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Associations between open-field behaviour and stress-induced hyperthermia in two breeds of sheep

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Abstract

*In sheep (*Ovis aries*) and other farm animals, routine husbandry procedures can cause negative emotions, such as fear, which are generally considered to reduce animal welfare. The open-field test (OFT) is the most widely used test to measure fearfulness in animals. The induction of psychological stress is often accompanied by an elevation of core body temperature, referred to as stress-induced hyperthermia (SIH) and both OFT and SIH were used in this study to measure fearfulness in sheep: the aim being to examine associations between behaviour in the OFT and the SIH response, using data from two breeds of sheep tested repeatedly over time. Twenty-four ewes from two breeds, Lacaune and Ripollesa, were tested for 10 min with all behaviours recorded throughout. Rectal temperature was measured immediately prior to the start of the test (T1) and 10 min after its completion (T2). SIH was measured as the difference between T2 and T1. Sheep were tested over three periods of three experimental days each. Ewes of both breeds showed consistent changes in behaviour in the OFT and a clear SIH response. Bleats and visits to the water bucket showed a clear pattern between rounds. Differences between T1 and T2 were found, T2 was higher than T1 suggesting that exposure to a novel arena caused SIH. Breed differences were found whereby T2 was 0.12°C higher in Ripollesa than Lacaune. These findings have implications for selection programmes, creating the possibility of selecting less fearful animals that will cope better with handling procedures that may induce fear. Further, they also demonstrate the importance of using both behavioural and physiological variables to evaluate fear.*

Keywords: *animal welfare, fear, open-field test, sheep, stress, stress-induced hyperthermia*

Introduction

Fear can be defined as a set of behavioural defence sequences protecting individuals from environmental dangers, social aggressions or abiotic aversive stimuli (Misslin 2003). Fear can also be induced by social isolation, which is known to be one of the most important fear-eliciting situations in sheep (*Ovis aries*), inducing behavioural and physiological perturbations (Minton & Blecha 1990; Romeyer & Bouissou 1992; Vandenheede *et al* 1998). In order to cope with a challenging situation, the individual evaluates the psychophysical and environmental properties of the event (Desire *et al* 2002). In addition to these environmental influences, the expression of fear is the result of interactive processes related to past experiences and the animal's genetic background (Boissy *et al* 2005). Fear reactions have an obvious adaptive value in the wild, for example detecting and escaping predators (Vierin & Bouissou 2002). Fear plays a crucial role in this process by motivating animals to avoid potentially harmful situations (Rushen *et al* 1999). Under farm conditions, however, acute or chronic fear reactions can lead to reduced productivity and welfare (for a review, see Dawkins 1990; Boissy 1998; Rushen *et al* 1999). The open-field test (OFT) or arena test is a behavioural test in which the animal is isolated from its conspecifics and introduced into an unfamiliar and barren environment. OFT is the most commonly used test to measure fearfulness in animals, and was developed for laboratory animals (Gray 1987). It has been widely used in farm animals (for a review, see Forkman *et al* 2007). Validation of the OFT, as a measure of fear in sheep, can be done by correlating behaviour in the OFT with physiological changes known to be associated with some forms of stress. Correlations between adrenocortical and behavioural responses to novelty have been found in calves (van Reenen *et al* 2005). Physiological responses associated with an emotional state of fear are generally believed to include increased activity of the sympathetic nervous system, eg increased heart rate and catecholamine secretion, and of the hypothalamo-pituitary-adrenal (HPA) axis, eg elevated plasma corticosteroids (Boissy 1995; Boissy & Le Neindre 1997; Ramos & Mormède 1997; Rushen *et al* 1999). When faced with the same challenge, fearful individuals show more pronounced behavioural (eg immobility or panic) and physiological (eg quicker, greater, longer) responses than less fearful ones (van Reenen *et al* 2005). Stress-induced hyperthermia (SIH) is mediated by the autonomic nervous system and is well known to occur prior, to and during, exposure to some stress- and/or anxiety-inducing situations (Spooren *et al* 2002). This phenomenon of SIH has been reported across a large variety of species (for a review, see Bouwknecht *et al* 2007). Psychological and physical stressors, such as mild disturbance (ie checking the availability of food and water in a mouse cage without handling [Bouwknecht *et al* 2001], handling [silver fox (*Vulpes vulpes*) and rat (*Rattus norvegicus*)] [Moe & Bakken 1997; Sundgren-Andersson *et al* 1998], predator smell [silver fox, rat and mice (*Mus musculus*)] [Moe & Bakken 1997; Sundgren-Andersson *et al* 1998; Hashimoto *et al* 2001], restraint stress [silver fox and rat] [Moe & Bakken 1997; Sundegre-Andersson *et al* 1998] and fear-conditioning paradigms) induce hyperthermia. Other behaviour-based induction methods for a hyperthermic response are exposure to a novel environment, an open-field arena or a light-dark box, as well as participation in social interactions in resident-intruder paradigms (for a review, see Bouwknecht *et al* 2007). The aim of this study, therefore, was to examine associations between behaviour in an OFT test and a physiological parameter known to be altered by fear (SIH), using data from two breeds of sheep tested repeatedly over time during three rounds. This was done using an experimental design that acknowledged that learning and habituation could have an effect on both behaviour and SIH.

