Copyright is owned by the Author of the thesis. Permission is given for a copy to be downloaded by an individual for the purpose of research and private study only. The thesis may not be reproduced elsewhere without the permission of the Author.
Pain assessment and alleviation in the domestic cat (*Felis catus*)

A thesis presented in fulfilment of the requirements for the degree of

Doctor of Philosophy

in

Veterinary Science

at Massey University, Manawatū, New Zealand.

Mark James Farnworth

2014
This thesis is dedicated to my parents and my Grandma without whom I may never have realised the value of education and found my love of biology.
Abstract

This thesis begins by exploring current knowledge around the domestic cat population and gonadectomy as well as pain assessment tools and pain alleviation for cats. It identifies a number of areas where knowledge is either absent or in need of updating and limitations in tools for the assessment of pain in cats. It therefore proposes the undertaking of the projects which can be found in the subsequent chapters.

Chapters two and three compared the attitudes and practices of veterinarians in New Zealand, Australia and the United Kingdom (UK) around pre-pubertal gonadectomy and provision of analgesia for cats. This used an electronic questionnaire which received 717 responses. Most respondents believed pre-pubertal gonadectomy was either entirely or ‘sometimes’ desirable (556/621). Age of patient at gonadectomy was significantly affected by country surveyed and respondents’ provision or non-provision of services for pounds. Post hoc Tukey HSD analysis indicated the mean age of both spaying and castration (both 4.3 months) in the UK was significantly different from both Australia (spaying: 3.4 months, castration: 3.2 months) and New Zealand (spaying: 3.4 months, castration: 3.2 months) (all p < 0.001). Mean ages at spaying and castration were also significantly different (p=0.008; p=0.019 respectively) for non-providers (spaying: 3.9 months, castration: 3.8 months) of services to pounds when compared to providers (spaying and castration: both 3.6 months).

With respect to the use of analgesics there has been a substantial increase in provision of analgesia to cats undergoing gonadectomy when compared to the early literature. There were significant differences in prevalence of analgesia provision prior to and
following spaying and castration (both p < 0.001). There were also significant post-
operative and post-discharge differences in provision of analgesia for castration, as
compared to spaying (both p < 0.001), and a similar effect was seen pre/intra-
operatively (p = 0.002).

Significant effects amongst countries and between genders relative to the desirability
of pre-pubertal gonadectomy were identified. Respondents from the UK were more
likely to answer ‘no’ (p=0.004) or ‘sometimes’ (p=0.05) as compared to those from
New Zealand or Australia. Females were more likely to respond with ‘sometimes’ as
opposed to ‘yes’ than males. Reasons for considering pre-pubertal gonadectomy
desirable or sometimes desirable focussed on reducing unwanted pregnancies and
improving population control, as well as improving rates of adoption, owner
compliance and cat behaviour and health. Post-operative provision of analgesia
following both castration (p < 0.001) and spaying (p < 0.001) also differed amongst
countries of practice. Veterinarians in Australia and New Zealand were more likely to
provide post-operative analgesia than those from the UK. Veterinarians from the UK
more commonly used non-steroidal anti-inflammatory drugs (NSAID) in the pre/intra-
operative phase (P < 0.001) than veterinarians from either New Zealand or Australia.

Differences in attitudes towards pre-pubertal gonadectomy amongst countries may
relate to the specific Veterinary Association’s guidelines or possibly differences in
social discourse which affect perception of cats. There is substantial overlap between
the reported minimum age of gonadectomy and the age at which cats can enter early
puberty, allowing a window for unintentional pregnancy when pre-pubertal
gonadectomy does not occur. The differences in use of analgesics amongst the UK,
Australia and New Zealand may reflect differing professional considerations of the
risks associated with the use of NSAID. In the interests of animal welfare, pain relief should perhaps be provided or offered more frequently for owner administration.

