

New Zealand Society of Animal Production online archive

This paper is from the New Zealand Society for Animal Production online archive. NZSAP holds a regular annual conference in June or July each year for the presentation of technical and applied topics in animal production. NZSAP plays an important role as a forum fostering research in all areas of animal production including production systems, nutrition, meat science, animal welfare, wool science, animal breeding and genetics.

An invitation is extended to all those involved in the field of animal production to apply for membership of the New Zealand Society of Animal Production at our website www.nzsap.org.nz

[View All Proceedings](#)

[Next Conference](#)

[Join NZSAP](#)

The New Zealand Society of Animal Production in publishing the conference proceedings is engaged in disseminating information, not rendering professional advice or services. The views expressed herein do not necessarily represent the views of the New Zealand Society of Animal Production and the New Zealand Society of Animal Production expressly disclaims any form of liability with respect to anything done or omitted to be done in reliance upon the contents of these proceedings.

This work is licensed under a [Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License](#).



You are free to:

Share— copy and redistribute the material in any medium or format

Under the following terms:

Attribution — You must give [appropriate credit](#), provide a link to the license, and [indicate if changes were made](#). You may do so in any reasonable manner, but not in any way that suggests the licensor endorses you or your use.

NonCommercial — You may not use the material for [commercial purposes](#).

NoDerivatives — If you [remix, transform, or build upon](#) the material, you may not distribute the modified material.

<http://creativecommons.org.nz/licences/licences-explained/>

Physiological indices of pain-induced distress

D.J. MELLOR AND K.J. STAFFORD¹

Animal Welfare Science and Bioethics Centre, IFNHH, Massey University, Palmerston North, New Zealand

ABSTRACT

To date, most assessments of the pain and distress caused by dehorning of calves and castration plus tail docking of lambs have employed changes in plasma cortisol concentrations. Although this approach can aid selection of the most appropriate methods in animal welfare terms, the use of cortisol as the sole physiological index allows conclusions to be drawn only about those features of acute responses to treatment which are reflected in plasma cortisol concentrations. Accordingly, in addition to the well-established cortisol responses to these treatments, that last hours, we now report on adrenaline responses that last minutes, and noradrenaline responses with an intermediate duration are described. Blood pressure, heart rate, adrenocorticotrophic hormone and cortisol responses to ring castration plus tail docking of lambs are described, and their relative sensitivity as indices of low-grade pain as the acute responses to treatment wane are considered.

Keywords: physiology, pain, distress

INTRODUCTION

The subjective experience of pain cannot be quantified physiologically. When interpreting physiological indices of pain, therefore, it is important to be clear about this limitation. We can examine the function of the body's pain perception apparatus by studying the physiological mechanisms that underlie pain experiences – i.e., stimulation of pain receptors, transmission of nerve impulses in pain pathways and electrical activity in those areas of the somatosensory cortex which apparently translate impulse traffic in pain pathways into perceived pain (Mellor *et al.*, 2000). We can also explore wider physiological changes that accompany, or that are induced by, heightened activity in the body's pain apparatus' – i.e., different features of physiological stress responses (Mellor *et al.*, 2000). These two approaches are complementary and informative.

Exploration of stress responses has been used most during studies designed to assess and alleviate the pain and distress caused by routine husbandry practices that cause injury. While these husbandry practices continue to be used routinely, they offer the opportunity to study acute and chronic responses to injuries caused by cautery, cryoacautery, cutting, crushing, constriction and corrosion of ears, skin, bone, horn, scrotum, testes and/or tail (Mellor & Stafford, 1999).

We use the term "pain-induced distress" when referring to some physiological responses to these practices. Before proceeding, therefore, it is necessary to clarify the meaning of the term "pain-induced distress" and how it can be assessed (Mellor & Stafford, 1999; Mellor & Stafford, 2000; Mellor *et al.*, 2000). The response to unpleasant experiences may be largely emotional (e.g., fear), largely physical (e.g., vigorous exercise), or both (e.g., pain). The level of distress is assessed by variables used to measure physiological stress and may be described as "minor", "moderate", "marked" and "very marked". Although changes in these variables are objective measurements, any conclusions about the subjective experiences that cause those changes remain judgements and not statements of fact. That is because

without sharing with us a common language, an animal cannot tell us how painful or pleasant a particular experience is.

Two physiological systems are used to assess distress. The first is the sympathetic adrenomedullary system which is primarily concerned with fast-acting "fight-flight" responses reflected in measurable responses in adrenaline, noradrenaline, heart rate and other related parameters. The second is the hypothalamic-pituitary-adrenocortical (HPA) system which initiates longer-lasting metabolic and anti-inflammatory responses that can promote healing. Indices of HPA activity include plasma concentrations of cortisol, adrenocorticotrophic hormone (ACTH) and corticotropin releasing factor (CRF). These hormones are useful indices because HPA activity generally increases in a graded way in response to the presumed noxiousness of different experiences (Mellor & Stafford, 2000).