Materials and methods

Animals and standard housing conditions

Twenty-four ewes from two different breeds: Lacaune (age 5 months, weight 30.07 [± 5.68] kg; n = 12) and Ripollesa (age 8 months, weight 35.63 [± 2.75] kg; n = 12) from the experimental farm of the Universitat Autonoma de Barcelona, Spain, were used for this study. All the tests were carried out prior to the ewes starting their first reproductive cycle. Animals went to pasture (5 h per day) every morning and remained in their home pens in the afternoon (fed with 200 g of pellets [CAC Valles, Barcelona, Spain] and *ad libitum* hay). Animals were randomly assigned into two subgroups (6 animals from each breed per subgroup). This procedure was approved by the Institutional Animal Care and Use Committee of the Universitat Autonoma de Barcelona, Spain.

Open-field test and stress-induced hyperthermia

Ewes were tested in an arena measuring 5 × 2.5 m (length × width) marked out in a grid of squares each measuring 0.83 × 0.83 m. Water and a familiar food (hay) were placed in a known bucket within the pen against the wall facing the entrance door. Adjoining one end of the arena was a pen measuring 2 × 3 m containing a group of 10 to 12 sheep, which were not visible from the arena due to the presence of a plastic-covered barrier (Figure 1). Animals waited in the adjoining pen to be tested. For each test, the animal was gently driven individually to the starting wooden cage (120 × 60 × 95 cm; length × width × height) where rectal temperature was measured for 1.5 min (Testo/Testo 110, Germany). Following this, the door of the test room was opened and the animal entered voluntarily. The test sessions lasted for 10 min and at the end of the test the door was opened and the animal gently pushed into the starting cage where rectal temperature was measured again (T2). Finally, the animal was released. Each one of the 24 animals was subjected individually to the test situation. Tests were conducted over three rounds of three days between 0800 and 1300h. Time interval between each round was 30 days. Each day, the animals entered into the open-field test using the same order. The behaviour of the animals was observed and video recorded when placed individually in the test pen without any additional fear-inducing stimuli. Ewes experienced the OFT each day for three days in three rounds (nine days total for each sheep) in order to examine trait consistency.

Measurement of behaviour

Behaviours recorded consisted of the number of: bleats, squares entered, visits to the food bucket, visits to the water bucket, times the ewe sniffed ground or walls (from now on exploring), urinations, defaecations, flight or escape attempts (rearing or jumping against the walls or entrance door) and grooming events. All behavioural variables were measured cumulatively for over 10 min. Between tests, animals were kept together as one flock on the farm.