Chapters four through six explored the value of a thermal carbon dioxide (CO$_2$) laser for the assessment of nociceptive thresholds in cats. To begin repeatabilities were established based on individual responses to three thermal tests on the same day and across 4 consecutive days. A total of 12 thermal tests were conducted on 16 adult cats (50% male). A non-thermal helium aiming laser was used as a control to ensure the animals were responding to the thermal component of the device. All thermal tests elicited a behavioural response 97% of which were a skin twitch known as the panniculus reflex. No control tests resulted in this reflex behaviour. There was no evidence that cats became sensitised or habituated to the low power thermal stimulus on any given day (p=0.426) or across days (p=0.115). There was also no difference in latency to respond between males and females (p=0.094), although there was a significant day of testing and sex interaction (p=0.042). Significant intra-class correlations (ICC) demonstrated that individual responses were repeatable over days 1 to 3 (all p<0.05) but not over day 4 (p=0.096). A significant intra-class correlation was also evident across all days when data were combined (p<0.0001).

Significant repeatabilities in the first laser-based experiment were low ranging from 0.241 to 0.414 therefore a larger sample was used (n=113) to establish any other factors, including age or sex effects, that impacted upon thermal sensitivity. In this next phase cats were exposed to a more powerful (500mW) CO$_2$ thermal laser three times during a 45-60 min test period with a minimum of 15 min elapsed between consecutive tests on any one individual. Again time to display a behavioural response was repeatable across tests for any given cat (ICC=0.482; p<0.001). Analyses of co-variance established that the body weight of females significantly affected response
threshold (p=0.013) but for males this effect was marginal (p=0.058). All other factors included in the analyses were non-significant. A post hoc t-test for males and females with overlapping body weights found no significant differences between the sexes (p=0.721). The precise reason for the effect of body weight on latency to respond is unknown and further exploration is needed.

Finally the CO₂ laser’s ability to assess analgesia in pain-free cats was explored. Sixty healthy adult female cats were used and randomly allocated to one of six treatments 1) saline 0.2 ml/cat; 2) morphine 0.5 mg/kg; 3) buprenorphine 20µg/kg; 4) medetomidine 2 µg/kg; 5) tramadol 2mg/kg; 6) ketoprofen 2mg/kg. Latency to respond to thermal stimulation was assessed prior to intramuscular injection and at 6 time periods following injection (15-30; 30-45; 45-60; 60-75; 90-105; 120-135 min). Thermal thresholds were again assessed using time to respond behaviourally to stimulation with a 500mW CO₂ laser. Maximum latency to respond was set at 60 sec but given that this technique was found to cause minor skin blistering in individuals that reached the 60s exposure limit, a cut off time of <45s is recommended.

Differences in response latency for each treatment across the duration of the experiment were assessed using a Friedman’s test. Differences between treatments at any given time were assessed using an independent Kruskal-Wallis test. Where significant effects were identified, pair-wise comparisons were conducted to further explain the direction of the effect. Cats treated with morphine (p=0.045) and tramadol (p=0.002) showed significant increases in latency to respond over the duration of the test period. Treatment with buprenorphine also resulted in increases in latency to respond although only at the level of a statistical trend (p=0.091). Injection of saline, ketoprofen or medetomidine showed no significant effect on latency to respond. The
longest latency to respond after injection of morphine was achieved at 60-75 min whilst that of buprenorphine occurred at 90-105 min.

These projects validated the CO₂ laser technique for use in cats and demonstrate that it can be used for assessment of analgesia and may be useful for differentiating amongst analgesic treatments. This technique may provide a simpler alternative to existing systems although further exploration is required both in terms of its sensitivity and comparative utility (i.e. relative to other thermal threshold systems). Future possible experiments using this technique are to be found in the discussion chapter.

