addition to the model because it had the lowest p-value associated with its effect on SNoRE score. The final model therefore contained HCPI score as well as group and the interaction between HCPI score and group (as this was significant at the p < 0.1 threshold in the initial model) as fixed effects. The results of this model are shown in Table 4. There was no significant effect of group on SNoRE score overall, however the effects of HCPI score and the interaction between HCPI score by group interaction were statistically significant. For both groups, higher HCPI scores were associated with higher SNoRE scores (more night-time restlessness and poorer sleep). However, the magnitude of this relationship was greater for control dogs than for osteoarthritic

Table 4	
---------	--

Results of final model for which the outcome was SNoRE score.	
---	--

Main and interaction effects	Beta estimate	95% Con Limits Lower	fidence Upper	z-value	p- value
Control Osteoarthritis HCPI score HCPI score*Group Interaction	Ref. 16.0958 1.1512 0.9008	0.0740 1.0717 0.8169	3503.1130 1.2365 0.9933	-1.0117 -3.8564 2.0944	0.3117 0.0001 0.0362

Ref. = reference category. P-values indicating significance at $\alpha=0.1$ are shown in bold.

dogs, as shown in Fig. 3.

4. Discussion

The significantly higher HCPI, CBPI Severity and CBPI Interference scores of osteoarthritic compared to control dogs suggest that osteoarthritic dogs were experiencing more pain and had more mobility impairment than control dogs, as expected. This indicates that the clinical examination used was successfully able to differentiate osteoarthritic and healthy control dogs.

According to actigraphy, osteoarthritic dogs spent a lower proportion of the night period resting than control dogs, suggesting that they spent less time asleep during the night. This is consistent with findings that human osteoarthritis patients report impaired sleep (Power et al., 2005; Taylor-Gjevre et al., 2011; Wilcox et al., 2000), and the findings of Fielden et al. (2003) that human osteoarthritic patients displayed significantly improved actigraphic measures of sleep following total hip replacement, indicating that osteoarthritis-related pain was the cause of their poorer sleep prior to surgery. Whilst Leigh et al. (1988) found no significant differences in actigraphic measurements between human osteoarthritic patients and healthy control volunteers, they did observe a non-significant trend for osteoarthritic participants to move around more during the night than control participants (Leigh et al., 1988). In a recent study of horses classified according to their lameness and inferred orthopaedic disease status, there was also no apparent relationship between (automated recordings of) daily recumbency times and lameness (Kelemen et al., 2021). On the other hand, a small study of eight video-recorded hospitalised horses indicated that animals with more severe osteoarthritis spent less time in lateral recumbency than those with milder disease (Oliveira et al., 2022). Because this is the first study to compare actigraphic measures of sleep in dogs with osteoarthritis to those without, our findings should be considered exploratory. Further research is warranted to confirm these effects are generalisable to the wider population of companion animal dogs.

There was no significant effect of group on SNoRE score, suggesting that osteoarthritis may not impair dogs' sleep quality as perceived by their owners. It is also possible that the sample size in this study may have been insufficient to detect an effect. However, a sample size calculation based on mean (sd) SNoRE scores for osteoarthritic (20.13 (8.2)) and control dogs (18.14 (8.7)) indicated that future studies would require a sample of c.280 dogs per group to detect a significant difference (t-test, p < 0.05 with 0.8 power) based on the small SNoRE score effect size observed here. The significant effect of HCPI score may indicate that dogs that experienced more severe pain due to osteoarthritis had impaired sleep quality. However, this effect was not evenly



Fig. 3. The HCPI and SNoRE scores of dogs in each group. Points represent mean observed values for each dog. Lines represent scores predicted by the model, with shaded areas representing interquartile ranges for model estimates.

observed - HCPI score had a greater effect on SNoRE scores of control dogs than osteoarthritic dogs. This could potentially be because the subset of control dogs with elevated HCPI scores may have had another undiagnosed pain-causing condition that affected their sleep quality more than osteoarthritis did in the osteoarthritic dogs, potentially masking an effect of osteoarthritis on sleep quality. Alternatively, it is possible that owners of dogs with elevated scores in both the HCPI and SNoRE questionnaires may have had a tendency to perceive their dogs' behaviour more negatively than other owners, and thus tended to give higher scores on both questionnaires.