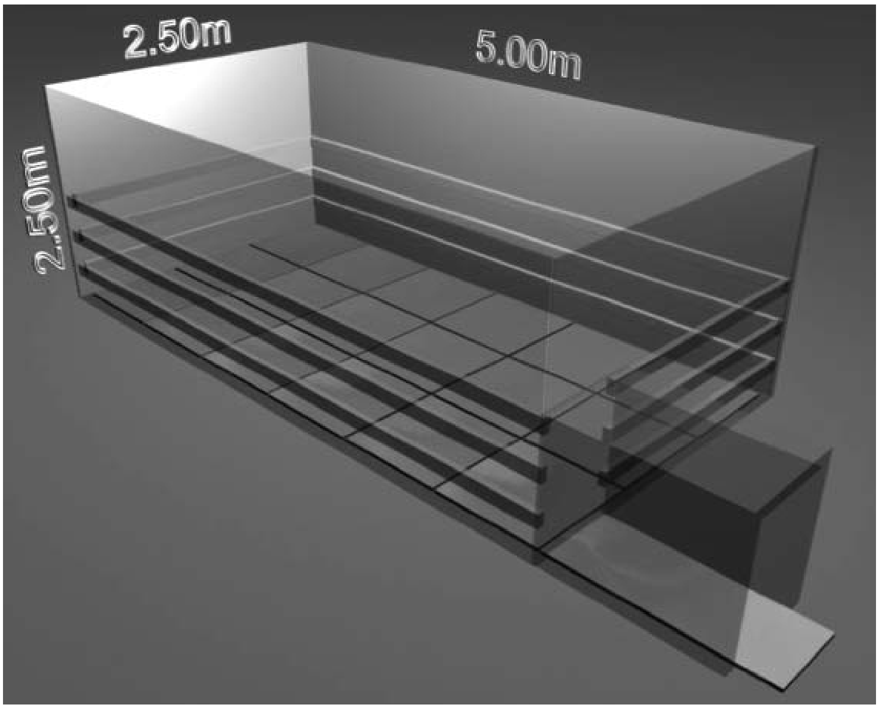
Statistical analysis

Statistical analysis was performed using SAS® v9.1.3 (SAS Institute, Cary, NC, USA) and with the exception of correlations between SIH and behaviours where significance was set at 0.01, the level was set at 0.05. Response variables were summarised using mean (± SD) or using relative and absolute frequencies when appropriate.

Continuous response variables (T2 and change in temperature [T2–T1]) were analysed using a mixed model. The variable animal was considered as a random factor in order to take into account the repeated measures on the same animal. Breed, day, replicate and T1 were included as fixed effects, as well as all possible interactions. This model allowed us to examine all main effects and possible interactions, and compare different levels as well as combination of levels of different explanatory variables (breed, replicate and day). Explanatory continuous variables (T1) were centred. Graphical plots of mean evolution of each parameter for each breed were obtained using least square means and their standard error provided from the model. Response variables based on counts which showed sufficient variability (bleats, visits to the food bucket, squares entered and exploring) were analysed using the former mixed model, assuming an appropriate distribution for the response variables. Generalised linear mixed models were used, assuming Poisson distribution or Negative-Binomial distribution depending on the presence of over dispersion. Graphical plots were also obtained using the same summary indices. Due to the exploratory character of the present study, multiple comparison corrections were not applied.

Figure 1

Schematic diagram of the open-field test.



Spearman correlations between behavioural measures were obtained as a descriptive measure of association for each breed. Observations from different days on the same animal were aggregated in order to obtain independent measures. Finally, for each response variable, Spearman correlations between all possible study days were evaluated for each breed as a descriptive measure of individual consistency. These correlation measures between pairs of days were pooled in order to obtain a global measure of time consistency.

Results

Behaviour

Bleats were affected by the day of the test and by the round, by the third day of test the mean number of bleats decreased, with the exception of Ripollesa on the first replicate (Figure 2). Differences in escape attempts were only seen between rounds where differences were found on visits to the water bucket, breed day and replicate. From the mixed model, Ripollesas made fewer visits to the water bucket than Lacaune (Figure 3). Comparing rounds, bleats — mean number on day one of each round — was similar on the first and second rounds and tended to decrease on the third for both breeds (Figure 2). Conversely, visits to the water bucket showed no differences on day one of each replicate (Figure 3). This behaviour was more stable between rounds.

Consistency was evaluated using Spearman correlations between the nine days of testing for Lacaune (L) and Ripollesa (R) (see Figure 4). Number of bleats presented the closest correlation in both breeds (L = 0.74 and R = 0.73). Some behaviours, such as exploring and visits to the water bucket differed between breeds (Figure 5); exploring being highly correlated on L = 0.51 and less so in the other R = 0.17. Escape attempts were similar in both breeds and presented a high correlation (L = 0.62 and R = 0.69).

Number of bleats showed high correlation throughout the 9 days of testing being one of the most consistent behaviours. Squares entered also showed high correlations between days, with the exception of day one. On visits to the water bucket, correlations were higher from day 5 to 9. Exploring events show high correlations between days 2, 5 and 8; high correlations were also observed from day 5 to 9. Escape attempts also showed high correlations during days with the exception of day one.

Stress-induced hyperthermia

Both breeds showed an increase in body temperature after the test that we considered SIH. From the mixed model T2, temperature change showed breed differences. Breed differences were observed on day two of the first round and on days two and three of the second round (Figure 5). T2 was 0.12ºC higher in Ripollesa compared to Lacaune ($t = -3.40$, $P = 0.003$). Day of test and round effects were not observed on the SIH, this physiological response may not be affected by repetition. SIH showed a low within-individual consistency (Figure 4) but increases in mean temperature were consistent between days and rounds.