Keywords: Analgesia; Cat; CO₂ laser; Gonadectomy; Pain assessment; Pre-pubertal; Veterinary attitudes
Contents

Abstract ........................................................................................................................................5

Contents ........................................................................................................................................11

List of tables and figures ..............................................................................................................18

Acknowledgements ......................................................................................................................19

Preface ........................................................................................................................................21

1. Literature Review: ..................................................................................................................23

1.1 The domestic cat population ..............................................................................................25

1.1.1 Problems associated with the cat population in New Zealand ......................................25

1.2 Reasons for Gonadectomy ..................................................................................................27

1.3 Nociception and pain ..........................................................................................................28

1.3.1 Defining nociception and pain ........................................................................................28

1.3.2 Acute pain .......................................................................................................................30

1.3.3 Inflammatory pain ...........................................................................................................31

1.3.4 Chronic pain ....................................................................................................................31

1.3.5 Pain severity ....................................................................................................................32

1.3.6 Pain duration ...................................................................................................................33

1.4 Impact of painful experiences .............................................................................................34
1.4.1 Central sensitization and the development of chronic/maladaptive pain

35

1.5 Gonadectomy of domestic cats ................................................................. 35

1.5.1 Timing of gonadectomy ....................................................................... 36

1.5.2 Impact of gonadectomy on cats .......................................................... 37

1.6 Current use of analgesia for pain in cats ................................................. 38

1.7 Managing the pain associated with gonadectomy in cats .................. 39

1.7.1 Peri-operative pain management ....................................................... 40

1.7.2 Post-operative and recovery pain management .................................. 42

1.8 Current limitations to effective pain management in cats .............. 44

1.9 Assessing pain ....................................................................................... 45

1.9.1 Behavioural assessment of pain .......................................................... 45

1.9.2 Limitations of behavioural assessment of pain ............................... 47

1.9.3 Behavioural measurement of pain in cats ........................................ 49

1.9.4 Pain scales .......................................................................................... 50

1.9.5 Quantitative sensory testing ............................................................... 53

1.10 Objectives of this study ....................................................................... 55

1.11 References ............................................................................................ 56

Survey Paper One .......................................................................................... 67
2. Veterinary attitudes towards pre-pubertal gonadectomy of cats: A comparison of samples from New Zealand, Australia and the United Kingdom. ............................................ 69
   
   2.1 Abstract ........................................................................................................ 69
   
   2.2 Introduction .................................................................................................. 71
   
   2.3 Materials and methods .............................................................................. 74
     
     2.3.1 Statistical analyses ............................................................................. 75
   
   2.4 Results .......................................................................................................... 77
     
     2.4.1 Basic demographics ........................................................................... 77
   
   2.5 Discussion .................................................................................................... 86
   
   2.6 References ................................................................................................... 92

Survey Paper Two .................................................................................................. 95

3. Veterinary provision of analgesia for domestic cats (*Felis catus*) undergoing gonadectomy: A comparison of samples from New Zealand, Australia and the United Kingdom. ................................................................. 97

   3.1 Abstract ........................................................................................................ 97
   
   3.2 Introduction .................................................................................................. 98
   
   3.3 Materials and methods .............................................................................. 102
   
   3.4 Statistical analyses ................................................................................... 103
   
   3.5 Results ........................................................................................................... 105
3.5.1 Basic demographics ................................................................. 105
3.5.2 Differences in analgesia use relative to procedure and phase........ 105
3.5.3 Differences in analgesia provision amongst respondents .......... 106
3.5.4 Provision of analgesia for owner administration ...................... 109
3.5.5 Analgesics used relative to country of practice ......................... 110
3.6 Discussion ....................................................................................... 112
3.7 References ..................................................................................... 117

Laser validation paper one ........................................................................ 121

4. Validating the use of a carbon dioxide laser for assessing nociceptive thresholds in adult domestic cats (Felis catus). ................................................................. 123