Our findings contrast with those of Knazovicky et al. (2015) that meloxicam analgesia significantly improved SNoRE scores, but not an actigraphic measure of sleep (total night-time activity), in dogs with osteoarthritis. There are several potential reasons for this. Different devices and algorithms were used, which are known to cause differences in actigraphic measures of sleep in humans (Paquet et al., 2007). Recruitment criteria were different; in particular the present study had no requirement for dogs to exhibit radiographic signs of osteoarthritis. Since radiographic signs of osteoarthritis are not always closely associated with clinical severity (Gordon et al., 2003; Hielm-Björkman et al., 2003), it was considered that radiography would have been unnecessarily invasive, require owners to visit the veterinary hospital, and would introduce unnecessary anaesthetic risks.

The present study also did not exclude dogs receiving analgesic treatment, in order to avoid biasing recruitment such that dogs with more severe pain from osteoarthritis that required analgesic treatment would have been excluded from the study and dogs with less severe pain from osteoarthritis that did not require analgesic treatment would not. Other than analgesics, one female dog with osteoarthritis was receiving Estriol for urinary incontinence and one control dog received phenobarbitone during the study period. The latter could potentially have affected this dog's behaviour but he had the seventh lowest mean proportion of time spent resting during the night and the joint sixth lowest mean SNoRE score in the control group (21 dogs), suggesting that his night time resting behaviour was not markedly different from the other control dogs.

The actigraphic outcome measures recorded were also different (the present study used mean proportions of night-time spent resting whereas Knazovicky et al., 2015 used mean activity counts per minute over the night-time period), which may be affected differently by osteoarthritis-related pain, since the night-time duration may have varied between individual dogs. It is also possible that meloxicam analgesia improves sleep in osteoarthritic dogs via alternative mechanisms than simply reducing the effects of osteoarthritis on sleep, and thus the differences in various measures of sleep between placebo-treated osteoarthritic dogs and meloxicam-treated osteoarthritic dogs may not directly reflect the differences between osteoarthritic and healthy control dogs. Additionally, intensity or duration of activity during the preceding day may have affected subsequent night-time activity, and we observed a weak positive relationship between the two suggesting that some dogs were more generally active across a day.

It is likely that owners were not regularly present in the same room as the dog whilst the dog was sleeping, and so may have guessed the answers to the SNoRE or based these on the dog's resting behaviour during the day. This is also possible in the study performed by Knazovicky et al. (2015) as dog or owner sleeping locations were not described in the inclusion criteria. Furthermore, presence or absence of the owner in the same room could have affected the dogs' sleep. In our study we know that all dogs slept indoors and, through informal communications during data collection, that the majority slept in different rooms to their owners, but we do not have quantitative data on the latter point. Whilst there is some conflicting evidence on how the presence of dogs can affect human sleep (Brown et al., 2018; Patel et al., 2017; Smith et al., 2018), it is currently unknown whether and how the presence of humans influences canine sleep. Whilst it was possible to blind owners as to whether their dog received placebo or nonsteroidal treatment in the study performed by Knazovicky et al. (2015), it is less easy to thoroughly blind owners as to whether their dogs had clinical signs of osteoarthritis, as most owners of osteoarthritic dogs were already aware of osteoarthritis-induced behavioural changes and described them within the dog's clinical history. However, it would be expected that the effects of owner perception would have caused an increased difference in SNoRE scores between osteoarthritic and control dogs, rather than preventing such a difference from being found. Additionally, because the SNoRE score has yet to be thoroughly validated, it is possible that it was unable to detect differences in night-time restlessness between osteoarthritic and control dogs, despite being able to detect differences between placebo-treated and NSAID-treated osteoarthritic dogs in Knazovicky et al.'s (2015) study.

These caveats and the small treatment effect size on SNoRE score observed here compared to our actigraphic findings suggest that SNoRE should be used with caution prior to further validation, especially when owners have little information on their dog's behaviour at night. Furthermore, future studies should address a limitation of this study and that of Knazovicky et al. (2015) by recording where dogs sleep and whether owners are present, and controlling for these factors in statistical analyses.

