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Assessment of Acute Pain in Farm Animals Using Behavioral and Physiological Measurements^{1,2}

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ABSTRACT: In this paper various aspects of animal pain and methods for its assessment are considered. The responses of lambs and calves to castration and of lambs to tail docking are used to illustrate quantitative approaches to the recognition and assessment of acute pain in farm animals. The

validation of physiological and behavioral measurements for assessment of pain is examined by relating measurements made from young lambs, after a range of treatments, to an independent ranking of the order of severity of the treatments.

Key Words: Pain, Hydrocortisone, Behavior, Castration, Docking, Discriminant Analysis

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Introduction

The development of methods of recognition and assessment of animal pain has been delayed by the unwillingness of some people to accept that animals are capable of experiencing or suffering pain when subject to injury, disease, or other noxious events. This may be due to expediency or to confusion of animal with human pain. For this paper it is assumed that animal pain generally serves the same purposes as human pain and that the experiences are similar, but that animal and human pain are not the same (Molony, 1986, 1992).

The following working definition of animal pain is used for this paper: animal pain is an aversive sensory and emotional experience representing an awareness by the animal of damage or threat to the integrity of its tissues; it changes the animal's physiology and behavior to reduce or avoid damage, to reduce the likelihood of recurrence and to promote recovery; unnecessary pain occurs when the intensity or duration of the experience is inappropriate for the damage

sustained or when the physiological and behavioral responses to it are unsuccessful at alleviating it.

Although physiological and behavioral changes are used here to define the presence and intensity of the experience, more studies are required to determine which changes to measure and how this can be achieved so that they can be applied to individual animals under clinical (field) conditions.

For unequivocal examples of animals in pain that might be ethically acceptable models for investigation, we turned to castration and tail docking of lambs and castration of calves. These practices are carried out with two main justifications: they improve the overall welfare of the animal, and the economic benefits outweigh the welfare costs. It is not intended to debate this here, but it seems reasonable that those carrying out such practices should be aware of how much pain they cause, and that they should support efforts to find the most humane ways of carrying them out.

The studies described in this paper were justified on two grounds: first, as part of the search for more humane methods for the procedures; and second, because the lambs or calves would normally be subjected to the procedure as part of an accepted husbandry system. This helped to obtain the permission of the licensing authorities in the UK (Home Office).

The studies are based on those used for the general assessment of pain (Chapman et al. 1985; Sandford et al., 1989), pain in young children (McGrath, 1987), and for assessment of pain produced in experimental animals by subcutaneous formaldehyde (Dubuisson and Dennis, 1977; Coderre et al., 1993; Abbott et al., 1995) or by sciatic ligatures (Bennett and Xie, 1988;

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Attal et al., 1989; Attal et al., 1990; Kupers et al., 1992).

Following the introduction of some principles for assessment of pain, evidence for acute pain from castration and tail docking will be discussed, and an attempt to validate some indices for assessment will be described.

Principles for Assessment of Animal Pain

Because direct measurement of subjective experiences is not possible, assessment of animal pain is of necessity a value judgment relying on physiological and behavioral indices to provide indirect evidence of this particular mental state. Several different indices ought normally to be used and their evaluation should be improved by training and experience. Those in the best position to make judgments will know the species, breed, and individual animal well; they include veterinary surgeons, farmers, and stockmen and stockwomen. To give animals the benefit of any doubt, where there is a choice, judgments should overestimate the intensity of pain to avoid missing animals in pain at the cost of treating some that are not.

Humans have a highly developed capacity for accurately appreciating the feelings of at least some other humans; this capacity may be misused, however, by applying it to humans from very different cultural backgrounds, to animals that have different cerebral capacities, and even to inanimate objects such as soft toys. Observation of an event that would be noxious if applied to the observer may thus illicit unwarranted empathetic feelings and emotional responses, and observers should make allowance for this in their assessment of animal pain.

Types of Animal Pain

Acute and chronic pain occur over different time courses: acute pain does not outlast the healing process, whereas chronic pain persists beyond the expected healing time for an injury. Acute pain is generally accompanied by autonomic changes and responds to analgesic treatment. Acute recurrent pain is a term that can be used to describe prolonged pain, such as cancer pain, which has a definable cause and consists of repeated attacks of acute pain. Chronic pain may have no obvious cause or temporal onset (American Pain Society, 1987).

Somatic and visceral pain originate in different parts of the body and have other notable differences (e.g., somatic pain is generally well localized, whereas visceral pain is poorly localized and may be referred to distant parts of the body).

Pain originating within the peripheral or central nervous system is often chronic and may not be

dependent on activity from nociceptors; it seems to be produced by damage to the mechanisms underlying the pain process and its control.