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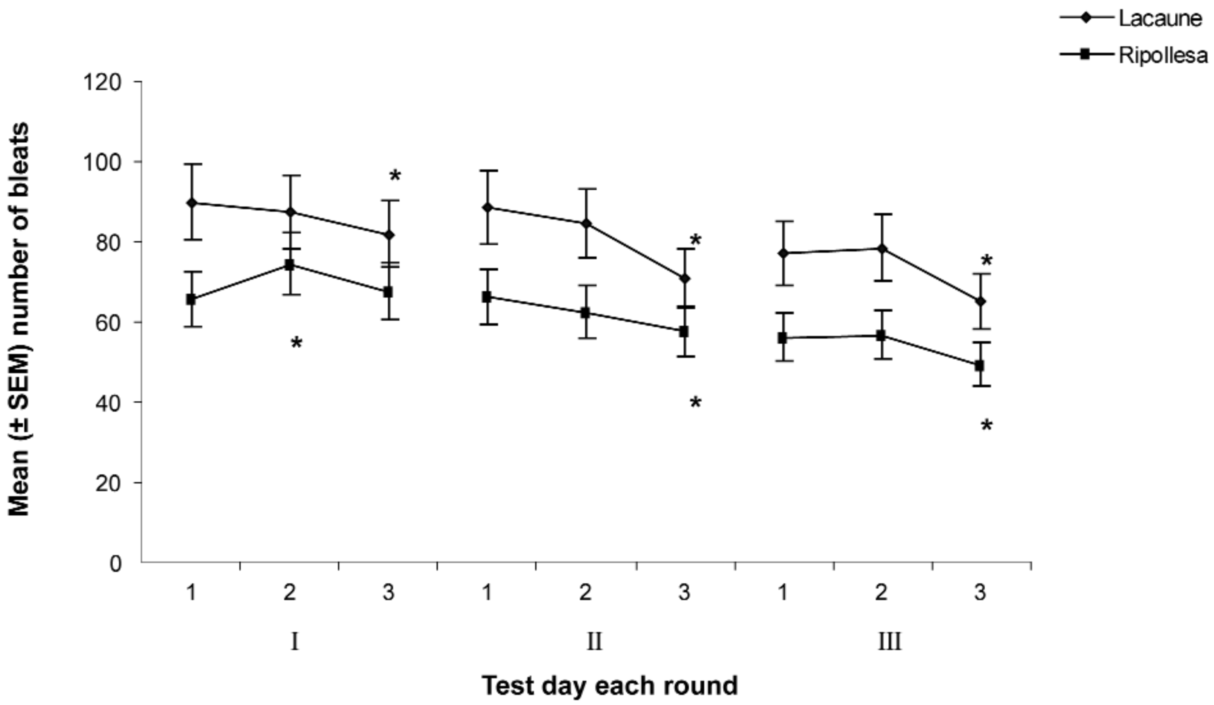
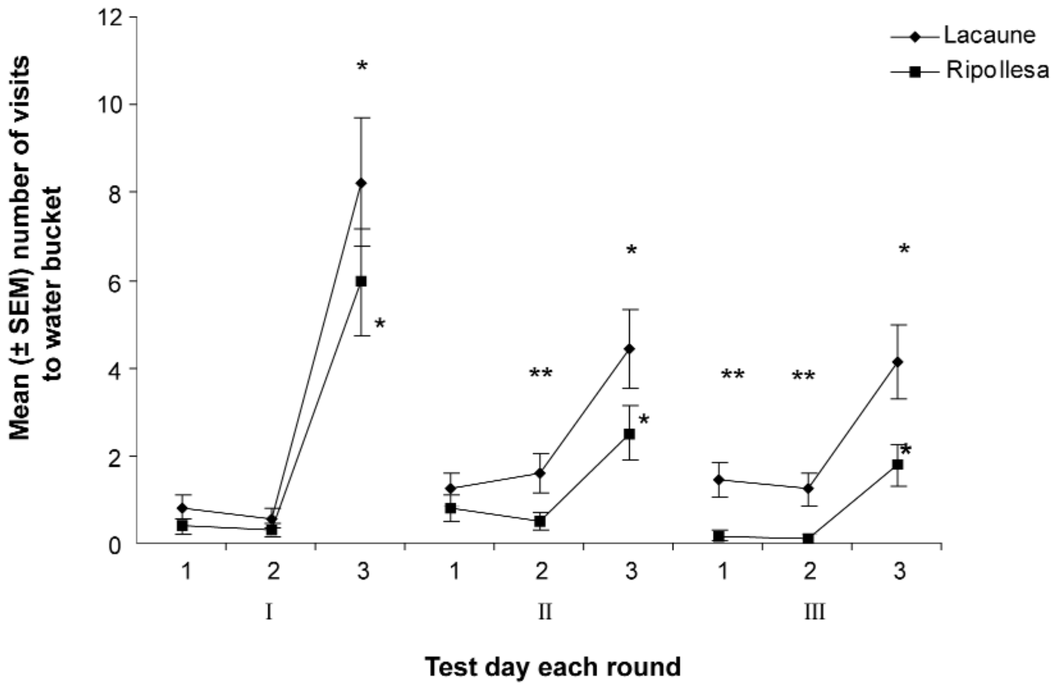
Figure 2



Mean (± SEM) number of bleats for each breed when tested in an open-field test during three days during the three rounds. * Significantly different from day one at $P < 0.05$.

