

Use of activity monitors for assessment of pruritus in an acute model of canine atopic dermatitis

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Background – We developed a canine model of acute atopic dermatitis to evaluate the potential of compounds to treat pruritus and skin lesions induced in *Dermatophagoides farinae* (Df)-sensitized dogs.

Hypothesis/Objectives – The aim was to investigate the effectiveness of long-term recording activity monitors to assess pruritus induced by allergen challenges.

Animals – Thirty-two Df-sensitized laboratory dogs.

Methods – In two blinded crossover studies, 28 Df-sensitized dogs were challenged on 3 days with a Df slurry applied to clipped abdominal skin. Dogs were treated with a positive control (prednisolone 1 mg/kg once daily for 5 days, starting 1 day before challenge) or left untreated; all were fitted with activity monitors. To confirm pruritus, a parallel study with four dogs was conducted, filming the dogs before and during challenge and assessing the film for pruritic behaviour.

Results – The activity of dogs treated with prednisolone was significantly lower between 00.00 and 03.00 h and between 03.00 and 06.00 h compared with untreated dogs (repeated-measures ANCOVA; $P < 0.0001$). To determine whether the recorded night-time activity corresponded to pruritic manifestations, we compared activity monitor and video recordings of four dogs for two periods (16.30–20.30 and 24.00–03.00 h) before and during a Df challenge. The correlation between night-time activity monitor activity and observed pruritic behaviour was highly significant (test of correlation coefficient versus zero: $r = 0.57$, $P < 0.0001$).

Conclusions and clinical importance – Determination of night-time activity with activity monitors after allergen challenge appears to be an objective and practical way to assess pruritus in this experimental model of canine atopic dermatitis.

Introduction

Canine atopic dermatitis (cAD) is a common dermatological disease in dogs and is defined as a genetically predisposed inflammatory and pruritic allergic skin disease with characteristic clinical features associated with IgE antibodies most commonly directed against environmental allergens.¹ The pathogenesis of cAD is complex and not fully understood. It involves a compromised barrier function, which induces an initial T-helper (Th)2-prone response leading to modulated keratinocyte differentiation and further epidermal barrier impairment.

Mechanical injury by scratching or tape stripping perpetuates or induces epidermal barrier disruption and expression of cytokines such as thymic stromal lymphopoietin, inducing a Th2-skewing milieu.^{2–4} However, in chronic lesions Th1, Th17 and Th22 cells prevail.² During this process, pruritogenic cytokines such as interleukin-

31 are released, stimulating neuronal pruritus and linking the immune reaction to the nervous system.⁵ This chain of events leads initially to an acute and subsequently to a chronic allergic skin reaction, with the accompanying characteristic clinical features. Chronic pruritus is a cardinal sign of cAD and is very often the reason for the owner to consult a veterinarian. The evaluation of itch is important for the diagnosis and for subsequent monitoring of disease progress and effectiveness of treatment.⁶ Measuring pruritus objectively and for sustained periods is difficult. In a clinical setting, itch is most frequently assessed by the owner using a visual analog scale.⁶ This has been shown to be relatively accurate and reproducible, but it remains subjective. One study described use of activity monitors to evaluate itch in dogs with cAD in their homes and demonstrated that night-time activity of dogs suffering from cAD is increased compared with that of healthy dogs.⁷ Another study showed correlation of accelerometer-measured motion and observed nocturnal pruritus in 15 kennelled dogs.⁸

We have a model of house dust mite (HDM)-allergic dogs following a standardized sensitization procedure. Once successfully sensitized, these dogs can be chal-

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lenged with HDM and they develop pruritus and skin lesions comparable to dogs suffering from naturally occurring cAD and to other HDM-allergic dog models that have been published.^{9–11} We use this model to test potential therapies for treatment of allergic dermatitis using the clinical end-points of pruritus and lesion score. The objective of the present studies was to evaluate whether we could use activity monitors to assess pruritus objectively and over long periods of time.

Materials and methods

Animals

The dogs used in these studies were purpose-bred laboratory beagles from two approved facilities. All procedures included in this work were approved by the local institutional and governmental veterinary authorities on animal care and use. A total of 32 dogs were used, 28 in two crossover-design studies and four in a parallel-design study. The ages of the dogs ranged from 1 to 4 years at the time the studies were conducted. Fifteen dogs were females (one spayed) and 17 were males (11 castrated). These dogs were housed in a mite-poor environment and did not present with clinical signs of allergic dermatitis prior to sensitization.

All dogs enrolled in studies were judged to be in good condition and healthy, based on general physical and dermatological examination, and were not receiving any medication that could influence the outcome. Regular blood samples were taken for evaluation to ensure the good health of the dogs.

Sensitization and challenge

The dogs had been sensitized epicutaneously to the house dust mite *Dermatophagoides farinae* (Df; Greer Laboratories, Lenoir, NC, USA). Successful sensitization was confirmed with two challenges, in which all dogs had to develop skin lesions over a predefined score. In the majority of selected dogs, subsequent studies showed that they also had serum Df-specific IgE and positive intradermal tests to Df.