Types of Pain Response

Several types of responses can be recognized: 1) those that modify the animal's behavior by learning and so enable the animal to avoid recurrence of the experience; 2) those, often automatic, that protect parts or the whole animal (e.g., withdrawal reflexes); 3) those that minimize pain and assist healing (e.g., lying or standing still); and 4) those that are designed to elicit help or to stop another animal (including humans) from inflicting more pain (e.g., communication by vocalization, posture, or other means such as smell).

Physiological and Behavioral Evidence for Acute Pain After Castration and(or) Tail Docking

Activity in Afferent Nerves. It has been shown that castration and tail docking of lambs with rubber rings produces significant increases in the afferent activity from nociceptors in the testes and tail (Cottrell and Molony, 1995; Graham, personal communication 1996). Increased activity of nociceptors with similar properties can be recorded directly from the nerves of conscious humans who report the stimulation as painful (Rice and Casale, 1994). The time course of the increase in nociceptor activity after these procedures can be related to increases in plasma cortisol and increases in abnormal behavior.

Activity of the Sympathetic Nervous System. There are several ways of measuring the activity of the sympathetic nervous system, including changes in heart rate, pupillary diameter, skin resistance, and peripheral blood flow. Because the system generally works as an integrated whole, several of these changes may occur in parallel. The state of the system can most easily be assessed by monitoring the heart rate from an electrocardiogram or by serial measurements of plasma catecholamines. Changes in heart rates of a limited number of animals subjected to castration have been measured (Kent et al., unpublished observations), and although changes consistent with predicted pain were detected, there were many interfering variables such as eating, exercise, and extraneous noises. It would therefore be difficult to use such changes in heart rate as a practical index for assessment of pain.

Activity of the Hypothalamo-Pituitary-Adrenal Axis. This is most easily measured from levels of corticosteroid hormones in plasma or saliva. A series of measurements must be made both before and after the treatment to accommodate the characteristics of release and elimination of the hormones and to determine the changes produced. Changes in plasma

cortisol concentrations closely follow the time course of changes in posture and activity after castration and tail docking (Kent et al., 1993). There are, however, interfering variables that can limit the use of such measurements for assessment of pain, including individual variation, diurnal changes, and the wide variety of stressors that activate the hypothalamic-pituitary-adrenal system.

Changes in Posture. Postural changes can be voluntary or involuntary. Involuntary spinal and brainstem reflexes can be initiated by activity from nociceptors, some of which may cause hyper-reflexia, including increased muscle tone; an example of this may be seen after castration of lambs with rubber rings as full extension of the hind limbs (Molony et al., 1993b). A voluntary change in posture after castration may be the adoption of an immobile stance (statue standing) to avoid or reduce stimulation of hyperalgesic tissues.

Under experimental conditions, the changes in posture after different methods of castration or tail docking can be compared with changes exhibited by animals subjected to sham treatments. Many different postures are available for use as indices, including various forms of lying and standing categorized according to the positions of the limbs and head. These postures have been divided somewhat arbitrarily for lambs into 1) normal lying, ventral (sternal) with the head down (V_1), with the head up (V_2), both occurring frequently in sham-treated lambs; 2) abnormal lying, ventral with partial extension of one leg (V_3) or full extension of one or more legs (V_4), and lateral lying with a shoulder down and the head up (L_1) or down (L_2), none of which occurred in control lambs under the environmental conditions for these experiments experienced in Scotland; 3) standing postures including normal standing/walking (S_1), abnormal standing/walking with just detectable ataxia, swaying, or abnormal stance (S_2), grossly abnormal standing/walking with stilted gait walking on knees or walking backward (S_3), and immobile or statue standing (SS) (Molony et al., 1993b, 1995).

The time spent by lambs in these postures after castration and(or) tail docking when compared with that spent by control lambs indicates how much the treatments changed behavior. The prevalence of particular postures or activities after treatments of different severities helps determine any weighting given to them as indices.

Changes in Locomotor Activity. In addition to changes in posture, castration and tail docking produce increases in locomotor activity, including restlessness, kicking, stamping, rolling, jumping, easing quarters, licking/biting at the site of damage, and tail wagging; the incidence of these behaviors can increase until all of the animal's time is spent in "abnormal" active behavior (Molony et al., 1993b). Although some of these active responses seem to have no beneficial effects, they may be generally described as attempts to escape and may represent specific pain

behavior. They are usually replaced by abnormal postures when the animal alters its strategy from active to passive attempts at avoidance.