A further study limitation is that the researcher evaluating osteoarthritis (MS) also carried out the statistical analysis and was not blind to treatment group identities. Questionnaire results were entered by another researcher, but it was not possible for multiple veterinary staff to go on home visits to collect osteoarthritis information independently to MS. This would have been more feasible had the study been performed on-site at Bristol Veterinary School, but this may have affected dog behaviour during clinical examination and, from previous experience, would likely have impeded owner recruitment.

The actigraphic findings from this study suggest that dogs with osteoarthritis may experience impaired sleep, as seen in human patients with osteoarthritis (Power et al., 2005; Taylor-Gjevre et al., 2011; Wilcox et al., 2000) and other chronic pain conditions (Nicassio and Wallston, 1992; Riley et al., 2001). This could potentially be a welfare concern because sleep disturbance is thought to exacerbate pain severity in human chronic pain patients (Affleck et al., 1996; Morin et al., 1998), therefore impaired sleep may also cause increased pain severity in osteoarthritic dogs. It is not yet known whether the relatively small increases in night-time activity observed in this study represent sufficiently impaired sleep to exacerbate dogs' pain, but due to the potential welfare impacts this is worthy of future investigation.

Impaired sleep is also associated with impaired working memory in humans (Chee and Choo, 2004; Steenari et al., 2003), therefore sleep impairments may affect the ability of dogs with osteoarthritis to solve problems or navigate around their environment, which could alter their ability to respond to training and to engage with the environment when walking with owners. In line with these suggestions, recent dog studies show that memory improvements in command learning tasks are related to EEG spectral features and spindle density during pre-test sleep periods (Kis et al., 2017; Iotchev et al., 2017, 2020a), and that EEG sleep spindle frequency characteristics of individual dogs are associated with their reversal learning ability (Iotchev et al., 2020b). These findings suggest that, as in humans, there are links between sleep and cognitive performance in dogs and therefore that disrupted sleep may indeed have detrimental effects on dog learning and memory.

Furthermore, since sleep disturbance in human chronic pain conditions is often preceded by increased pain severity (Drewes et al., 2000; Nicassio and Wallston, 1992; Riley et al., 2001), sleep disturbance in canine osteoarthritis may also reflect increased pain and hence be useful as a welfare indicator. Because of these potential implications, further research is needed to confirm whether the findings of this study are generalisable to the wider canine population.

5. Conclusions

Osteoarthritic dogs in this study spent less time resting during the night than healthy control dogs, but did not have significantly different SNoRE scores. This suggests that dogs with osteoarthritis may spend less time sleeping during the night than control dogs and may experience impaired sleep similar to that reported in human osteoarthritis patients, and with potentially negative implications for their welfare.

Conflict of interest statement

The authors acknowledge no conflicts of interest regarding this study.

Data Availability

Data for this article are available on request from the authors.

Acknowledgements

This research was funded by the UK Biotechnology and Biological Sciences Research Council (BBSRC) South West Biosciences Doctoral Training Partnership (SWBio DTP) programme, grant number BB/J014400/1. We are grateful to the owners of the dogs for their enthusiastic participation in the study, and to three anonymous referees for their helpful and constructive comments.

Appendix A. Supplementary material

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.applanim.2022.105661.