4.1 Abstract ....................................................................................... 123
4.2 Introduction ..................................................................................... 124
4.3 Materials and methods ................................................................... 127
4.3.1 Subjects and housing conditions ............................................... 127
4.3.2 Experimental protocol .............................................................. 128
4.4 Statistical analyses ......................................................................... 131
4.5 Results .......................................................................................... 132
4.5.1 Latency to respond ................................................................. 133
4.5.2 Repeatability .............................................................................. 133
5. Body weight affects behavioural indication of thermal nociceptive threshold in adult female domestic cats (*Felis catus*). ................................................................. 145

5.1 Abstract ..................................................................................................... 145

5.2 Introduction ............................................................................................. 146

5.3 Materials and methods ............................................................................. 148

5.3.1 Subjects and housing conditions .......................................................... 148

5.3.2 Experimental protocol .......................................................................... 149

5.3.3 Additional data collection .................................................................... 151

5.4 Statistical analyses.................................................................................... 152

5.5 Results ...................................................................................................... 154

5.5.1 Provisional analyses................................................................................ 154

5.5.2 Effects of individual variables on response latency............................. 155

5.6 Discussion ................................................................................................. 157

5.7 Conclusions ............................................................................................... 161

5.8 References ................................................................................................. 162
6. Assessment of a carbon dioxide laser for the measurement of thermal nociceptive thresholds following intra-muscular administration of morphine, buprenorphine, tramadol, ketoprofen and medetomidine to pain-free female cats

6.1 Abstract

6.2 Introduction

6.3 Materials and methods

6.3.1 Cats and housing conditions

6.3.2 Laser device

6.3.3 Thermal threshold testing procedure

6.3.4 Drug treatments

6.3.5 Statistical analyses

6.4 Results

6.4.1 Weight

6.4.2 Effect of treatments on latency to respond to thermal stimulation

6.4.3 Side effects of treatment and procedure

6.5 Discussion

6.6 References

7. General discussion
7.1 Gonadectomy and pain in cats ................................................................. 189
7.2 Value of these studies ............................................................................. 191
7.3 Summary of key findings ....................................................................... 192
7.4 Implications of findings for veterinary practice and pain research in cats.. 195
7.5 Limitations of the research .................................................................... 198
  7.5.1 Survey studies .................................................................................. 198
  7.5.2 Laser-based studies ......................................................................... 199
7.6 Future enquiry ....................................................................................... 202
7.7 References ............................................................................................. 206
8. Appendix 1 ............................................................................................. 209
9. Appendix 2: DRC 16s Statements of contribution to doctoral thesis containing publications for chapters 2-6 inclusive. ................................................. 213
List of tables and figures

Table 2-1: Respondent variables ................................................................. 78

Table 2-2: Minimum age of gonadectomy ................................................... 79

Table 2-3: Minimum age of spay relative to service provision ...................... 80

Table 2-4: Is pre-pubertal gonadectomy desirable? Response by gender ........ 82

Table 2-5: Responses to open ended questions about pre-pubertal gonadectomy ........................................................................................................ 85

Table 3-1: Analgesia use for cats undergoing gonadectomy ......................... 106

Table 3-2: Provision of analgesia relative to country of practice ................... 109

Table 3-3: Analgesics used during and after gonadectomy relative to country of practice ........................................................................................................ 111

Table 4-1: Intra-class correlations and repeatability of laser protocol .............. 134

Table 5-1: Cat characteristics ..................................................................... 155

Table 6-1: Number of cats reaching 60 s cut-off by treatment ....................... 178

Figure 5-1a/b: Body weight and response latency ........................................... 156

Figure 6-1: Individual variation in latency to respond to buprenorphine ........ 179

Figure 6-2: Latency to respond relative to treatment and across the testing period. ........................................................................................................... 180
Acknowledgements

This thesis would not have been possible without the help of my supervisors and co-authors all of whom are named further within this thesis. Honourable mention must also go to those who assisted in the dissemination of the survey used in chapters one and two, particularly Sue Blakie, Tim Sainty and M Cole. A final thanks to the staff and students of the Massey University Feline Unit for assistance with cat care and management.