Fatigue also contributes, because prolonged active behavior uses up reserves of energy (changes plasma glucose and FFA), produces heat (increases body temperature), and causes metabolic and electrolyte changes including acidosis and dehydration, all of which can be measured as physiological changes but none of which has been shown to be a specific index for pain.

Changes in Evoked Behavior. Intense noxious stimulation by castration and tail docking leads, in some lambs, to periods of inert lateral lying (Molony et al., 1993b) during which it can be difficult to elicit any evidence of conscious awareness. Some ewes paw vigorously at their lambs when they see them lying immobile in this lateral posture; this seems to be a way of evoking activity to help alleviate the ewe's concern for the "state" of its offspring. It illustrates a common approach to assessment of the "state" of a lamb by both ewe and shepherd.

Part of any assessment of pain should include the animal's response to standard stimuli, the commonest being its response to the approaching shepherd or sheepdog. Systematic experimental use of evoked responses has been by means of tests such as the open field test (Fell and Shutt, 1989).

Reduction of Physiological and Behavioral Changes by Local Anesthetic Treatment. Local anaesthetic treatment can reduce or eliminate both physiological and behavioral changes produced by castration and tail docking by blocking transmission of neural activity from the affected tissues, thus confirming the peripheral nociceptive basis of this acute pain (Wood et al., 1991).

Reduction of Physiological and Behavioral Changes by Analgesic Treatment. Although some analgesia has been achieved in sheep with opioids, α_2 agonists and nonsteroidal anti-inflammatory drugs (NSAID) (Nolan et al., 1987; Waterman et al., 1991; Ley et al., 1991; Welsh et al., 1992), no systematic dose-related reductions of the physiological and behavioral changes produced by castration and tail docking have been achieved. Of the analgesics tried, xylazine (an α_2 agonist) reduced both physiological and behavioral responses to tail docking (Molony et al., 1993a), and diclofenac, a NSAID, was effective against the pain produced by burdizzo castration but not against that produced by rubber ring castration or tail docking (unpublished observations). The opioids morphine and etorphine, however, when administered intrathecally, had no effect on responses to castration and tail docking (Wood, 1991; Molony and Wood, 1992). More studies are required to demonstrate a clear dose-response relationship between indices of pain from castration and tail docking and increasingly effective doses of analgesics. However, it seems that the visceral (testicular) pain produced by rubber ring

castration may be resistant to alleviation by commonly used analgesics, and indices for measuring this pain cannot be validated if they are also required to assess the effectiveness of the analgesic.

Validation of Indices and Elimination of Redundant Indices

For clinical assessment of pain it is necessary to determine the validity and sensitivity of each index and to eliminate as many redundant indices as

possible. This has been attempted using indices alone or in combinations, to assign animals to a series of groups ranked in order of decreasing severity of treatment based on alternative independent indices. An abstract with some results is included to illustrate the approach.

Methods

Forty-nine Dorset crossbred lambs weighing 3 to 6 kg were penned (3.6 m × 1.5 m) with their dams and

