Evaluation of the Environmental Bias on Accelerometer-Measured Total Daily Activity Counts and Owner Survey Responses in Dogs with Osteoarthritis

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Abstract

Objective To determine if environmental variables affect the average daily activity counts (AC) of dogs with osteoarthritis (OA) and/or owners’ perception of their dog’s clinical signs or quality of life.

Methods The AC and Canine Brief Pain Inventory (CBPI) owner questionnaires of 62 dogs with OA were compared with daily environmental variables including the following: average temperature (°C), high temperature (°C), low temperature (°C), relative humidity (%), total precipitation (mm), average barometric pressure (hPa) and total daylight hours.

Results Daily AC significantly correlated with average temperature and total daylight hours, but average temperature and total daylight hours accounted for less than 1% of variation in AC. No other significant relationships were found between daily AC and daily high temperature, low temperature, relative humidity, total precipitation or average barometric pressure. No statistical relationship was found between daily AC and the CBPI, nor between environmental variables and the CBPI. Canine Brief Pain Inventory scores for pain severity and pain interference decreased significantly over the test period.

Clinical Significance The relationship between daily AC and average temperature and total daylight hours was significant, but unlikely to be clinically significant. Thus, environmental variables do not appear to have a clinically relevant bias on AC or owner CBPI questionnaires. The decrease over time in CBPI pain severity and pain interference values suggests owners completing the CBPI in this study were influenced by a caregiver placebo effect.

Keywords ► osteoarthritis ► osteoarthritis management ► clinical orthopaedics ► clinical studies

Introduction

Historically, people with osteoarthritis (OA) report that their symptoms of pain and joint stiffness are influenced by weather conditions and worsen with cold temperature, precipitation or both.1–4 It has been reported that 62 to 92% of people believe that they are weather-sensitive and experience aggravation of their OA symptoms in relation to weather.1,3–5 Anecdotally, veterinary clients report similar worsening of clinical signs in relation to weather in their pet dogs suffering from OA.
However, scientific literature addressing the relationship between weather and clinical symptoms in dogs with OA is scarce.

A multitude of studies have evaluated the association between weather conditions and the symptoms related to OA in humans yielding conflicting results. Pain and function of a cohort of 222 Dutch patients with hip OA, who participated in a 2-year prospective, randomized, controlled clinical trial evaluating the efficacy of glucosamine sulphate, was studied in relation to weather variables. The authors found a significant relationship between weather variables and pain and function as measured by the self-administered Western Ontario and McMaster University Osteoarthritis Index (WOMAC) subscale. However, they reported the changes were not clinically relevant as the overall contribution of the weather variables to variation in the pain or function scores was small (≤1%). For perspective, they found a 10% increase in relative humidity corresponded to an increase of WOMAC pain score of 1 (1–100) and a 10-hPa increase in barometric pressure corresponded to a decrease of the WOMAC function score by 1 (1–100).

One of the largest weather-related studies involved 2,942 patients with OA across six European countries as part of the European Project on OSteoArthritis. The study looked for associations between self-reported joint pain, self-perceived weather sensitivity (individuals who believe their pain is affected by damp/rainy weather, cold weather or hot weather), emotional distress such as anxiety and depression, mastery or the feeling that one is in control of their environment, frequency and duration of physical activity, body mass index, number of comorbidities, local climate and seasonal weather patterns. The study found that those who perceived that their symptoms were weather-sensitive experienced significantly more joint pain overall that was more intense than that of their non-weather-sensitive counterparts in their local climate. Interestingly, most of the weather-sensitive participants reported to be sensitive to damp, rainy weather, cold weather or both. However, it was shown that those living in a cold, wet climate reported lower pain intensity levels than those in a warm and wet or dry climate. A psychological bias was suggested to explain these findings. Also, they found six significant predictors of weather sensitivity including sex, education, country, anxiety, depression and mastery—all but one of which are psychological factors.