Once successfully sensitized, the dogs were used in challenge studies. For a challenge, the dogs were sprayed with a Df slurry at a concentration of 31 mg/mL on three consecutive days to the clipped and tape-stripped ventral abdomen. Phosphate-buffered saline (pH 7.2) was used as a diluent. Daily lesion scoring and pruritus evaluation were conducted to monitor the allergic reactions of the dogs.

Study design

The activity monitor data were collected during two studies, which were conducted using a crossover design. Briefly, the dogs were randomly allocated to either the positive control or the untreated group. Each dog acted as its own control by being included in both treatment groups in sequential phases. The order in which the dogs were enrolled in either group was random. The

dogs were housed in pairs, and each pair of dogs was in the same treatment group to avoid potential contamination. There was a minimum of 4 weeks washout between the phases. The lesion scoring of the dogs was always performed by a trained person blinded to the treatment groups to ensure unbiased scoring. An overview of the design of the crossover studies is depicted in Figure 1. The positive control was oral prednisolone at a dose of ~1 mg/kg once daily. Treatment was initiated 1 day before the challenge and terminated 4 days after the first day of challenge.

Activity monitors

The activity monitors (Actical®; Mini Mitter Company, Respironics, Bend, OR, USA) were attached to the dogs' collars. For data interpretation, the Actireader® and Actical® Software (Mini Mitter Company, Respironics) were used.

Activity monitors are piezoelectric accelerometers that can detect and record movement. They were programmed to record cumulative activity with an epoch of 1 min for ~2 weeks continuously. At the end of the study, using the proprietary reader (Actireader®) the activity monitor data were downloaded to a computer and then sent for statistical analysis. For every 24 h, the 1 min data were condensed to 1 h means and then to 3 h means (24.00–03.00, 03.00–06.00, ..., and 21.00–24.00 h), 6 h means (24.00–06.00, 06.00–12.00, 12.00–18.00 and 18.00–24.00 h), day and night means (06.00–18.00 and 18.00–06.00 h of the next day) and total means (06.00–06.00 h of the next day).

The monitors were attached to the individual dog collars 5–7 days before each challenge to collect individual baseline activity data; they were removed and the data downloaded 2 days after the last allergen application.

Video recording of pruritic behaviour

Data used for evaluation of pruritus by video recording were from one parallel-design study with a group of four sensitized, untreated dogs (two females and two males, aged 1 year). This study was designed to be comparable to one arm of the crossover studies with additional video recording.

To film the dogs, we used GoPro 3 Silver Edition cameras (Woodman Labs Inc., San Mateo, CA, USA). The cameras were mounted on the ceiling above the dog pens, allowing a complete overview of each pen. The dogs were housed in pairs. One dog of each pair was marked with sheep marker crayon to allow individual identification of the animals. The dogs were filmed two nights before the challenge and every night during and after the challenge. They were filmed at two time intervals, i.e. from 16.00 to 20.30 h and from 24.00 to 03.00 h of the following day. The lights in the kennel were switched on ~30 min before each recording period and turned off at the end of the recording.

The pruritic behaviour was determined by observing the recorded film of the dogs at 30 min intervals and recording the duration (in minutes) of each pruritic episode with a stopwatch. Scoring was performed by two independent observers. The exact

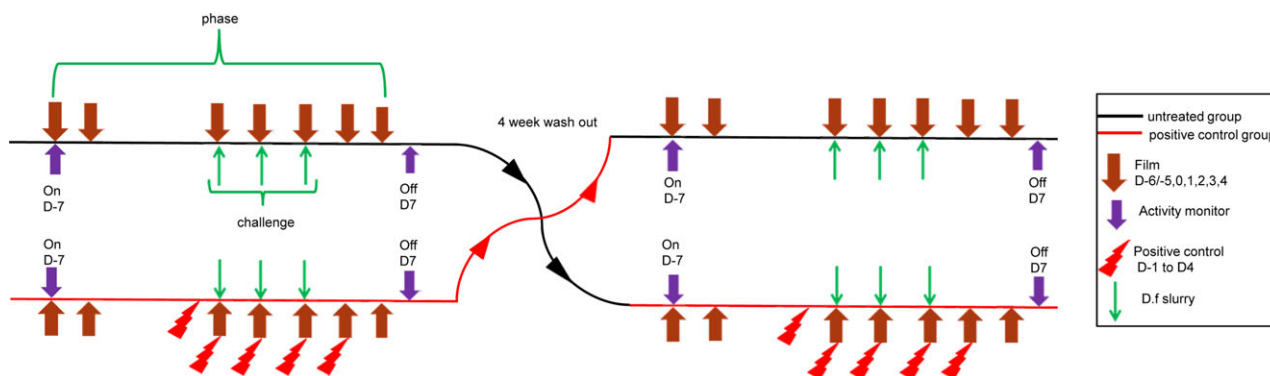


Figure 1. Outline of crossover studies with activity monitor measurements.

time intervals and length of time of pruritic behaviour were recorded in a prepared Excel spreadsheet that was used for statistical evaluation.