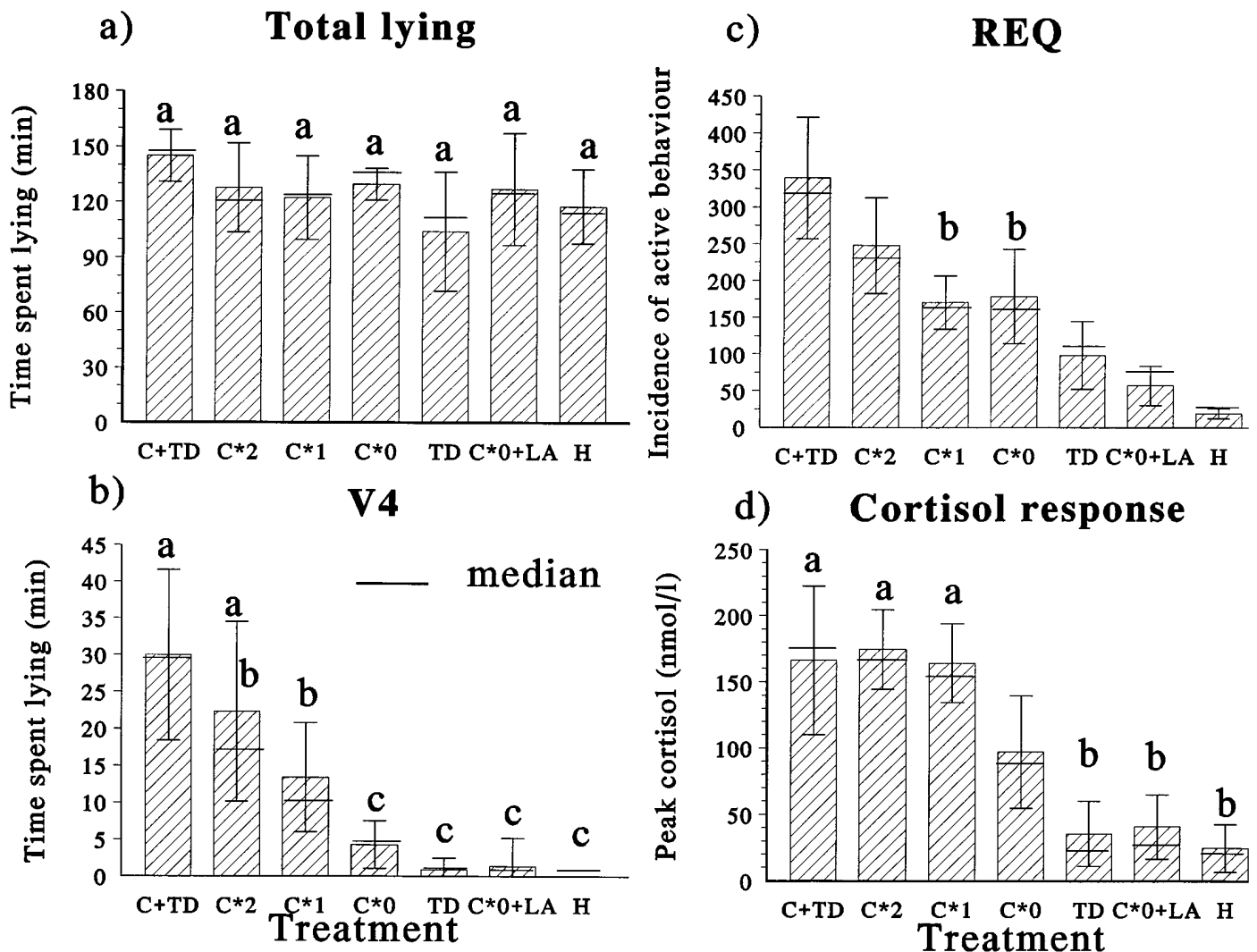


Figure 1. Responses of groups of 5- to 6-d-old Dorset crossbred lambs ($n = 7$) to the following treatments of decreasing severity: castration and tail docking (C+TD); bilateral castration (C*2); unilateral castration (C*1); short scrotum castration (C*0); tail docking (TD); short scrotum castration + local anesthesia (C*0+LA); or handled controls (H). (a) The mean (\pm SD) times spent lying during the 180 min after treatment. (b) The mean (\pm SD) times spent lying abnormally (V_4) during the 180 min after treatment. (c) The mean incidences (\pm SD) of restlessness + roll/jumping + foot stamp/kicking + easing quarters (REQ) during the 180 min after treatment. (d) The mean (\pm SD) peak cortisol concentrations (nmol/L) reached during the 180 min after treatment. The median value for each group is indicated by the full-width horizontal line. Mean values for treatment groups labelled with the same letter are not significantly different ($P > .05$).

siblings. Groups of seven lambs were treated at 5 or 6 d old. The treatments were ranked before the experiment in decreasing order of severity according to the amount of tissue involved and the established effectiveness of local anesthetics, thus providing a rank order of severity.

1. Bilateral castration and tail docking with rubber rings (**C+TD**).
2. Bilateral castration with a rubber ring (**C*2**).
3. Unilateral castration with a rubber ring (**C*1**).
4. Short scrotum castration with a rubber ring: the testes were pushed up into the inguinal region and the ring placed around the neck of the scrotum (**C*0**).
5. Tail docking with a rubber ring (**TD**).
6. Short scrotum castration with a rubber ring plus .3 mL of local anesthetic (Bupivacaine .25%) into the neck of the scrotum on each side just proximal to the rubber ring (**C*0+LA**).
7. Handled controls (**H**).

It was considered that the increments in severity between treatments C*0, C*1, and C*2 were most likely to be similar. Ranking of TD was uncertain because different tissue and a different location were involved.

Plasma cortisol concentrations were measured before (-20 min and 0 min) and at intervals for 180 min after treatment (nine samples). Postures (scanned at 2-min intervals) and active behaviors (continuous) have been described above; they were recorded by direct observation for 180 min as in previous studies (Molony et al., 1993b). Statistical analysis was by one-way analysis of variance; significant differences between groups were established using Student's *t*

tables and the standard error of the difference. To investigate the value of different indices alone and in combination, cross-validated discriminant analysis (Minitab v9) was carried out. This measured the proportion of lambs that could be assigned to appropriate (correct) treatment groups using the values obtained for particular indices.