Figure 3



Mean (± SEM) number of visits to the water bucket for each breed when tested in an open-field test during three days during the three rounds. * Significantly different from day one at $P < 0.05$; ** Differences between breeds at $P < 0.05$.

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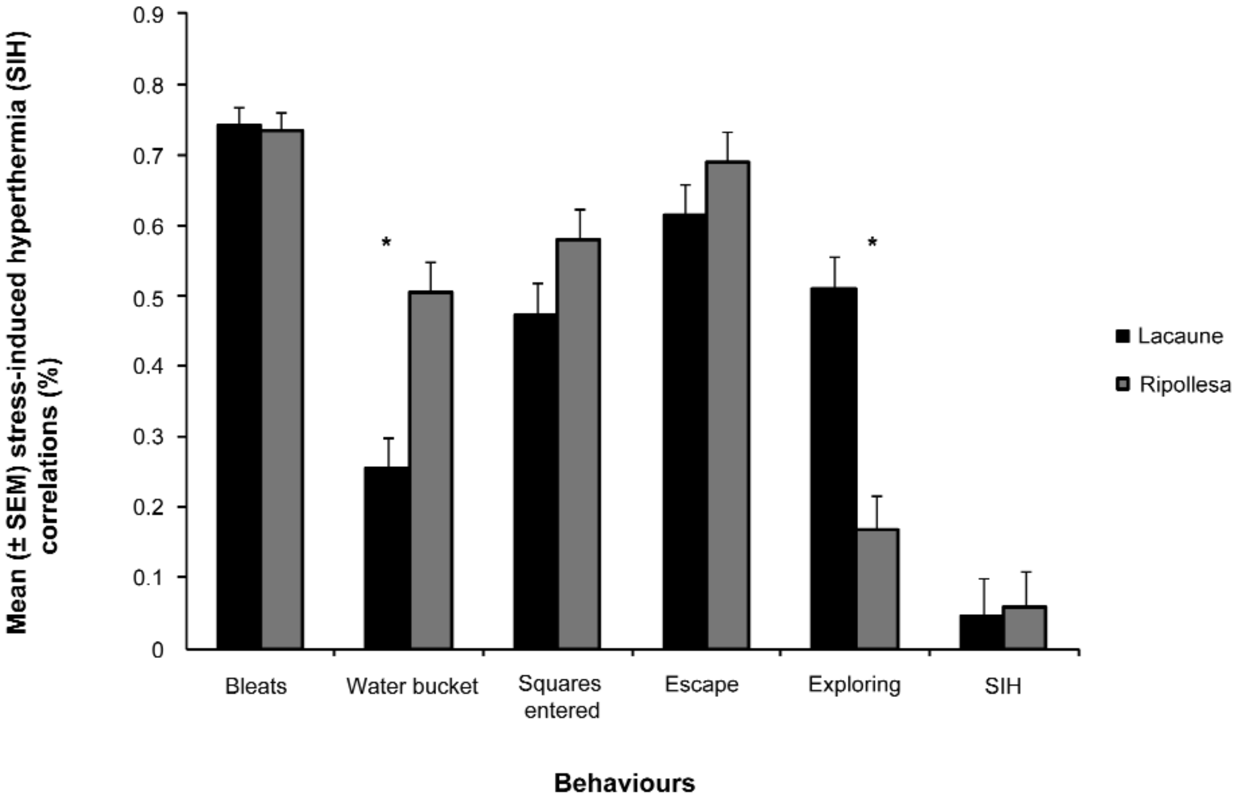
Figure 4



Behaviours and SIH mean correlations between nine days of testing for each breed: Lacaune and Ripollesa. * Breeds differ significantly at $P < 0.05$.

From Spearman correlations between behaviour displayed in the OFT and body temperature: T1 was correlated positively with escape attempts ($r = 0.20$, $P = 0.004$) while change in temperature showed a negative relationship with exploring ($r = -0.32$, $P = 0.000072$), the remaining correlations were excluded because we considered using a lower *P*-value (0.01) due to low correlations.