Lesion score

During the challenge, the dogs were examined daily and skin lesions recorded. We used our own lesion score adapted from the CADESI-03¹² scoring system. Our scoring system involved examination of 22 defined and specific body sites on each dog. Each body site was scored according to the clinical signs of erythema, papules and excoriation. Each clinical sign was graded from 0 to 5 (0, nothing; 1 and 2, mild; 3 and 4, moderate; and 5, severe). Using this lesion score, we arbitrarily considered a dog to have shown an allergic reaction when it had reached a total daily score of ≥ 40 , which corresponds to a moderate reaction.

Statistical methods

A repeated-measurements analysis of covariance (RMANCOVA) model was fitted to the data of the crossover-design study with the following effects: treatment, day, interaction of treatment and day, sequence, animal number, phase, baseline value, unit (animal number within each phase) as a random effect and an autoregressive of first-order covariance structure [AR(1)] for the repeated measurements. Interaction of treatment and day takes into account the potential differences of the effect of treatment on any given day and the effect of the day on any given treatment. The AR(1) allows for correlation of an individual to the study days. Without this, instead of comparing two animals on four study days, it would be like comparing eight animals on four study days.

In addition to the RMANCOVA model, for the parallel-design study an analysis of (co)variance model (ANCOVA) was fitted to the data of each day after baseline with the same effects as in the RMANCOVA model, except for day, interaction of treatment and day, and the repeated-measurements structure.

To compare the baseline values over groups, an ANOVA model was fitted to the baseline data.

All statistical tests in these studies were two sided, and those with a corresponding P value ≤ 0.05 were considered statistically significant.

For activity, a logarithmic transformation was applied, in order to improve normality of the residuals. To avoid taking logarithms of zero, a small value (1) was added before the transformation. Treatment groups were compared in a pairwise manner, without and with correction for multiplicity. All calculations were carried out using the software SAS[®] version 9.2 (SAS Institute Inc., Cary, NC, USA).

Results

Evaluation of activity monitor data

In Figure 2a, the mean activity measured by activity monitor during a quiet period in the kennel (between 03.00 and 06.00 h) is depicted and shows a significant difference between prednisolone-treated and untreated Df-sensitized dogs.

For comparison, during a time slot in which the dogs were all very active due to the feeding and exercise routine in the kennel, between 09.00 and 12.00 h, we saw a lack of difference between the two groups (Figure 2b) before and after challenge.

Table 1 shows the differences in mean activity recorded over 24 h in two independent crossover studies. The results show that in both studies the measured mean activity in the prednisolone-treated dogs was significantly lower compared with the untreated Df-challenged dogs for some of the 3, 6 and 12 h time periods (see Table 1 for details).

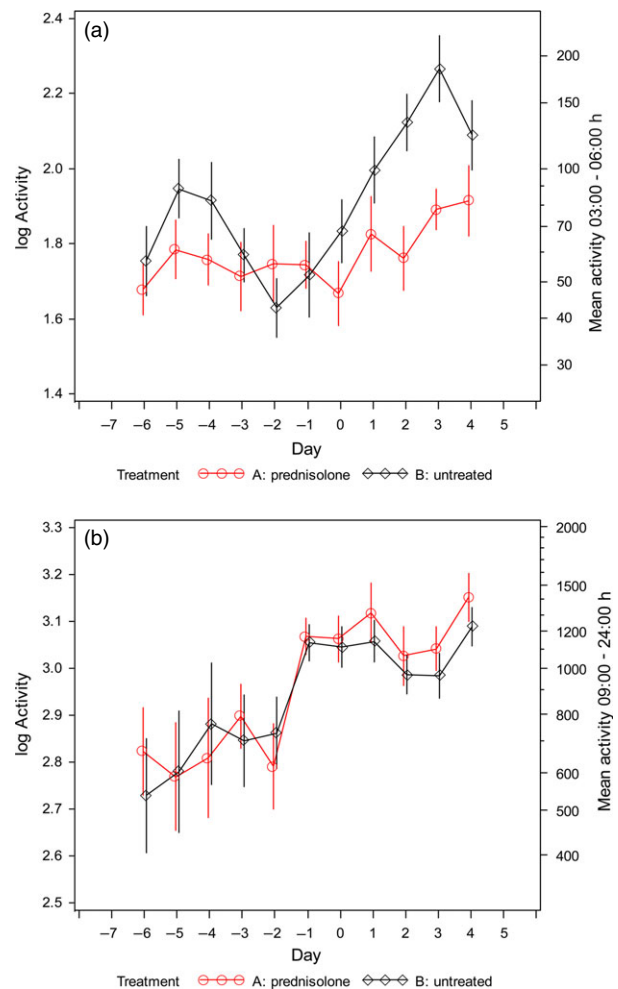


Figure 2. (a) Mean activity (means $\pm$ SEM) measured by activity monitors of positive control treated (A, prednisolone) and untreated sensitized dogs (B; $n = 16$) in a crossover design before (days -7 to -1) and during challenge (days $0-4$) between 03.00 and 06.00 h. The difference in mean activity levels at baseline of the two groups was taken into account as a covariant in the RMANCOVA model used in the statistical analysis. (b) Mean activity (means $\pm$ SEM) measured by activity monitors of positive control treated (A, prednisolone) and untreated sensitized dogs (B; $n = 16$) in a crossover design before (days -7 to -1) and during challenge (days $0-4$) between 09.00 and 12.00 h.