Results

Examples are presented of the relationships between the different indices investigated and the intensity of pain as predicted from the order of severity of the treatment.

Lying (total) during the 180 min after treatment (Figure 1a) was not different in any of the treatment groups ($P > .05$). Abnormal ventral lying (V_4) separated the four most highly ranked groups from the rest ($P < .05$; Figure 1b), and the sum of the scores over 180 min for restlessness, rolling, foot-stamping/kicking and easing quarters (**REQ**) separated the treatments from each other ($P < .05$) except C*1 from C*0 (Figure 1c). Peak plasma cortisol changes did not distinguish between either the three most or three least highly ranked treatments but distinguished a treatment of intermediate severity (C*0) from both the least and most severe groups ($P < .01$; Figure 1d).

To find the most economical combination of the indices used, they were subjected to cross-validated discriminant analysis. A combination of V_4 and REQ gave one of the best results, placing 63% of the lambs in their appropriate treatment groups (Table 1); addition of the peak cortisol response reduced this to 59% (Table 2).

Table 1. Discriminant analysis with cross-validation using posture V_4^a and the REQ^b score^c

Assigned group	Actual group						
	C+TD	C*2	C*1	C*0	TD	C*OLA	H
C+TD	5	1	0	0	0	0	0
C*2	1	4	1	0	0	0	0
C*1	1	1	4	0	0	0	0
C*0	0	1	2	4	1	0	0
TD	0	0	0	3	4	2	0
C*OLA	0	0	0	0	1	3	0
H	0	0	0	0	1	2	7
Total no. ^d	7	7	7	7	7	7	7
No. correct ^e	5	4	4	4	4	3	7
Proportion ^f	.71	.57	.57	.57	.57	.43	1.00

^a V_4 = ventral lying with full extension of the hindlegs.

^bREQ = summation of restlessness, roll/jumping, foot stamp/kicking, and easing quarters.

^cLambs in different treatment groups (Actual) are assigned to a group according to the V_4 /REQ values obtained after treatment.

^dNo. = 49.

^eNo. correct = 31.

^fProportion correct = .633.

Table 2. Discriminant analysis with cross-validation using posture V_4^a , REQ^b score, and peak plasma cortisol concentration

Assigned group	Actual group						
	C+TD	C*2	C*1	C*0	TD	C*OLA	H
C+TD	4	1	0	0	0	0	0
C*2	2	4	1	0	0	0	0
C*1	0	2	5	1	0	0	0
C*0	1	0	1	4	0	0	0
TD	0	0	0	2	4	2	0
C*OLA	0	0	0	0	2	2	1
H	0	0	0	0	1	3	6
Total no. ^c	7	7	7	7	7	7	7
No. correct ^d	4	4	5	4	4	2	6
Proportion ^e	.57	.57	.71	.57	.57	.29	.86

^a V_4 = ventral lying with full extension of the hindlegs.

^bREQ = summation of restlessness, roll/jumping, foot stamp/kicking, and easing quarters.

^cNo. = 49.

^dNo. correct = 29.

^eProportion correct = .592.

Discussion

These results are consistent with the hypothesis of Wood (1991) and Molony (1991) that plasma cortisol can exhibit a ceiling effect, a maximal response being obtained when only one testis (C*1) was involved. Some behavioral indices also showed ceiling effects, but for rubber ring castration and tail docking of lambs of this breed and age, a more economical index for assessment of acute pain was obtained by combining the time spent lying ventrally (V_4) and the incidence of the active behaviors (REQ). Weighting of the values of V_4 and REQ according to their contributions to the discriminant analysis could help provide a single measuring instrument similar to those used for assessment of formalin-induced pain in rats (Coderre et al., 1993; Abbott et al., 1995). Further analysis should determine the requisite minimum measurement time for these indices to obtain a similar level of discrimination, and if less than about 20 min, this approach may be of clinical use for assessment of this type of pain in individual lambs.

Implications

Animal pain can be recognized and assessed using physiological and behavioral indices but different types of pain in different species should be considered separately before generalizations are made about the value of particular sets of indices for assessment. Assessment is improved by using several indices, each of which changes over different parts of the range of intensities of pain. Multivariate analysis can help determine the weighting of indices to obtain the most robust and economical methods of assessment for each type of pain in each species. If assessments with such

methods are shown to be consistent with those made by suitably experienced veterinary surgeons, stockmen, and stockwomen, it will help in appreciation of the methods used by such experienced people, and in standardizing the assessment of acute pain in farm animals.

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