References

- Affleck, G., Urrows, S., Tennen, H., Higgins, P., Abeles, M., 1996. Sequential daily relations of sleep, pain intensity, and attention to pain among women with fibromyalgia. Pain 68, 363–368.
- Alves, A., Panis, Y., Trancart, D., Regimbeau, J.-M., Pocard, M., Valleur, P., 2002. Factors associated with clinically significant anastomotic leakage after large bowel resection: multivariate analysis of 707 patients. World J. Surg. 26, 499–502.
- Anderson, K.L., O'Neill, D.G., Brodbelt, D.C., Church, D.B., Meeson, R.L., Sargan, D., Summers, J.F., Zulch, H., Collins, L.M., 2018. Prevalence, duration and risk factors for appendicular osteoarthritis in a UK dog population under primary veterinary care. Sci. Rep. 8, 5641.
- Arendt-Nielsen, L., Nie, H., Laursen, M.B., Laursen, B.S., Madeleine, P., Simonsen, O.H., Graven-Nielsen, T., 2010. Sensitization in patients with painful knee osteoarthritis. Pain 149, 573–581.
- Bates, D., Mächler, M., Bolker, B., Walker, S., 2015. Fitting linear mixed-effects models using lme4. J. Stat. Softw. 1 (1).
- Bogaert, D., Hermans, P.W.M., Boelens, H., Sluijter, M., Luijendijk, A., Rümke, H.C., Koppen, S., Belkum, Av, de Groot, R., Verbrugh, H.A., 2005. Epidemiology of nasopharyngeal carriage of neisseria meningitidis in healthy dutch children. Clin. Infect. Dis. 40, 899–902.
- Brown, D.C., Boston, R.C., Coyne, J.C., Farrar, J.T., 2007. Development and psychometric testing of an instrument designed to measure chronic pain in dogs with osteoarthritis. Am. J. Vet. Res. 68, 631–637.
- Brown, D.C., Boston, R.C., Coyne, J.C., Farrar, J.T., 2008. Ability of the canine brief pain inventory to detect response to treatment in dogs with osteoarthritis. J. Am. Vet. Med. Assoc. 233, 1278–1283.
- Brown, D.C., Boston, R.C., Coyne, J.C., Farrar, J.T., 2009. A novel approach to the use of animals in studies of pain: validation of the canine brief pain inventory in canine bone cancer. Pain Med. 10, 133–142.
- Brown, C.A., Wang, Y., Carr, E.C., 2018. Undercover dogs: pet dogs in the sleep environment of patients with chronic pain. Soc. Sci. 7, 157.
- Bursac, Z., Gauss, C.H., Williams, D.K., Hosmer, D.W., 2008. Purposeful selection of variables in logistic regression. Source Code Biol. Med. 3, 17-17.
- Di Cerbo, A., Sechi, S., Canello, S., Guidetti, G., Fiore, F., Cocco, R., 2017. Behavioral disturbances: an innovative approach to monitor the modulatory effects of a nutraceutical diet. J. Vis. Exp. 119, e54878.
- Chee, M.W.L., Choo, W.C., 2004. Functional imaging of working memory after 24 hr of total sleep deprivation. J. Neurosci. 24, 4560–4567.
- Conzemius, M.G., Aper, R.L., Corti, L.B., 2003. Short-term outcome after total elbow arthroplasty in dogs with severe, naturally occurring osteoarthritis. Vet. Surg. 32, 545–552.
- Dormann, C.F., Elith, J., Bacher, S., Buchmann, C., Carl, G., Carré, G., Marquéz, J.R.G., Gruber, B., Lafourcade, B., Leitão, P.J., 2013. Collinearity: a review of methods to

M. Smith et al.

deal with it and a simulation study evaluating their performance. Ecography 36, 27–46.