Evaluation of pruritic behaviour by filming

By comparing the activity measured by activity monitor and the pruritic behaviour score expressed as minutes of pruritic behaviour, we found that the correlation between observed pruritic behaviour and activity monitor measurement was highly significant (correlation coefficient versus zero: $r = 0.57$, $P < 0.0001$; Table 2). Additionally, all dogs had an overall increase in pruritic behaviour compared with baseline during the challenge, but not in every observed time period (Figure 3).

Discussion

The aim of this work was to determine the usefulness of activity monitors to determine pruritic behaviour in a model of HDM-sensitized dogs.

Pruritus is one of the hallmarks of canine atopic dermatitis. One study showed that the correlation between

Table 1. Differences in mean activity during different time slots measured by activity monitors in two crossover-design studies

Response	A versus B, Study 1 (<i>n</i> = 16)	A versus B, Study 2 (<i>n</i> = 12)	
Mean activity 24.00–03.00 h	<0.0001 A*	<0.0001 A*	Mean activity in 3 h periods
Mean activity 03.00–06.00 h	0.0006 A*	0.0085 A*	
Mean activity 06.00–09.00 h	0.6881	0.7413	
Mean activity 09.00–12.00 h	0.2245	0.2591	
Mean activity 12.00–15.00 h	0.0387 A*	0.9266	
Mean activity 15.00–18.00 h	0.0001 A*	0.0166 A*	Mean activity in 6 h periods
Mean activity 18.00–21.00 h	<0.0001 A*	<0.0001 A*	
Mean activity 21.00–24.00 h	<0.0001 A*	<0.0001 A*	
Mean activity 24.00–06.00 h	<0.0001 A*	0.0010 A*	
Mean activity 06.00–12.00 h	0.9106	0.3735	
Mean activity 12.00–18.00 h	0.0014 A*	0.7301	Mean activity in 12 h periods
Mean activity 18.00–24.00 h	<0.0001 A*	<0.0001 A*	
Mean activity, day 06.00–18.00 h	0.9995	0.3091	
Mean activity, night 18.00–06.00 h	<0.0001 A*	<0.0001 A*	Mean activity over a 24 h period
Mean activity, total 06.00–06.00 h	0.1767	0.6990	

Mean activity, RMANCOVA group comparisons (adjusted *P* values for comparison); A, prednisolone-treated group; and B, untreated group.

*Significant value.

Table 2. Correlation and *P* value for correlation

	First variable	Second variable	All dogs	Dog 1	Dog 2	Dog 3	Dog 4
Nonzero correlation	Pruritus minutes	Mean activity	0.570*	0.480	0.718*	0.386	0.440
<i>P</i> value for correlation	Pruritus minutes	Mean activity	<0.0001	<0.0001	<0.0001	0.0004	<0.0001

'Pruritus minutes' is the duration (in minutes) of each observed pruritic episode. 'Mean activity' is the activity of the dogs determined with activity monitors during the period that the film was observed, i.e. 16.30–20.30 and 24.00–03.00 h. *A nonzero correlation of 0.5 is highly significant.

