LASA 3Rs Section / UFAW Meeting

25th September 2019

Pain assessment and control

~ PROGRAMME ~

GlaxoSmithKline
David Jack Centre for R & D
Park Road, Ware
Herts, SG12 0DP.

LASA has awarded this meeting 5 CPD points

Programme

09:50-10:30	Arrival, coffee and registration
10:30	Welcome & Introduction
	Session 1- Chair, Robert Hubrecht
10:40-11:15	**Working with Wildlife and minimising Pain and Stress** Dr M G I Brash, Fera and University of York
11:15-11:45	**Pain sensitivity & analgesia in fish – a practical guide for the laboratory fish vet** Paul Schroeder, University of Oxford
11:45-12:15	**Assessing the long-term consequences for pain in tail amputated pigs: A cautionary tail?** Dale Sandercock, Roslin Institute
12:15-12:45	**The identification and limitation of pain in commercial laying hens and broiler** Gina Caplen, University of Bristol
12:45-14:00	Lunch and networking
	Session 2- Chair, Patricia Pimlott
14:00-14:30	**Monitoring welfare in laboratory dogs** Jackie Boxall, GSK
14:30-15:00	**NHP – title TBC** Caroline Bergmann, University of Oxford
15:00-15:30	**Recent advances in assessing pain in animals** Matthew Leach, Newcastle University
15:30-16:00	**Pain assessment and analgesia in laboratory animals: what have we learned so far?** Carl Bradbrook, Anderson, Moores Veterinary Specialists
16:00	Final comments and close of meeting

Abstracts

Working with Wildlife and minimising Pain and Stress

Dr M G I Brash B Vet Med Cert Zoo Med MRCVS
NVS for Fera and York University

The Animals (Scientific Procedures) Act 1986, and the advice note for 'Working with animals taken from the wild' (Advice note 02/2016) acknowledges that working with these animals has inherent problems and provides good advice about the level of competencies that a project licence holder must have.
This includes being familiar with the signs of common disease and injuries in the species, and with the behavioural indicators of pain, distress and disease which is often more difficult to interpret in wild animals.
Furthermore there is a requirement that wild animals found to be injured or in poor health are not subjected to a regulated procedure, unless and until it has been examined by a veterinary surgeon, or other competent person, and action been taken to minimise the suffering of the animal.
However health assessment of wild animal is often not possible prior to capture, and is further complicated by the animals ability to mask pain, disease and discomfort. This also means that the risk status of the animal to stressors cannot be underestimated.
In this context stress refers to the generalized nonspecific response of the body to any factor that threatens to overwhelm its compensatory abilities to maintain homeostasis. These may be eustressors, helping the animal to survive, but can also be harmful, such as in severe pursuit of the animal, poor capture or restraint, pain or anaesthesia.
Simple mechanical capture has been shown to result in statistically less problems, especially losses, than chemical capture (Spraker 1993). So bizarrely using e.g. traps or netting, are safer than a drug delivered to a free roaming animal, even though the animal may suffer acute stressors for a period of time whilst being caught.
It is essential that these stressors are minimised with capture undertaken carefully, judiciously, with good planning and appropriate legal permits and licenses in place to ensure successful capture, research and release back to the wild.
Capture and anaesthetic related mortality is usually more frequent than in domestic or laboratory species, but to accept this without having first ensured that one has done all in ones power to prevent this by minimising stressors would be unforgivable.
Added to this working with wild animals especially in the field at POLE's has added problems, with risks to both operator and animal and therefore increased responsibilities.
This talk concentrates upon the common stressors affecting wildlife, focusing on the recognition of pain, its potential treatment, and ways to minimise these. It aims to assist compliance with the Act and a successful outcome to the research.
Any scientist working with wild animals should ensure that they are familiar with the Guidance on Operation of the ASPA, and 'Working with animals taken from the wild' (Advice note 02/2016).