As noted before, changes in the above parameters do not measure pain, but they do provide an indication of how unpleasant the experience is emotionally and physically. The fast response time of the sympathetic-adrenomedullary system makes it likely to be more useful during the first few minutes after application of a noxious procedure, whereas the slower response time of the HPA axis means that it is likely to be more useful subsequently. This is illustrated below.

To date, most physiological assessments of the distress caused by painful husbandry practices have been conducted using plasma cortisol concentrations. The strengths and weaknesses of this approach have been explored in detail elsewhere (Stafford & Mellor, 1993; Mellor *et al.*, 2000) and will be summarised here. We will then describe recent observations in which catecholamine, blood pressure, heart rate and other acute physiological responses to noxious stimulation were examined in addition to acute cortisol responses. Chronic responses will not be considered.

It is noteworthy that observing pain-related behaviours can also be helpful in assessing pain-induced distress. The value of such observations is discussed by Stafford and

¹Institute of Veterinary, Animal and Biomedical Sciences, Massey University, Palmerston North, New Zealand

Mellor in these proceedings (2002).

General considerations

Stafford & Mellor (1993) considered five factors which can confound assessments of distress. They are as follows:

First, all parameters which might be chosen to indicate the presence of distress must by definition also show variations or frequencies of occurrence that indicate the absence of distress. The values in distress-free and distressed states both need to be determined.

Second, it is important to determine whether or not deviations of chosen indices from control values to levels indicating distress actually do reflect the expected type of distress or indeed reflect distress at all. For instance, in anaesthetised animals, cortisol responses can be elicited by hypoxaemia and/or hypotension as well as by surgery-induced pain, so that the first two need to be prevented before cortisol responses can be interpreted in terms of stimulation of pain receptors.

Third, the significance of different distress-specific behaviours should be checked, where possible, against physiological indices in order to assess the validity of conclusions drawn using behaviour alone. For instance, cortisol responses question conclusions based on cursory observation of behaviour regarding the relative distress caused by castration with a rubber ring or a knife (Lester *et al.*, 1996).

Fourth, taking recommendations based on unchecked or poorly checked assumptions must be avoided, especially when extrapolating from one species to another, as unexpected differences can arise between the distress responses of different species to the same treatment.

Fifth, studying the distress caused by husbandry practices is complex, time-consuming and expensive, if it is to be done rigorously, as allowance must be made for possible effects of the species, breed, sex and age of the animals, the different methods used, and even factors such as the rearing methods of young animals.

Acute cortisol responses

There are six additional points which need to be borne in mind when interpreting cortisol responses to noxious stimulation (Mellor *et al.*, 2000).

First, the HPA system responds to a wide range of physically, physiologically and emotionally challenging situations. Although some argue that this is an impediment to the use of cortisol, we consider that this non-specificity adds credibility to its use to assess distress. We have demonstrated that, provided the stimuli used are obviously noxious and that appropriate control groups are used, cortisol responses can be informative (Mellor & Stafford, 1999; Mellor & Stafford, 2000; Mellor *et al.*, 2000).

Second, cortisol concentration-time curves need to be derived by repeated blood sampling as the response manifests and recedes. This allows the magnitude and speed of change, and the duration and pattern of the whole response or each part of it, to be determined. Differences between groups in initial or later concentration changes, peak concentration and time to reach it, and time of return

to pretreatment values are informative, but only if they can be related to the whole response. Only comparing concentrations before treatment with those at one or two arbitrary times after it provides little valuable information and can be misleading.

Third, cortisol responses vary in complexity. They may be simple (e.g., rising to a peak and then returning to pretreatment values, as is usual with castration and/or tailing of lambs), or they may be more complex (e.g., first rising to a peak, then declining to a plateau and finally returning to pretreatment values, as usually occurs with amputation dehorning of calves). Further complexity arises when responses include two (or more) peaks.

Fourth, quantitative tools for characterising cortisol distress responses include numerical representation of individual facets of the response (e.g., peak height, response duration, area under the cortisol curve) and statistical evaluation of concentration-time curves to detect within-group deviations from pretreatment values and between-group differences after treatment. There is no single numerical factor that adequately defines distress responses, even simple ones, and it is obvious that the more complex a response, the less likely it is that a single number could represent it effectively. Quantitative definition of cortisol responses may best be achieved by using a range of numerical approaches, with the chosen combination depending on the characteristics of the particular response (Mellor *et al.*, 2000).