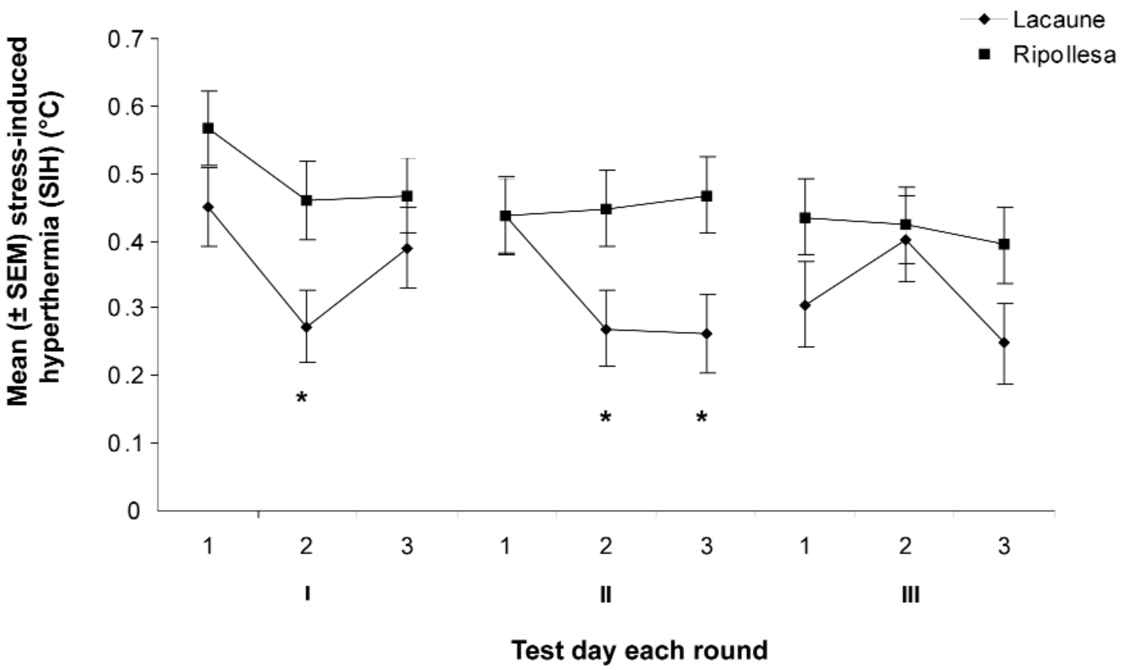
Discussion

Ewes on the OFT showed consistent changes in behaviour and a clear SIH response. Numbers of bleats and visits to the water bucket were the more consistent behaviours, they showed a pattern between days and rounds. This pattern was expected, due to the assumption that fear is an individual characteristic and should therefore be consistent. The change in behaviours over days (a decrease in the number of bleats) is consistent with a general habituation, resulting in reduced levels of fear. The major change in visits to the water bucket was seen between the first and third day of the test, with behaviours in the third day differing very slightly from the second. Number of bleats showed a decreasing trend. Differences between the first and third day may have been influenced by learning and habituation to the test situation, therefore animals were less reactive.

Numbers of bleats and visits to the water bucket were also consistent between rounds, at least on day one. That means that every time the test started again, ewes displayed the same behavioural response. This will allow future repetition of the experiment without the need for rounds; measuring the fear response on day one is sufficient.

Although there is no consensus regarding the manner in which fear-related reactions can be recognised and measured in farm animals, in the OFT, fear of the stimulus may be expressed as avoidance and the suppression of active behaviours, such as locomotion, vocalisation and exploration (Beausoleil *et al* 2005; Erhard *et al* 2006). There is no clear interpretation for domestic mammals since we do not know exactly what is measured in this situation, eg fear, social motivation, exploration or a combination of the three. Frequency of bleating may be more difficult to explain, as it may reflect a tendency for animals to re-establish contact with their flock mates and would thereby be a measure of sociability as opposed to general fearfulness (Forkman *et al* 2007). Nevertheless, a number of studies have found a correlation between frequency of bleats and behaviours thought to be related to fear, suggesting that, at least in certain circumstances, frequency

Figure 5



Mean (± SEM) SIH by breed during the nine test days (divided into three-day blocks). * Breeds differ significantly at $P < 0.05$.

of bleats may be affected by general fearfulness (Vandenheede *et al* 1998). An important concern when repeating behavioural tests is the possibility of habituation. Animals were expected to learn during the three consecutive days, both bleats and visits to the water bucket varied within the three days on each replicate suggesting habituation. After numerous runs through the OFT, sheep may not perceive it as a novel environment therefore becoming less fearful and more exploratory but the effect of isolation may remain a major source of stress (Erhard *et al* 2006).

We found a negative correlation between exploratory behaviour and SIH. Exploratory behaviours directed to an object reflect a low level of fear, combined with high motivation to explore (Moberg & Wood. 1982; Romeyer & Bouissou 1992; Boissy & Bouissou 1995; Vandenheede *et al* 1998).