- Drewes, A.M., Nielsen, K.D., Hansen, B., Taagholt, S.J., Bjerregård, K., Svendsen, L., 2000. A longitudinal study of clinical symptoms and sleep parameters in rheumatoid arthritis. Rheumatology 39, 1287–1289.
- Everitt, B., Skrondal, A., 2002. The Cambridge Dictionary of Statistics. Cambridge University Press, Cambridge.
- Fielden, J.M., Gander, P.H., Horne, J.G., Lewer, B.M.F., Green, R.M., Devane, P.A., 2003. An assessment of sleep disturbance in patients before and after total hip arthroplasty. J. Arthroplast. 18, 371–376.
- Gordon, W.J., Conzemius, M.G., Riedesel, E., Besancon, M.F., Evans, R., Wilke, V., Ritter, M.J., 2003. The relationship between limb function and radiographic osteoarthrosis in dogs with stifle osteoarthrosis. Vet. Surg. 32, 451–454.
- Henrotin, Y., Sanchez, C., Balligand, M., 2005. Pharmaceutical and nutraceutical management of canine osteoarthritis: Present and future perspectives. Vet. J. 170, 113–123.
- Hielm-Björkman, A.K., Kuusela, E., Liman, A., Markkola, A., Saarto, E., Huttunen, P., Leppäluoto, J., Tulamo, R.-M., Raekallio, M., 2003. Evaluation of methods for assessment of pain associated with chronic osteoarthritis in dogs. J. Am. Vet. Med. Assoc. 222, 1552–1558.
- Hielm-Björkman, A.K., Rita, H., Tulamo, R.-M., 2009. Psychometric testing of the Helsinki chronic pain index by completion of a questionnaire in Finnish by owners of dogs with chronic signs of pain caused by osteoarthritis. Am. J. Vet. Res. 70, 727–734.
- Holm, S., 1979. A simple sequentially rejective multiple test procedure. Scand. J. Stat. 65–70.
- Hunt, J.R., Goff, M., Jenkins, H., Harris, J., Knowles, T.G., Lascelles, B.D.X.,
- Enomoto, M., Mendl, M., Whay, B., Murrell, J.C., 2018. Electrophysiological characterisation of central sensitisation in canine spontaneous osteoarthritis. Pain 159, 2318–2330.
- Iotchev, I.B., Kis, A., Bódizs, R., van Luijtelaar, G., Kubinyi, E., 2017. EEG transients in the sigma range during non-REM sleep predict learning in dogs. Sci. Rep. 7, 12936.
- Iotchev, I.B., Reicher, V., Kovács, E., Kovács, T., Kis, A., Gácsi, M., Kubinyi, E., 2020b. Averaging sleep spindle occurrence in dogs predicts learning performance better than single measures. Sci. Rep. 10, 22461.
- Iotchev, I.B., Szabó, D., Kis, A., Kubinyi, E., 2020a. Possible association between spindle frequency and reversal-learning in aged dogs. Sci. Rep. 10, 6505.
- Johnston, S.A., 1997. Osteoarthritis: joint anatomy, physiology, and pathobiology. Vet. Clin. N. Am. Small Anim. Pract. 27, 699–723.
- Kelemen, Z., Grimm, H., Long, M., Auer, U., Jenner, F., 2021. Recumbency as an equine welfare indicator in geriatric horses and horses with chronic orthopaedic disease. Animals 11, 3189.
- Kis, A., Szakadát, S., Gácsi, M., Kovács, E., Simor, P., Török, C., Gombos, F., Bódizs, R., Topál, J., 2017. The interrelated effect of sleep and learning in dogs (Canis familiaris); an EEG and behavioural study. Sci. Rep. 7, 41873.
- Kis, A., Szakadát, S., Kovács, E., Gácsi, M., Simor, P., Gombos, F., Topál, J., Miklósi, Á., Bódizs, R., 2014. Development of a non-invasive polysomnography technique for dogs (Canis familiaris). Physiol. Behav. 130, 149–156.
- Knazovicky, D., Tomas, A., Motsinger-Reif, A., Lascelles, B.D.X., 2015. Initial evaluation of nighttime restlessness in a naturally occurring canine model of osteoarthritis pain. PeerJ 3, e772.
- Koller, M., 2016. robustlmm: an R package for robust estimation of linear mixed-effects models. J. Stat. Softw. 75, 1–24.
- Kooby, D.A., Stockman, J., Ben-Porat, L., Gonen, M., Jarnagin, W.R., Dematteo, R.P., Tuorto, S., Wuest, D., Blumgart, L.H., Fong, Y., 2003. Influence of transfusions on perioperative and long-term outcome in patients following hepatic resection for colorectal metastases. Ann. Surg. 237, 860.