Fifth, cortisol has been used extensively to assess distress because its response magnitude, as indicated by peak height, response duration and/or area under the curve, usually accords with the predicted noxiousness of different procedures (for examples see Mellor *et al.*, 2000). However, care needs to be taken when interpreting responses at the lower and upper extremes of the response range, because different noxious stimuli applied simultaneously may not have additive effects on cortisol responses. At high concentrations this may manifest as a “ceiling effect” in which the overall noxiousness of two undoubtedly painful stimuli applied simultaneously may be underestimated because each one alone would elicit a maximum cortisol response.

Sixth, wide variation in cortisol responses to treatment is common. It is important to distinguish between variable effects of pretreatment stressors on different animals and animal-specific differences (some animals show consistently high and others consistently low responses to the same stimulus). This is accomplished easily by assessing how close cortisol concentrations are to non-stressed levels before treatment and whether or not they subsequently return to those levels.

It is important to note that assessment of the acute pain-induced distress response of animals using cortisol as the sole physiological index, allows conclusions to be drawn only about those features of the acute response that are reflected by changes in plasma cortisol concentrations (Mellor & Stafford, 1999; Mellor & Stafford, 2000; Mellor *et al.*, 2000). It is, therefore, valuable to include other indices of pain-induced distress.

Acute catecholamine responses

In addition to the longer-lasting HPA responses to painful stimuli, there is the well-known rapid-onset, short-lived catecholamine-centred response mediated by the sympathetic-adrenomedullary system that helps to activate "fight-flight" reactions. A less-well-known third component, having an intermediate time scale, which involves noradrenaline release probably by damaged tissues (Halter *et al.*, 1977), is also apparent when traumatic injury is involved (Chernow *et al.*, 1987; Udelsman *et al.*, 1987; Friedrich *et al.*, 1999). We examined these three responses in calves which were dehorned by amputation and in lambs castrated and tail docked with rings (Mellor *et al.*, 2002).

In calves, as expected, the plasma cortisol response to dehorning consisted of an initial rise to peak concentrations reached about 40 min after treatment, a decrease to high plateau values that were maintained between about 1.5 and 3 h, and then a further decrease back to pretreatment values by 7 h after treatment. At 5 min, when the first post-treatment blood sample was taken, plasma adrenaline concentrations were greater than pretreatment values, but by 10 min had returned to pretreatment values, where they remained subsequently. The high concentrations at 5 min indicate stimulation of the adrenal medulla and may represent the tail of a much greater response that occurred during the first seconds and minutes after horn amputation. Although adrenomedullary stimulation can also release noradrenaline, no elevation in its plasma concentrations was seen at 5 min, but other stressors in calves can cause increases in adrenaline with no corresponding increase in noradrenaline concentrations (Locatelli *et al.*, 1989; Agnes *et al.*, 1990a; Agnes *et al.*, 1990b). However, noradrenaline concentrations subsequently rose to a peak at 30 min and then returned to pretreatment values by 60 min after treatment. These changes are thought to reflect "wash-out" of noradrenaline from damaged tissues at the amputation sites, and may reflect the extent of tissue damage, as is apparently the case for human beings (Halter *et al.*, 1977; Hagenouw *et al.*, 1986; Friedrich *et al.*, 1999).

In lambs, as expected, the cortisol response to ring castration and tailing consisted of an initial rise to peak concentrations at about 50 min and a return to pretreatment values by 3.5 h after treatment. There was no detectable adrenaline response, but noradrenaline concentrations rose during the first 10 min, remained high until 30 min and then returned to pretreatment values by 60 min. It appeared that the gradual onset of hypoxia/anoxia in the scrotum and testes after ring application was not a sufficient insult to cause elevated adrenaline release at 5 min, but what occurred earlier remains unknown. "Wash-out" of peripherally-released noradrenaline from damaged tissues proximal to the ring may explain the pattern of its plasma concentrations during the first 60 min after treatment.

Overall these results show that adrenomedullary stimulation is likely to occur only during the first 5 min, "wash-out" of peripherally-released noradrenaline from damaged tissues for up to about 60 min, and HPA stimulation for several hours after treatment.

Acute blood pressure, heart rate and ACTH responses

In a study of two-month-old lambs, we examined the effects of ring castration and tail docking on systolic, diastolic and mean arterial blood pressure, heart rate, the plasma concentrations of ACTH, cortisol, renin, glucose, lactate, electrolytes, minerals, total carbon dioxide, urea, creatinine and total protein, plasma osmolality and the haematocrit (Peers *et al.*, 2002). Mean systolic, diastolic and mean arterial blood pressure, heart rate and the plasma concentrations of ACTH and cortisol all increased markedly during the first 60 min after ring placement. Although plasma ACTH and cortisol concentrations had returned to control values by 2.5 to 3 h, the blood pressures and heart rate were still elevated 4 h after ring application. In contrast, there were no significant changes in mean values for any other parameter measured. It follows that systolic, diastolic and mean arterial blood pressure and heart rate may be more sensitive than plasma ACTH or cortisol concentrations as indices of low-grade pain induced by ring castration and tail docking. Alternatively, it is possible that by 4 h after ring placement a small shift in sympathetic tone still persists in the absence of low-grade pain.