Even though many studies have found relatively good correlations between OFT and other tests, and OFT can be considered a good fear test for sheep and goats (Forkman *et al* 2007), it is interesting to continue to examine associations between different fear and stress measures in this species. The use of a physiological indicator, such as SIH, can be useful to validate the fear response. As we measured the difference between rectal temperature before and after the test, the first question was to ascertain whether this difference can be considered to be SIH. There are three possible reasons to explain an increase in rectal temperature after the test: fever, exercise and stress (Oka *et al* 2001). Fever could be eliminated because animals did not show any clinical signs of a pathological process. Due to the increase in activity of the animals submitted to the test, the exercise could be considered a cause of the hyperthermia. However, there are several reasons to discount this explanation. Previous studies in silver foxes (Moe & Bakken 1997) and in rats (Kluger *et al* 1987) have demonstrated that there is little or no correlation between SIH and increased physical activity, and that SIH in silver foxes (Moe & Bakken 1998) and mice (Zethof *et al* 1995) may be an expression of an emotional response, such as fear or anxiety. Bakken *et al* (1999) found that in silver fox vixens, 7% of the temperature increase could be explained by increased physical activity. However, our results showed no relationship between squares entered and escape attempts with change in temperature. So, we can infer that the differences in response obtained in the test are due to isolation and novelty. If we consider that the difference between rectal temperature before and after the test is indeed SIH, then behaviours associated with an increase in temperature, such as exploring ($r = -0.32$, $P = 0.000072$), can be considered to be indicative of stress or fear.

The results here reveal a relationship between SIH and behavioural responses within the OFT. When comparing rounds, similar distribution was found, thus animals showed consistency in both behavioural response and SIH. The rise in rectal temperature that is observed and the behavioural responses can be considered a reproducible phenomenon

Breed effects were also reflected in both behavioural and SIH responses. Lacaune ewes showed a lower SIH than Ripollesas.

Large differences in fear responses in ruminants have been observed between breeds, even in studies where they have been reared under the same management system and few studies have used the novel arena test to quantify behavioural differences between breeds in sheep (Boissy *et al* 2005). Differences between breeds in reactivity towards potentially fear-eliciting situations have often been reported in adult sheep. In general, less domesticated, 'light' breeds are reported to be more reactive than commercial, 'heavy' breeds (Romeyer & Bouissou 1992; Hansen *et al* 2001). We can consider Lacaune as being more modified by the domestication process than Ripollesa. One aspect that has to be considered is the interaction between the genotype of the animals and the characteristics of their environment. The acute response to alarming events may be influenced by the affective and cognitive processing of the individual (Boissy *et al* 2005).

Animal welfare implications

It is generally accepted that absence of chronic fear is necessary for good welfare. It follows that the development of a clear and accessible way of assessing fear would be very useful. Our study shows that the expression of fear can be measured at a behavioural and physiological level, using a simple OFT and the SIH paradigm. These basic tests could be further used for pharmacological validations of anti-anxiety drugs or combinations of stimuli that might induce fear. These findings have implications for selection programmes, having the possibility to select less fearful animals that will cope better with a handling procedure that may induce fear, and demonstrate the importance of using both behavioural and physiological variables to evaluate fear.

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References

Bakken M, Moe RO, Smith AJ and Selle GME 1999 Effects of environmental stressors on deep body temperature and activity levels in silver fox vixens (*Vulpes vulpes*). *Applied Animal Behaviour Science 64*: 141-151

Beausoleil NJ, Stafford KJ and Mellor DJ 2005 Sheep show more aversion to a dog than to a human in an arena test. *Applied Animal Behaviour Science 91*: 219-232

Boissy A 1995 Fear and fearfulness in animals. *The Quarterly Review of Biology 70*: 165-191

Boissy A 1998 Fear and fearfulness in determining behavior. In: Grandin T (ed) *Genetics and the Behavior of Domestic Animals* pp 67-111. Academic Press: New York, USA

Boissy A and Bouissou M 1995 Assessment of individual differences in behavioural reactions of heifers exposed to various fear-eliciting situations. *Applied Animal Behaviour Science 46*: 17-31

Boissy A and Le Neindre P 1997 Behavioral, cardiac and cortisol responses to brief peer separation and reunion in cattle. *Physiology & Behaviour 61*: 693-699

Boissy A, Fisher AD, Bouix J, Hinch GN and Le Neindre P 2005 Genetics of fear in ruminant livestock. *Livestock Production Science 93*: 23-32

Bouwknecht JA, Olivier B and Paylor RE 2007 The stress-induced hyperthermia paradigm as a physiological animal model for anxiety: a review of pharmacological and genetic studies in the mouse. *Neuroscience & Biobehavioral Reviews 31*: 41-59

