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Pain assessment and alleviation in the domestic cat (*Felis catus*)

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

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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 (CO₂) 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) CO₂ 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 covariance 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; CO₂laser; Gonadectomy; Pain assessment;Pre-pubertal; Veterinary attitudes

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