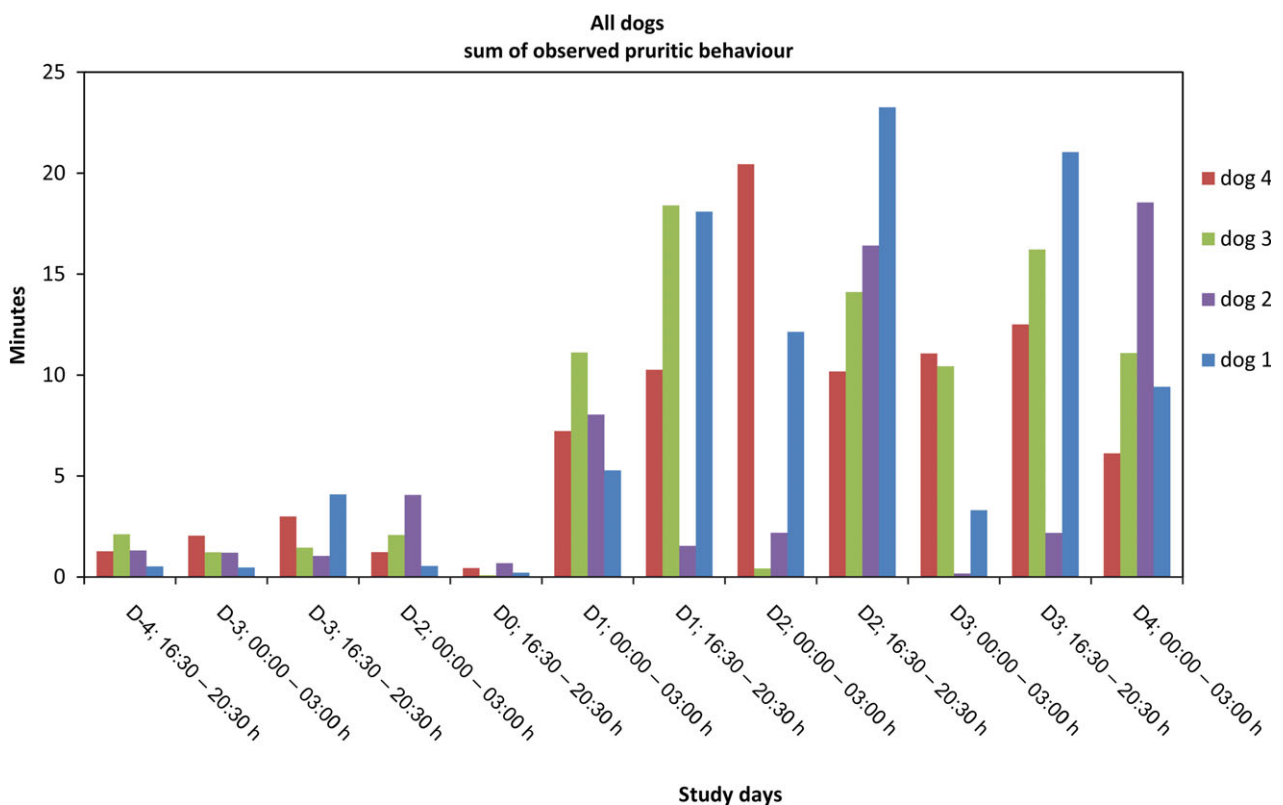


Figure 3. Observed pruritic behaviour of four sensitized dogs before (days –4 to –2), during (days 0–2) and after house dust mite challenge (days 3 and 4) scored from video recording. The columns represent the hourly sum (in minutes) of pruritic behaviour for each dog within the time periods 16.30–20.30 and 24.00–03.00 h. Days –4 and 4 only have one observational period each because they are the days on which the filming was started and ended, respectively.

quality of life and pruritus in dogs suffering from pruritic skin disease and of their owners was significant ($P = 0.001$ and 0.023 , respectively).¹³ This suggests the

importance of controlling itch and of monitoring it during treatment as an indication of success of antipruritic therapy.⁶ In spontaneous cAD, owners typically assess

pruritus with a visual analog scale, but this is not practical in a laboratory setting where there is not a continuous cohabitation of the dog-handling staff with the dogs. This means that in the presence of personnel during the feeding, exercising and handling routines of the day, the dogs will be very active and not settle down to itch. Other disadvantages of the visual analog scale scoring system are that it is subjective and allows periodic pruritus assessments as opposed to a continuous objective evaluation.

This is the first study that looks at an objective and standardized measurement of pruritus in a canine model of allergic dermatitis. Accelerometers have been tested and found useful in humans as an objective and practical method to assess nocturnal itch in children and adults suffering from atopic dermatitis.^{14–16} Children suffering from atopic dermatitis and healthy children wearing accelerometers on limbs were filmed at night in their homes using infrared video cameras.¹⁵ There was a significant correlation between video analysis and accelerometer recordings ($r = 0.54–0.62$). In a subsequent study, the use of wrist activity monitors for the measurement of nocturnal scratching in patients with atopic dermatitis concluded that wrist activity monitors enabled measurement of nocturnal itch with satisfactory sensitivity.¹⁴

Thus far, the evaluation of treatment effects in HDM-sensitized laboratory dogs has focused primarily on changes in lesion scores (CADESI scores) and pruritus observed over short periods of time, therefore missing the treatment effect on established pruritus over time.^{9–11} Only a few studies have described the use of activity monitors to assess pruritus in dogs.^{7,8}

We attached activity monitors to the collars of the dogs 1 week before and during HDM challenge studies. We perceived that during the day the measured activity was strongly influenced by the schedule of feeding, visiting of personnel and exercise provided in the outdoor runs. In two different studies, we observed highly significant differences in activity between the groups at certain time periods, i.e. late afternoon (15.00–18.00 h), evening (18.00–24.00 h) and night (24.00–06.00 h; Table 1). These are the times of absence of the personnel. Subsequent studies (data not shown) confirmed that the night period (24.00–06.00 h) was the most repeatable time to see significant differences in activity between untreated and prednisolone-treated dogs. This is in line with results from a report monitoring activity in a smaller number of healthy dogs and dogs with cAD at home.⁷ In that study, a significantly decreased median epoch activity was measured only during the night when comparing healthy and atopic dogs.⁷ Filming of the dogs was not performed. In order to prove that increased activity was caused by pruritus, a report described the correlation of activity measurements and nocturnal behaviour in kennelled dogs.⁸ Those dogs were not specifically selected for the presence of pruritic behaviour. In that study, head shaking of the dogs was noted as a potentially confounding factor.⁸ We did not observe this phenomenon in our dogs.