- Leigh, T.J., Hindmarch, I., Bird, H.A., Wrisght, V., 1988. Comparison of sleep in osteoarthritic patients and age and sex matched healthy controls. Ann. Rheum. Dis. 47, 40.
- Moreau, M., Dupuis, J., Bonneau, N.H., Desnoyers, M., 2003. Clinical evaluation of nutraceutical, carprofen and meloxicam for the treatment. Vet. Rec. 152, 323–329.
- Morin, C.M., Gibson, D., Wade, J., 1998. Self-reported sleep and mood disturbance in chronic pain patients. Clin. J. Pain 14, 311–314.
- Nicassio, P.M., Wallston, K.A., 1992. Longitudinal relationships among pain, sleep problems, and depression in rheumatoid arthritis. J. Abnorm. Psychol. 101, 514.
- Oliveira, T., Santos, A., Silva, J., Trindade, P., Yamada, A., Jaramillo, F., Silva, L., Baccarin, R., 2022. Hospitalisation and disease severity alter the resting pattern of horses. J. Equine Vet. Sci. 110, 103832.
- Paquet, J., Kawinska, A., Carrier, J., 2007. Wake detection capacity of actigraphy during sleep. Sleep 30, 1362–1369.
- Patel, S.I., Miller, B.W., Kosiorek, H.E., Parish, J.M., Lyng, P.J., Krahn, L.E., 2017. The effect of dogs on human sleep in the home sleep environment. Mayo Clin. Proc. 92, 1368–1372.
- Peat, G., McCarney, R., Croft, P., 2001. Knee pain and osteoarthritis in older adults: a review of community burden and current use of primary health care. Ann. Rheum. Dis. 60, 91–97.
- Power, J.D., Perruccio, A.V., Badley, E.M., 2005. Pain as a mediator of sleep problems in arthritis and other chronic conditions. Arthritis Care Res. 53, 911–919.
- R Core Team, 2014. R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing, Vienna, Austria.
- Reicher, V., Bunford, N., Kis, A., Carreiro, C., Csibra, B., Kratz, L., Gacsi, M., 2021. Developmental features of sleep electrophysiology in family dogs. Sci. Rep. 11, 22760.
- Riley, J.L., Benson, M.B., Gremillion, H.A., Myers, C.D., Robinson, M.E., Smith Jr, C.L., Waxenberg, L.B., 2001. Sleep disturbance in orofacial pain patients: pain-related or emotional distress? CRANIO® 19, 106–113.
- Sadeh, A., 2011. The role and validity of actigraphy in sleep medicine: an update. Sleep Med. Rev. 15, 259–267.
- Smith, B.P., Browne, M., Mack, J., Kontou, T.G., 2018. An exploratory study of human–dog co-sleeping using actigraphy: do dogs disrupt their owner's sleep? Anthrozoös 31, 727–740.
- Sofat, N., Ejindu, V., Kiely, P., 2011. What makes osteoarthritis painful? The evidence for local and central pain processing. Rheumatology 50, 2157–2165.
- Steenari, M.-R., Vuontela, V., Paavonen, E.J., Carlson, S., Fjällberg, M., Aronen, E.T., 2003. Working memory and sleep in 6-to 13-year-old schoolchildren. J. Am. Acad. Child Adolesc. Psychiatry 42, 85–92.
- Stone, A.A., Broderick, J.E., Porter, L.S., Kaell, A.T., 1997. The experience of rheumatoid arthritis pain and fatigue: examining momentary reports and correlates over one week. Arthritis Rheumatol. 10, 185–193.
- Taylor-Gjevre, R.M., Gjevre, J.A., Nair, B., Skomro, R., Lim, H.J., 2011. Components of sleep quality and sleep fragmentation in rheumatoid arthritis and osteoarthritis. Musculoskelet. Care 9, 152–159.
- Wilcox, S., Brenes, G.A., Levine, D., Sevick, M.A., Shumaker, S.A., Craven, T., 2000. Factors related to sleep disturbance in older adults experiencing knee pain or knee pain with radiographic evidence of knee osteoarthritis. J. Am. Geriatr. Soc. 48, 1241–1251.
- Wiseman, M.L., Nolan, A.M., Reid, J., Scott, E.M., 2001. Preliminary study on ownerreported behaviour changes associated with chronic pain in dogs. Vet. Rec. 149, 423–424.
- WSAVA Nutritional Assessment Guidelines Task Force Members, 2011. WSAVA nutritional assessment guidelines. J. Feline Med. Surg. 13, 516–525.