An important limitation of studies of human patients with OA is that they largely rely on patient self-reported activity and pain questionnaires rather than objectively measured physical activity. These retrospective recall methods may overlook work- or transportation-related physical activities. Additionally, they significantly overestimate the rates of moderate and vigorous physical activity among elderly patients. Accelerometers objectively measure all physical activity, including short bouts of light intensity activity such as walking, which may go unrecorded with aforementioned questionnaires. A 3-year cohort study was performed relating the accelerometer-measured physical activity of 241 arthritis patients, enrolled in an arthritis physical activity trial, to weather variables. The study found that reduced total daylight hours (TDH), daily average temperature (AT) of <20 or ≥75°F and light or heavy rainfall were significantly associated with lower total daily activity counts (AC). Cold days were associated with fewer (and often no higher intensity) activity minutes. Hot days were associated with short bursts of high-intensity activity, with less overall activity than moderate temperature days. However, a significant limitation of this study was the fact that participants were randomized into treatment groups to evaluate the efficacy of different physical activity promotion methods in arthritics. Even the control group received advice to increase physical activity. While this study design may reduce the psychological bias of the participants, it is difficult to discern whether the activity changes reported are from environmental conditions or the instructions to exercise.

Induced animal models of joint pain have been used to investigate the relationship between weather variables and OA pain. A rat model of arthritis, induced via an intra-articular injection of complete Freund’s adjuvant into the knee joint, was used to study the relationship between pressure changes and pain intensity. Sixteen young adult male Sprague Dawley rats with induced knee OA were placed in a hyperbaric pressure chamber and exposed to pressures of 1 or 2.5 atm for periods of 5 hours daily for 14 days. Pain was assessed daily after a 30-minute decompression period by measuring the weight placed on the affected knee and comparing it to the pre-injection weight-bearing value. The study found that the rats in the 2.5-atm test group showed more significant improvement in weight-bearing than the control (1 atm) and, therefore, less pain throughout the test period.

Osteoarthritis affects as many as one in 3 of the human senior population. While it has been reported that approximately 20% of dogs will experience chronic pain associated with OA, empirically the frequency of clinical symptoms from OA may be higher especially in some populations of dogs. It is important to further evaluate the relationship between weather variables and OA pain to elucidate mechanisms of pain and disease progression, to aid in the development of novel therapies and to potentially control for variables affecting clinical study design.

The objective of this study was to determine if environmental variables (daily AT, high temperature [HT], low temperature [LT], relative humidity [RH], total precipitation [TP], average barometric pressure [ABP] and TDH) affect average daily AC of dogs with OA and/or owners’ perception of their dog’s clinical symptoms or quality of life. Based upon the conflicting data in the human literature, our null hypothesis was that there is no association between the dependent variables (AC and Canine Brief Pain Inventory [CBPI] outcomes) and the independent variables (weather and time) in dogs exhibiting clinical signs of OA.

**Methods**

A prospective cohort study was performed utilizing AC and owner questionnaires of dogs receiving the placebo from two randomized, double-blinded, placebo-controlled clinical trials evaluating the safety and efficacy of oral nutraceuticals for the management of pain and inflammation associated with OA.
Both clinical studies used in this study had identical inclusion and exclusion criteria, blinding and randomization procedures, technical and professional staff, and quality assurance oversight. The number of dogs screened, dogs enrolled and study initiation dates for the two studies differed. Both clinical studies were approved by the Institutional Animal Care and Use Committees and completed within the University of Minnesota Veterinary Medical Center. Dogs were enrolled and tested from April 2013 to September 2015. All dogs resided within Minnesota for the duration of the study period.

One hundred and sixty client-owned dogs with clinical signs secondary to OA were enrolled in both studies. Inclusion criteria included informed owner consent, overall healthy, weight 5 to 85 kg, older than 8 months of age, lameness and/or disability secondary to OA in one or more joints, joint pain on orthopaedic examination performed by a veterinary surgeon and radiographic confirmation of OA in at least one joint. Overall systemic health was evaluated by a thorough history, physical examination, haematology and blood biochemistry panel.

Dogs were excluded if they were pregnant, lactating, intended for breeding or if their owners had significant changes in their day-to-day activity planned (e.g. vacation, moving) during the study period. Dogs could not be treated with oral corticosteroids for 30 days; nonsteroidal anti-inflammatory drugs for 7 days; other oral analgesic medications for 7 days; or glucosamine, chondroitin, omega-3 fatty acid products (including veterinary diets) or any combination of these for 14 days prior to enrolment. Injections of hyaluronic acid, corticosteroids and polysulphated glycosaminoglycan 3 months prior to enrolment also precluded participation. Dogs that underwent joint surgery within 6 months of enrolment were excluded.