Pain sensitivity & analgesia in fish – a practical guide for the laboratory fish vet

Paul Schroeder
Department of Biomedical Services, Oxford University, UK

The question of whether fish have the capacity to experience a state akin to pain was first empirically addressed in Jan Verheijen's seminal study on carps in 1983. Subsequently, comprehensive evidence has been presented not only on the anatomical prerequisites for a pain system in several fish species, but also for a behavioural component. Opinions against fish perceiving pain focus on the difference in neuroanatomy between higher mammals and lower vertebrates who do not possess a neocortex.
True to Bateson's criteria, the successful (behaviour sparing) use of analgesics in a variety of fish species of different developmental stages is to be interpreted as further evidence that fish are able to perceive pain and can be adversely affected by a painful event, while wider recognition of pain sensitivity in fish may be tied to future functional anatomy revelations – as has already happened in birds.

Finally, with the increased understanding of pain sensitivity in fish there is also scope for a re-evaluation of the principles of anaesthesia and how they apply to fish, with special focus on the delivery of analgesia as part of the anaesthetic triad.

Assessing the long-term consequences for pain in tail amputated pigs: A cautionary tail?

DA Sandercock[1], P Di Giminiani[2], SA Edwards[2], SH Smith[3], MW Barnett[3], TC Freeman[3]

[1]Animal and Veterinary Sciences, Scotland's Rural College (SRUC), UK
[2]School of Natural and Environmental Sciences, Newcastle University, UK
[3]The Roslin Institute and Royal (Dick) School of Veterinary Studies, University of Edinburgh, UK

Tail amputation by tail docking or as a consequence of tail biting in pig production systems has serious implications for animal welfare, has been implicated in peripheral nerve injury and may result in chronic pain. The current study, part of the 'FareWellDock' project investigating the long-term consequences of pain in tail amputated pigs, provides new evidence to support this. Histopathological analysis of tail stumps collected 1, 4, 8 and 16 weeks after tail docking revealed widespread development of traumatic neuromas from 4 weeks after amputation injury. Traumatic neuromas are often associated with residual stump and phantom limb pain, both recognised as neuropathic pain states. Neuronal dispersion and proliferation within a granulation tissue bed was observed 16 weeks after amputation, in conjunction with epidermal re-innervation. Mechanical nociceptive thresholds were quantified in pigs with intact, 1/3rd and 2/3rds tail amputation pigs at 8 weeks. Significant decreases in tail sensitivity thresholds were observed in both tail amputated groups, 1 and 16 weeks post-amputation ($p<0.05$). Transcriptome analysis was performed on dorsal root ganglia (DRG) from 2/3rds tail amputated and sham-treated pigs 1, 8 and 16 weeks following amputation at either 3 or 63 days of age. Amputation induced significant changes in gene expression (up and down) compared to sham-treated intact controls for both treatment ages and all time points after tail treatment ($p<0.05$). Sustained changes in gene expression in tail-amputated pigs were evident four months after tail injury. Correlation network analysis revealed two gene clusters associated with tail amputation: Cluster A (759 down-regulated) and Cluster B (273 up-regulated) genes. Gene ontology analysis identified 124 genes in Cluster A and 61 genes in Cluster B associated with both 'inflammatory pain' and 'neuropathic pain'. In Cluster A, ion channel gene family members, e.g. voltage-gated potassium channels, and receptors, e.g. GABA receptors, were significantly down-regulated compared to shams, both of which are linked to increased peripheral nerve excitability after axotomy. Up-regulated gene families in Cluster B were linked to transcriptional regulation, inflammation, tissue remodelling and regulatory neuropeptide activity. These transcriptomic findings, coupled with observations of long-term reductions in tail stump mechanical nociceptive thresholds, support the suggestion that tail amputation causes sustained changes in peripheral nerve DRG neuron and glial cell function involving key mediators of inflammation and neuropathic pain, which might cause long-term stump pain in pigs.