Bouwknecht JA, Hijzen TH, van der Gugten J, Maes RAA, Hen R and Olivier B 2001 Absence of 5-HT1B receptors is associated with impaired impulse control in male 5-HT1B knock-out mice. *Biological Psychiatry 49*: 557-568

Dawkins MS 1990 From an animal's point of view: motivation, fitness, and animal welfare. *Behavior and Brain Science 13*: 54-61

Desire L, Boissy A and Veissier I 2002 Emotions in farm animals: a new approach to animal welfare in applied ethology. *Behavioural Processes 60*: 165-180

Erhard HW, Elston DA and Davidson GC 2006 Habituation and extinction in an approach-avoidance test: an example with sheep. *Applied Animal Behaviour Science 99*: 132-144

Forkman B, Boissy A, Meunier-Salaün M-C, Canali E and Jones RB 2007 A critical review of fear tests used on cattle, pigs, sheep, poultry and horses. *Physiology & Behavior 92*: 340-374

Gray JA 1987 *The Psychology of Fear and Stress.* Cambridge Univeristy Press: Cambridge, UK

Hashimoto M, Watanabe T, Fujioka T, Tan N, Yamashita H and Nakamura S 2001 Modulating effects of prenatal stress on hyperthermia induced in adult rat offspring by restraint or LPS-induced stress. *Physiology & behavior 73*: 125-132

Hansen II, Christiansen F, Hansen HS, Braastad B and Bakken M 2001 Variation in behavioural responses of ewes towards predator-related stimuli. *Applied Animal Behaviour Science 70*: 227-237

Kluger MJ, O'Reilly B, Shope TR and Vander AJ 1987 Further evidence that stress hyperthermia is a fever. *Physiology & Behavior 39*: 763-766

Minton JE and Blecha F 1990 Effect of acute stressors on endocrinological and immunological functions in lambs. *Journal of Animal Science 68*: 3145-3151

Misslin R 2003 The defense system of fear: behavior and neurocircuitry. *Neurophysiologie Clinique/Clinical Neurophysiology 33*: 55-66

Moberg GP and Wood VA 1982 Effect of differential rearing on the behavioral and adrenocortical response of lambs to a novel environment. *Applied Animal Ethology 8*: 269-279

Moe RO and Bakken M 1997 Effects of handling and physical restraint on rectal temperature, cortisol, glucose and leucocyte counts in the silver fox (*Vulpes vulpes*). *Acta Veterinaria Scandinavica 38*: 29-39

Moe RO and Bakken M 1998 Anxiolytic drugs inhibit hyperthermia induced by handling in farmed silver foxes (*Vulpes vulpes*). *Animal Welfare 7(4)*: 97-100

Oka T, Oka K and Hori T 2001 Mechanisms and mediators of psychological stress-induced rise in core temperature. *Psychosomatic Medicine 63*: 476-486

Ramos A and Mormède P 1997 Stress and emotionality: a multidimensional and genetic approach. *Neuroscience & Biobehavioral Reviews 22*: 33-57

Romeyer A and Bouissou M 1992 Assessment of fear reactions in domestic sheep, and influence of breed and rearing conditions. *Applied Animal Behaviour Science 34*: 93-119

Rushen J, Taylor AA and de Passille AM 1999 Domestic animals' fear of humans and its effect on their welfare. *Applied Animal Behaviour Science 65*: 285-303

Spooren WPJM, Schoeffter P, Gasparini F, Kuhn R and Gentsch C 2002 Pharmacological and endocrinological characterisation of stress-induced hyperthermia in singly housed mice using classical and candidate anxiolytics (LY314582, MPEP and NKP608). *European Journal of Pharmacology 435*: 161-170

Sundgren-Andersson AK, Ostlund P and Bartfai T 1998 Simultaneous measurement of brain and core temperature in the rat during fever, hyperthermia, hypothermia and sleep. *Neuroimmunomodulation 5*: 241-247

Van Reenen CG, O'Connell NE, Van der Werf JTN, Korte SM, Hopster H, Jones RB and Blokhuis HJ 2005 Responses of calves to acute stress: individual consistency and relations between behavioral and physiological measures. *Physiology & Behavior 85*: 557-570

Vandenheede M, Bouissou MF and Picard M 1998 Interpretation of behavioural reactions of sheep towards fear-eliciting situations. *Applied Animal Behaviour Science 58*: 293-310

Vierin M and Bouissou MF 2002 Influence of maternal experience on fear reactions in ewes. *Applied Animal Behaviour Science 75*: 307-315

Zethof TJJ, Van Der Heyden JAM, Tolboom JTBM and Olivier B 1995 Stress-induced hyperthermia as a putative anxiety model. *European Journal of Pharmacology 294*: 125-135

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