Dogs were randomized for each study using a random number generator into a placebo control group, product control group and/or a test nutraceutical group. Study personnel that had no interaction with the client or patient performed the randomization procedure. The study veterinarian and client were blinded to the dog’s treatment group assignment. A patient’s treatment group was revealed upon completion of the study, and only dogs randomized to placebo treatment were included in this evaluation. Outcome measures included the CBPI, daily AC and weather variables. Clients completed a CBPI prior to enrolment (day −7) and at each subsequent visit (days 30 ± 3, 60 ± 3 and 90 ± 3). Day −7 served as the baseline score for CBPI. Canine Brief Pain Inventory questions 1 to 4 were summed to establish pain severity score (PSS) and questions 5 to 10 were summed to establish pain inference score (PIS); only dogs with a PSS and PIS ≥ 2 were enrolled. Activity counts were measured by Actical accelerometer (AM) attached to device-specific collars worn ventrally on the neck. The AM was placed on the dog at the end of the day −7 hospital visit. Owners were instructed to have the dogs wear the AM continuously for the duration of the study and not to attach a leash to the AM collar. The days between days −7 and 0 served to establish a baseline value, or control, for each patient so that change in the patient’s AC after the administration of an intervention could be assessed. The AM measures frequency and duration of movement in all six planes. A voltage generated by acceleration is converted into a digital value and adjusted by a baseline value representative of acceleration due to gravity. The raw activity value is the difference between the digital value generated during the sampling period, or epoch, and the baseline value. The raw activity value is converted by software to an AC for that epoch. The epoch length used was 60 seconds.

A rescue analgesic protocol and additional interventions were implemented if medically indicated and the dog was withdrawn from the study. Pet owners incurred no costs for participation and were compensated with a 6-month supply of the test nutraceutical upon completion of the study.

Quality controlled local climatological data nearest to the clients’ zip code were obtained from the National Oceanic and Atmospheric Administration’s (NOAA) National Centers for Environmental Information. Daily environmental variables of AT, HT, LT, dew point (°C), TP, ABP and TDH reported by the NOAA’s weather stations nearest to each dog’s home were utilized for comparison. Relative humidity was calculated using the following formula, \( r_h = \frac{T - 100}{T - T_d} \times 100 \), where actual vapour pressure \( e = 6.11 \times 10^{(t/237.7)} \), and saturated vapour pressure \( e_s = 6.11 \times 10^{(t/237.7)} \). Actual vapour pressure is calculated from the dew point temperature, \( T_d \), and \( e_c \) is calculated from the air temperature, \( T \).

The objective of statistical analysis was to discover clinically useful relationships between the dependent variables (AC and CBPI outcomes) and the independent variables (weather and time). Clinically useful relationships were defined as ones that could be used to model or control for confounding weight and time variables. We investigated linear models (ANOVA, linear models including higher-order linear models, e.g. quadratic models), transformations, subset analyses (e.g. weekdays vs. weekends, high temperatures vs. low temperatures) and visual identification of patterns. When regression models were performed, the variance of the error terms was explored to ascertain the validity of the model. Black-box models, machine learning and other methods that are not generally available to users were not explored.

Conventional models from the simplest to the most sophisticated were constructed, noting those models that fit the data. The cumulative effect of type I error from multiple testing was not controlled since this study was exploratory, not confirmatory. The goal was to find a set candidate model and relationship that might be confirmed with a future study that restricted type I error to 0.05. There is no statistical framework to correct type I error inflation in the multiple model scenario. The Bonferroni correction does not apply directly to the multiple model situations, only to post hoc tests in ANOVA models.

Study populations were compared on number of dogs rescued, sex, body weight or age using the Wilcoxon rank-sum test or Fisher’s exact test, depending on the type of response.

**Results**

Sixty-two (33 and 29 dogs from the two studies) different client-owned dogs received placebo and were included in this
study. Eleven dogs (17.7%) were prescribed rescue medication for worsening of clinical symptoms and discontinued from the study. Data until the dog was removed or rescued were included in the analysis. Twenty-eight different breeds were represented—the most common being the Labrador Retriever ($n = 19$), Golden Retriever ($n = 5$), Mixed breed ($n = 4$) and Pug ($n = 3$). Twenty-six (41.9%) of the dogs were neutered males; the remaining were spayed females. On average, dogs weighed 27.8 kg (6.7–53 kg; SD: 10.7 kg) and were 8.0 years old at the time of enrolment (1–14 years; SD: 3.1 years). There were not any significant differences in the sex ratio, mean body weight, age or the number of dogs that received rescue analgesia between the study populations.