We observed a significant correlation between the activity monitor data at night and the observed pruritic behaviour (Table 2; $r = 0.57$). This correlation is highly

significant despite the lack of specificity of the activity monitor data and our observation that the activity monitor data and observed behaviour did not always coincide. The reason for this discrepancy can be explained partly by the fact that the monitors were attached to the dog's chain collars, meaning that they could not be in very tight contact with the skin. Thus, certain very slight movements, such as licking, were not always picked up by the activity monitor. Fixation of the activity monitor on a harness would have allowed closer contact to the skin, but would have been even less sensitive in identifying the slight head movements that occur during licking.

Activity monitors and filming of the dogs are both methods for assessment of pruritus, and each approach has its own advantages and disadvantages. Filming the dogs and subsequent assessment of pruritus is highly specific. The disadvantages are the labour-intensive analysis of the film and the relatively short time intervals, i.e. several hours observed. The risk with selecting small time windows on specific days is evident in the data of the visual analysis of the dogs (Figure 3). In three of the four dogs (dogs 1, 2 and 3), an overall increase in pruritus during challenge was observed although it was not evident at every time period. Only one dog (dog 4) had an increase in pruritus compared with baseline in every period evaluated during and after the challenge.

In comparison, activity monitor data are not specific; they record all activity and not pruritus. However, they allow objective evaluation over long periods of time (weeks) and the data can be analysed quickly.

In our model of allergic dogs, we demonstrated that in a crossover design they are an effective means of determining pruritus. The crossover design means that every dog is its own control. This is important due to the lack of specificity of the activity monitor data and the individual differences in 'normal' activity levels of the individual dogs. Despite extensive activity monitor recording pre-challenge (2 weeks) in a parallel design, the interpretation of the activity monitor data remained inconclusive (data not shown). Work is ongoing to characterize further the usefulness of activity monitors for the assessment of pruritus.

In conclusion, pruritus is a hallmark of atopic dermatitis and an important indicator of success of a treatment. Thus, it is important to be able to determine the effect of new potential compounds on pruritic behaviour. We have shown that the determination of night-time activity with activity monitoring after allergen challenge appears to be an objective and practical way to assess the effects of a compound on pruritus in this experimental model of allergic dogs.

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References

- Halliwell R. Revised nomenclature for veterinary allergy. *Vet Immunol Immunopathol* 2006; 114: 207–208.

2. Kabashima K. New concept of the pathogenesis of atopic dermatitis: interplay among the barrier, allergy and pruritus as a trinity. *J Dermatol Sci* 2013; 70: 3–11.
3. Klukowska-Rötzler J, Chervet L, Müller EJ *et al.* Expression of thymic stromal lymphopoietin in canine atopic dermatitis. *Vet Dermatol* 2013; 24: 54–59. e13–e14.
4. Oyoshi MK, Larson RP, Ziegler SF *et al.* Mechanical injury polarizes skin dendritic cells to elicit a Th2 response by inducing cutaneous thymic stromal lymphopoietin expression. *J Allergy Clin Immunol* 2010; 126: 976–984.
5. Marsella R, Sousa C, Gonzales A *et al.* Current understanding of pathophysiologic mechanisms of canine atopic dermatitis. *J Am Vet Med Assoc* 2012; 241: 194–207.
6. Hill PB, Lau P, Rybníček J. Development of an owner-assessed scale to measure the severity of pruritus in dogs. *Vet Dermatol* 2007; 18: 301–308.
7. Nuttall T, McEwan N. Objective measurement of pruritus in dogs: a preliminary study using activity monitors. *Vet Dermatol* 2006; 17: 348–351.
8. Plant JD. Correlation of observed nocturnal pruritus and actigraphy in dogs. *Vet Rec* 2008; 162: 624–625.
9. Marsella R, Nicklin C, Lopez J. Atopy patch test reactions in high-IgE beagles to different sources and concentrations of house dust mites. *Vet Dermatol* 2005; 16: 308–314.
10. Marsella R, Olivry T, Nicklin C *et al.* Pilot investigation of a model for canine atopic dermatitis: environmental house dust mite challenge of high-IgE-producing beagles, mite hypersensitive dogs with atopic dermatitis and normal dogs. *Vet Dermatol* 2006; 17: 24–35.
11. Pucheu-Haston CM, Jackson HA, Olivry T *et al.* Epicutaneous sensitization with *Dermatophagoides farinae* induces generalized allergic dermatitis and elevated mite-specific immunoglobulin E levels in canine model of atopic dermatitis. *Clin Exp Allergy* 2008; 38: 667–679.
12. Olivry T, Marsella R, Iwasaki T *et al.* Validation of CADESI-03, a severity scale for clinical trials enrolling dogs with atopic dermatitis. *Vet Dermatol* 2007; 18: 78–86.
13. Noli C, Minafò G, Galzerano M. Quality of life of dogs with skin diseases and their owners. Part 1: development and validation of a questionnaire. *Vet Dermatol* 2011; 22: 335–343.
14. Ebata T, Iwasaki S, Kamide R *et al.* Use of a wrist watch activity monitor for the measurement of nocturnal scratching in patients with atopic dermatitis. *Br J Dermatol* 2001; 144: 305–309.
15. Benjamin K, Waterston K, Russell M *et al.* The development of an objective method for measuring scratch in children with atopic dermatitis suitable for clinical use. *J Am Acad Dermatol* 2004; 50: 33–40.
16. Brighurst C, Waterston K, Schofield O *et al.* Measurement of itch using actigraphy in pediatric and adult populations. *J Am Acad Dermatol* 2004; 51: 893–898.