The identification and limitation of pain in commercial laying hens and broiler chickens

Gina Caplen, University of Bristol

It is widely accepted that birds, like mammals, are capable of experiencing pain. This belief is supported by multiple lines of evidence, including the existence of various cutaneous thermal, mechanical and chemical nociceptors, the observation of physiological and behavioural responses to noxious stimulation, and the demonstration that non-steroidal anti-inflammatory drugs and opioids have analgesic properties in birds. In the context of commercial poultry welfare, pain assessment is important to identify which pathologies or husbandry procedures are responsible for producing pain. This allows us to preferentially target the most impactful pathologies, reduce or alter husbandry procedures, and/or develop effective analgesic strategies. In this talk we summarise the evidence for pain experience in chickens, review the main likely causes of pain in commercial flocks and consider how these factors can be mitigated. The current limitations to the assessment and management of poultry pain will also be discussed. In brief, laying hens are prone to outbreaks of injurious (vent and feather) pecking, hyperkeratosis with abscess formation (bumblefoot), and keel-bone fractures due to the conditions in which they are housed and, in the case of bone fractures, genetic selection for increased egg production. Modern strains of broiler chicken have a tendency to become lame and develop contact dermatitis and breast blisters, due to housing

conditions and genetic selection for increased growth rate and an altered morphology. Potentially painful practices include mutilations such as beak trimming (to prevent feather pecking in layers) and comb/wattle trimming, toe-clipping and de-spurring in parent stock.

Monitoring welfare in laboratory dogs
Jackie Boxall and Helen Murphy
Global Laboratory Animal Medicine, Ware, GSK

Recognition and management of pain in laboratory dogs used in safety assessment studies will be explored with a focus on maintaining high welfare standards in the post-surgical period and when pain results as an adverse effect of compound administration. Staff training and knowledge of normal dog behaviour are important considerations when undertaking welfare and pain assessments, and familiarity with individual variation and strain effects is essential. Bespoke scoring systems can be used post-operatively and their use in two different telemetry models will be described along with an overview of multimodal analgesic regimes for dogs.

Caroline Bergmann, University of Oxford
Abstract pending

RECENT ADVANCES IN ASSESSING PAIN IN ANIMALS

MC Leach[1], AL Miller[1] and PA Flecknell[2]

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Assessing emotional states such as pain in non-human animals remains challenging as they are unable meaningfully communicate pain or any other emotional state to those who care for them, i.e. have self-report. Therefore, we have to rely on proxy indices of pain, but in many cases, we cannot be sure how these indices relate to the underlying emotional state experienced by the animal. There is increasing interest in developing new indices that potentially are a more direct assessment of the emotional component of pain in non-human animals. In this presentation, I will describe some of these new methods and discuss how they might more directly relate to pain experienced as well as any potential limitations of these techniques. These novel methods will include; spontaneous 'complex' behaviour, a range of operant behavioural assays (including self-administration, conditioned discriminations) and the relatively new method of using facial expressions to assess pain.

Pain assessment and analgesia in laboratory animals: what have we learned so far?
CA Bradbrook
Anderson Moores Veterinary Specialists, Winchester, Hampshire, SO21 2LL

Pain assessment in any non-verbal species is a vital component of any work with laboratory animals, and a fundamentally essential component of any laboratory-based research. Good pain assessment and provision of analgesia is a key part of the 3R's. Paying close attention to pain and analgesic refinement will ensure scientific data output and data collection is of the highest quality and improve reliability.

The challenge facing both the veterinary and scientific communities is that of ensuring pain assessment itself is valid, consistent and also reproducible and can be applied to the relevant species. A number of pain assessment tools have been developed in several species during recent years. The species with pain scales currently available include rodents, rabbits, dogs and cats, all of which are used in the laboratory environment. A number of these assessment tools are based on the use of facial expression, which in itself may be affected by environmental and individual factors, and most importantly cannot be ported between different species. Recent research into new ways to assess pain in non-human primates (NHPs) using both behaviour and facial expression has proved promising,

with the aim to improve welfare and scientific output in neuroscience research. Pain assessment in NHPs is further complicated by the difficulty in interacting with this species.

The use of analgesia in the experimental setting may also prove a difficult area, as the drugs themselves may have an effect that could interfere with the scientific data to be collected. In this situation consultation with an expert in anaesthesia and analgesia, and discussion of the scientific aims and concerns at the planning stage may lead to better outcomes and improve animal welfare.

This presentation will explore the pain assessment tools that are currently available, those in development and how they may be integrated into the research laboratory. It will then focus on how we should be using these tools to provide the most appropriate analgesia to ensure valid and reproducible scientific output.