Over the study period, there were a large range of daily AC and weather variables within and between dogs (–Fig. 1). In one dog, daily AC ranged from 35,882 to 331,098 and over the course of the entire study daily AT ranged from −28 to 31°C. A significant relationship between weather and AC was identified. Daily AC increased as daily AT increased ($p < 0.001$) and as TDH increased ($p < 0.001$; –Fig. 2). Although the $p$-value is significant, the independent weather variables contributed to less than 1% ($R^2 < 0.01$) of the variation in AC. No statistical relationship was found between daily AC and the CBPI or weather and the CBPI.

Using a mixed-effects model with dog identification number as the random effect to account for the repeated measures and study day as the fixed effect, daily AC and weather variables did not change over time ($p = 0.728$ that the means of daily AT were different over time). However, the sum of the CBPI PSS (sum of questions 1–4; $p = 0.004$) and PIS (sum of questions 5–10; $p = 0.005$) significantly decreased with subsequent questionnaires (–Table 1). A regression line was calculated and plotted for these data (–Fig. 3). Residuals were calculated and plotted to validate quality of fit for a linear model and $R^2$ was calculated. For CBPI PSS and PIS, $R^2 = 0.96$ and 0.99, respectively.

**Discussion**

A significant relationship between weather and time variables and AC was discovered. However, because their contribution to the variation in AC was exceptionally low (<1%), it is believed to be clinically irrelevant. Thus, environmental variables do not appear to bias the AC of dogs with OA. This is consistent with the aforementioned study in people, where they found a statistical relationship between RH, ABP and pain and function in patients with hip OA, but the relationship was not clinically relevant because the change was very small (1%). However,
Similarly, in this study we failed to find a statistical relationship between CBPI and an objective outcome measure in patients with OA (patient activity). Like force platform gait analysis, accelerometers detect patient movement that may go unnoticed by the owner. Documenting the owner’s opinion regarding the status of a veterinary patient is important, similar to gathering a patient history for any dog that presents to the hospital. For dogs with OA, owner questionnaires have proved to be valuable, as they have demonstrated a treatment effect for many nonsteroidal anti-inflammatory drugs. However, since it has been determined that owner questionnaires do not correlate with direct measurements of the patient, it may be prudent to balance outcome measures including information from the owner and objective measurements of the patient.

It is imperative to understand that accelerometer data are highly variable within a dog between days and between dogs and that they are affected independently by age and body weight.14,15,23,24 When other variables are controlled, it has been suggested that advancing age or increasing body weight decreases AC in a linear fashion.23 Additionally, with respect to change in a patient with OA, it is unclear how to interpret a change in AC. For example, how does an increase in AC by 10% relate to distance travelled or intensity of activity? Until we better understand the relationship between AC and clinically translatable outcome measures, activity monitoring may be best suited to evaluate changes in AC within individual dogs over time in response to a treatment.15 Furthermore, while age and body weight were included in statistical modelling, we did not measure patient height, stride length or other morphometric features that might influence AC. We did not control for how much time the dogs spent indoors or outdoors. Finally, no single dog wore the activity monitor for more than two seasons in Minnesota. A more appropriate study design might have patients wear activity monitors to span all of the seasons.

In this evaluation of dogs with OA, we found that environmental weather variables do not appear to have a clinically important bias on AC or owner CBPI responses. CBPI PSS and the PIS significantly decreased with time, suggesting a measurable caregiver placebo effect should be expected when using this questionnaire.

References

Fig. 3 Linear regression lines providing an overview of change over time for the sum of the Canine Brief Pain Inventory severity scores 1 to 4 (dotted line; $R^2 = 0.96$), the sum of the Canine Brief Pain Inventory pain inference scores 5 to 10 (dashed line; $R^2 = 0.99$) and mean daily activity count (solid line; $R^2 = 0.13$). Canine Brief Pain Inventory questions significantly decreased with time; average daily activity count did not.
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