Résumé

Contexte – Nous avons développé un modèle canin de dermatite atopique aiguë afin d'évaluer le potentiel des traitements du prurit et des lésions cutanées chez les chiens sensibilisés à *Dermatophagoides farinae* (Df).

Hypothèses/Objectifs – Le but était d'étudier l'efficacité au long cours des moniteurs d'activité d'évaluation du prurit lié aux tests allergéniques.

Sujets – Trente-deux chiens de laboratoire sensibilisés à Df.

Méthodes – Dans deux études croisées en aveugle, 28 chiens sensibilisés à Df ont été testés sur 3 jours, avec un mélange de Df, appliqué directement à la peau abdominale tondu. Les chiens ont été traités avec un contrôle positif (prednisolone 1 mg/kg une fois par jour pendant 5 jours, démarré un jour avant le début du test) ou sont restés sans traitement; tous ont été monitorés. Afin de confirmer le prurit, une étude parallèle avec quatre chiens a été menée, filmant les chiens avant et au cours du test et évaluant le comportement de prurit.

Résultats – L'activité des chiens traités avec la prednisolone était significativement plus faible entre 00.00 et 03.00 h et entre 03.00 et 06.00 h comparé aux chiens non traités (mesures répétées ANCOVA; $P < 0.0001$). Pour déterminer si les données enregistrées au cours de la nuit correspondaient aux manifestations de prurit, nous avons comparé les enregistrements d'activité et des enregistrements vidéo de quatre chiens sur deux périodes (16.30–20.30 et 24.00–03.00 h) avant et au cours du test Df. La corrélation entre l'activité nocturne monitorée et le comportement de prurit observé étaient significativement élevés (test de corrélation coefficient versus zéro : $r = 0.57$, $P < 0.0001$).

Conclusions et importance clinique – Déterminer une activité nocturne avec des moniteurs actifs après un test allergénique semble être un moyen objectif et pratique de caractériser le prurit dans ce modèle expérimental de dermatite atopique canine.

Resumen

Introducción – hemos desarrollado un modelo canino de dermatitis atópica para evaluar fármacos potencialmente útiles en el tratamiento del prurito y de las lesiones inducidas por perros sensibilizados al *Dermatophagoides farinae* (Df).

Hipótesis/Objetivos – el propósito fue investigar la efectividad de monitores de seguimiento de actividad a largo plazo para obtener una valoración del prurito inducido por la exposición a alérgenos.

Animales – 32 perros de laboratorio sensibilizados a Df.

Métodos – se realizaron dos estudios ciegos cruzados, 28 perros sensibilizados a Df fueron expuestos durante tres días una preparación de extracto de Df aplicada en la piel del abdomen tras rasuramiento. Los perros fueron tratados con un control positivo (prednisolona a 1 mg/kg una vez al día durante cinco días, empezando un día después de la exposición), o se dejaron sin tratar; a todos se les pusieron monitores de seguimiento de actividad. Para confirmar el prurito, se realizó un estudio paralelo con cuatro perros obteniendo filmaciones de los perros antes y durante la exposición, y evaluando las filmaciones para un posible comportamiento indicativo de prurito.

Resultados – la actividad de perros tratados con prednisolona fue significativamente menor entre las cero y las tres horas, y entre las tres y las seis horas, comparados con los perros no tratados (repetidas mediciones ANCOVA; $P < 0,0001$). Para determinar si la actividad nocturna grabada correspondía manifestaciones pruríticas se compararon las actividades grabadas por el monitor y películas de video previamente obtenidas de cuatro perros durante dos periodos (16.30–20.30 y 24.00–03.00 h) antes y durante la exposición a Df. La correlación entre la actividad nocturna obtenida por el monitor y el comportamiento prurítico observado fue altamente significativa (prueba de correlación de coeficiente frente a cero: $r = 0,57$, $P < 0,0001$)

Conclusiones e importancia clínica – la determinación de la actividad nocturna con monitores de actividad tras la exposición a alérgeno parece ser una forma práctica y objetiva de asesorar el prurito en este modelo experimental de dermatitis atópica canina.

Zusammenfassung

Hintergrund – Wir entwickelten ein Hundemodell für die akute atopische Dermatitis, um das Potential verschiedener Wirkstoffe bei der Behandlung des Juckreizes und der Hautveränderungen, bei *Dematophagoides farinae* (Df)-sensibilisierten Hunden zu evaluieren.

Hypothese/Ziele – Das Ziel war es, die Wirksamkeit von Langzeitmonitoren zur Beurteilung von Juckreiz durch Allergenprovokationen zu untersuchen.

Tiere – Zweiunddreißig Df-sensibilisierte Laborhunde.