These observations highlight an important point about cortisol responses: the return of plasma cortisol concentrations to pretreatment values at the end of an acute response to a noxious stimulus does not necessarily indicate that the animal is pain free; it indicates that the noxious input occurring at that time, in relation to what preceded it, is not sufficient to elevate plasma cortisol concentrations. This understanding is implicit in our earlier statements that assessment of the acute pain-induced distress response of animals using cortisol as the sole physiological index, allows conclusions to be drawn only about those features of the acute response that are reflected by changes in plasma cortisol concentrations (Mellor & Stafford, 1999, 2000; Mellor *et al.*, 2000).

REFERENCES

- Agnes, F.; Sartorelli, P.; Abdi, B.; Locatelli, A. 1990a. Effect of transport loading or noise on blood biochemical variables in calves. *American journal of veterinary research* 51: 1679-1681
- Agnes, F.; Sartorelli, P.; Picotti, G.B.; Arrigoni, C.; Locatelli, A.; 1990b: Metyrapone and adrenal response in stressed calves. *Journal of veterinary medicine* 37: 771-774
- Chernow, B.; Alexander, H.R.; Smallridge, R.C.; Thompson, W.R.; Cook, D.; Beardsley, D.; Fink, M.P.; Lake, R.; Fletcher, J.R. 1987: Hormonal responses to graded surgical stress. *Archives of internal medicine* 147:1273-1278
- Friedrich, M.; Rixecker, D.; Friedrich, G. 1999: Evaluation of stress-related hormones after surgery. *Clinical and experimental obstetrics and gynaecology* 26: 71-75
- Hagenouw, R.R.P.M.; Bridenbaugh, P.O.; van Egmond, J.L.; Stuebing, R. 1986: Tourniquet pain: a volunteer study. *Anesthesia and analgesia* 65: 1175-1180
- Halter, J.B.; Pflug, A.E.; Porte, D. 1977: Mechanism of plasma catecholamine increases during surgical stress in man. *Journal of clinical endocrinology and metabolism* 45: 936-944
- Lester, S.J.; Mellor, D.J.; Holmes, R.J.; Ward, R.N.; Stafford, K.J. 1996: Behavioural and cortisol responses of lambs to castration and tailing using different methods. *New Zealand veterinary journal* 44: 45-54
- Locatelli, A.; Sartorelli, P.; Agnes, F.; Bondiolotti, G.P.; Picotti, G.B. 1989: Adrenal response in the calf to repeated simulated

- transport. *British veterinary journal* 145: 517-522
- Mellor, D.J.; Cook, C.J.; Stafford, K.J. 2000: Quantifying some responses to pain as a stressor. In: Moberg, G.P. and Mench, J.A. (ed) *The Biology of Animal Stress: Basic Principles and Implications for Welfare* Oxon, UK, CAB International, Wallingford, pp 171-198
- Mellor, D.J.; Stafford, K.J. 1999: Assessing and minimising the distress caused by painful husbandry procedures. *In practice* 21: 436-446
- Mellor, D.J.; Stafford, K.J. (2000). Acute castration and tailing distress and its alleviation in lambs. *New Zealand veterinary journal* 48: 33-43
- Mellor, D.J.; Stafford, K.J.; Todd, S.E.; Lowe, T.E.; Ward, R.N.; Gregory, N.G.; and Bruce, R.A.; 2002: Comparison of cortisol and catecholamine responses to ring castration and tailing of lambs and amputation dehorning of calves. *Australian veterinary journal* (in press)
- Peers, A.; Mellor, D.J.; Wintour, E.M.; Dodic, M. 2002: Blood pressure, heart rate, hormonal and other acute responses to rubber ring castration plus tailing of lambs. *New Zealand Veterinary Journal* (in press)
- Stafford, K.J.; Mellor, D.J. 1993: Castration, tail docking and dehorning - What are the constraints? *Proceedings of the New Zealand society of animal production* 53, 189-195
- Udelsman, R.; Norton, J.A.; Jelenich, S.E.; Goldstein, D.S.; Lineham, W.M.; Loriaux, D.L.; Chrousos, G.P. 1987: Responses of the hypothalamic-pituitary-adrenal and renin-angiotensin axes and the sympathetic system during controlled surgical and anaesthetic stress. *Journal of clinical endocrinology and metabolism* 64: 986-994