Methoden – In zwei geblindeten Cross-over Studien wurde bei 28 Df-sensibilisierten Hunden an drei Tagen mit einer Df Suspension, die auf geschorene Bauchhaut aufgetragen wurde, eine Provokation durchgeführt. Die Hunde wurden mit einer Positivkontrolle (Prednisolon 1 mg kg^{-1} einmal täglich für 5 Tage, Start einen Tag vor der Provokation) behandelt bzw blieben unbehandelt; allen wurden Aktivitätsmonitoren angepasst. Um den Juckreiz zu bestätigen wurde eine Parallelstudie mit vier Hunden durchgeführt, wobei die Hunde vor und während der Provokation gefilmt wurden und der Film auf Juckreizverhalten hin beurteilt wurde.

Ergebnisse – Die Aktivität von Hunden, die mit Prednisolon behandelt worden waren, war signifikant niedriger und lag zwischen 00.00 und 03.00 h sowie zwischen 03.00 und 06.00 h im Vergleich zu unbehandelten Hunden (ANCOVA mit wiederholten Messungen; $P < 0,0001$). Um zu bestimmen, ob die aufgenommene Nachtaktivität mit den Manifestationen des Pruritus übereinstimmten, verglichen wir den Aktivitätsmonitor und Videoaufzeichnungen von vier Hunden über zwei Perioden (16.30–20.30 und 24.00–03.00 h) vor und nach einer Provokation mit Df. Die Korrelation zwischen Nachtaktivität durch den Aktivitätsmonitor gemessen und dem beobachteten Juckreizverhalten war hochsignifikant (Test des Korrelationskoeffizienten versus null: $r = 0,57$, $P < 0,0001$).

Schlussfolgerungen und klinische Bedeutung – Die Feststellung der Nachtaktivität mit Aktivitätsmonitoren nach einer Allergenprovokation erscheint eine objektive und praktische Methode, um Juckreiz in diesem experimentellen Modell der atopischen Dermatitis des Hundes zu beurteilen.

摘要

背景 – 我们研发了犬急性异位性皮炎模型，粉尘螨致敏犬诱发瘙痒和皮肤病变，用以评估复合治疗的潜力。

假设/目的 – 目的是调查超长记录实时监视器评估过敏原激发的瘙痒效果。

动物 – 32只粉尘螨过敏患犬。

方法 – 在双盲交叉实验中，28只尘螨过敏的患犬，连续三天在剃毛腹部接触尘螨悬浊液。积极控制（泼尼松龙 1 mg/kg sid po 连续五天，实验前一天开始服用）或不治疗；均用监视器监视。为确认瘙痒，用4只犬进行了平行试验，记录接受尘螨刺激前后的视频，并评估瘙痒表现。

结果 – 经泼尼松龙治疗的犬，活动性在00.00到03.00小时和03.00和06.00小时期间，明显少于未治疗的犬（重复测量 ANCOVA; $P < 0,0001$ ）。为确定夜间的行为是否符合瘙痒的临床表现，我们对4只犬两个时期（16.30–20.30 和 24.00–03.00 小时）接受尘螨刺激前后的录像。夜间活动记录和观察到的瘙痒表现高度相关（先关系数测试对比零: $r = 0,57$, $P < 0,0001$ ）。

总结与临床意义 – 本次犬异位性皮炎模型研究中，确定接受尘螨刺激后犬的夜间活动记录，应该是一种客观而可行的评估瘙痒的方法。

要約

背景 – 筆者らはそう痒と *Dermatophagoides farinae* (Df) 感作犬において誘発した皮膚病変を治療できる可能性のある化合物を評価するため、急性アトピー性皮膚炎モデル犬を開発した。

仮説/目的 – 目的はアレルゲン負荷によって誘発される痒みを評価する為の長期間記録活動モニターの有効性を調査することである。

供与動物 – 32頭のDf感作済み実験犬

方法 – 2つの盲検化交差試験において、28頭のDf感作犬の毛刈りをした腹部皮膚へ3日間にわたりのDf懸濁液を塗布し、負荷を行った。イヌは陽性コントロール(1日1回 5日間プレドニゾロン、負荷前日から開始)として処置、あるいは無処置とし、全てを活動モニターに割り当てた。そう痒を確認する為に、4頭のイヌを用いた並行研究が実施され、負荷前と負荷中のイヌを撮影し、痒み動作を撮影フィルムで評価した。

結果 – プレドニゾロンで処置したイヌの活動性は00.00と03.00時の間、および03.00と06.00時の間において無処置のイヌと比較し有意に低かった(反復測定ANCOVA; $P < 0.0001$)。記録した夜間の活動性がそう痒の徴候を示しているかどうかを決定するため、筆者らは4頭で負荷前とDf負荷中の2つの時間帯(16.30–20.30 および 24.00–03.00 時)の活動性モニターとビデオ記録を比較した。夜間の活動性モニター活動性と観察された痒み動作の間の相関は有意に高かった(検査の相関係数対ゼロ: $r = 0.57$, $P < 0.0001$)。

結論および臨床的な重要性 – アレルゲン負荷後の活動性モニターを用いた夜間の活動性の決定はこのイヌアトピー性皮膚炎実験モデルにおいてそう痒の評価に客観的および実用的であった。