



Session IV-5: Can pain research benefit research animals?

Session IV-5: Oral presentations

IV-5-526

Assessment of pain in small laboratory animals using behaviour and facial expressions

M. Leach

Newcastle University, Newcastle, UK

m.c.leach@ncl.ac.uk

Considerable advances have been made in assessing pain in laboratory animals through the evaluation of behavioural and postural changes. Successful implementation of such assessments depends on establishing which behaviours and postures indicate pain and which areas of the body to focus on to observe these indicators. Failure to observe all relevant body areas will prevent successful use of behaviour-based assessment techniques.

Using eye-tracking equipment we have demonstrated that irrespective of experience observers' focus first, more frequently and for longer on the face compared to the abdomen, ears, back and hindquarters of rabbits when assessing pain following ovariohysterectomy. The general ability of the observers to identify rabbits in pain was very poor, with incorrect pain scores being positively correlated with increased observation of the face. Consequently, focusing on the face to assess abdominal pain based on behaviour is likely to reduce the effectiveness of the pain assessment.

Alternatively, if we can identify facial expressions in animals that are associated with pain as in humans then a fixation on the face may actually increase the effectiveness of pain assessment based upon such expressions. Recently Langford et al. (2010) convincingly demonstrated that mice exhibit facial expressions associated with pain and that it can be objectively measured using the Mouse Grimace Scale (MGS). We have further validated the MGS by demonstrating its effectiveness for assessing post-operative pain in mice (following vasectomy) and potentially rats (following adrenalectomy). In these studies changes in MGS paralleled those of behaviour-based indicators of pain.

Reference

Langford, D. J. et al. (2010). *Nat. Methods* 7, 447-449.

IV-5-658

Studying pain in rodents using facial expression

J. S. Mogil

McGill University, Montreal, Canada

jeffrey.mogil@mcgill.ca

Recent decades have seen an explosion in our understanding of the molecular and cellular underpinnings of pain, but virtually none of this knowledge has resulted in new clinical therapies. Many pain researchers believe that the problem may lie in the existing animal models of pain, which are of questionable clinical

relevance. Most basic science studies of pain continue to rely on the measurement of reflexive, evoked hypersensitivity responses after artificial neuropathic or inflammatory injuries, whereas clinical pain in humans features mostly spontaneous pain. The *status quo* also has relevance for the veterinary pain



literature, as research into postoperative pain management is conducted using likely irrelevant assays, or measures of uncertain specificity. We recently developed the Mouse (and Rat) Grimace Scale, in which spontaneous pain is quantified from

facial expression, as is commonly done in non-verbal humans. Applying this method has allowed us to reassess the true duration of spontaneous pain after surgery, and the true efficacy (or lack thereof) of commonly used analgesics.

IV-5-157

Non-invasive pain assessment in mice subjected to vasectomy

K. R. Jacobsen, O. Kalliokoski, A. C. Teilmann, J. Hau and K. S. P. Abelson

University of Copenhagen, Copenhagen, Denmark

kiroja@sund.ku.dk

Recognition of pain and stress is a common challenge when working with laboratory mice. The aim of this study was to identify non-invasive parameters to assess the severity and duration of possible pain and stress following vasectomy in BALB/c mice. Mice were subjected to isoflurane anesthesia and vasectomy or isoflurane anesthesia without surgery. Body weight, food and water intake, and fecal corticosterone were measured three days prior to and three days after the procedure. Behavioral observations were recorded 1, 2, 4 and 8 h after the procedure. Food and water consumption and defecation rate

were significantly reduced in the vasectomized group one day post-operatively compared to the mice subjected to anesthesia only. Fecal corticosterone was elevated the first day after isoflurane anesthesia but not in the vasectomized group. Vasectomy resulted in behavioral changes that were not seen in the group subjected to isoflurane anesthesia only. In conclusion, food and water consumption and pain specific behaviors could be useful as non-invasive parameters to assess post-operative pain and stress in mice subjected to vasectomy. However, fecal corticosterone was not useful for this purpose in the present setup.

IV-5-453

Can a focus on the translatability of preclinical pain research benefit research animals?

S. E. G. Duffus¹, G. Griffin¹ and J. Sawynok²

¹The Canadian Council on Animal Care, Ottawa, Canada; ²Dalhousie University, Halifax, Canada

sduffus@ccac.ca

Neuropathic pain, a chronic and debilitating condition in humans, is often modeled in animals by inducing nerve injury. Pain-related sensory changes studied in these models include hypersensitivity to thermal stimuli (hyperalgesia), light touch (mechanical allodynia), and the injection of painful chemicals (chemogenic hypersensitivity). In modeling neuropathic pain, it is important to closely replicate the clinical condition to improve translatability. The current study explored preventive analgesia for postoperative neuropathic pain. Since human patients routinely receive postoperative morphine as part of their analgesic regime, the impact of postoperative morphine on the preventive effects of drugs being studied needed to be determined. Previous research using the spared nerve injury (SNI) model of neuropathic pain demonstrated that amitriptyline has preventive anti-hyperalgesic effects that are not significantly al-

tered by postoperative morphine administration. In this study, propentofylline (1 h preoperatively and then daily for 7 days) alleviated long-term mechanical allodynia in the SNI model. This was not affected by morphine administration (postoperatively and daily for 3 days). When given in combination, propentofylline and amitriptyline maintain their individual long-term effects in the presence of postoperative morphine. Many nerve injury models, including the SNI model, involve extensive tissue manipulation to produce physical injury to a nerve(s), causing pain and inflammation that may not be related to the long-term sensory changes of interest. Here the exploration of postoperative morphine, to improve translatability, likely provided the rats with relief from pain which was not necessary for the study outcomes, and represents a potential refinement for further studies using this model.



IV-5-556

ATLAS: an evidence based web resource for pain control in laboratory animals

A. Z. Karas¹, L. Carbone² and H. L. Shafford³

¹Cummings School of Veterinary Medicine, Tufts University, North Grafton, USA; ²Lab Animal Resource Center, University of California San Francisco, San Francisco, USA; ³Veterinary Anesthesia Specialists, LLC, Clackamas, USA

alicia.karas@tufts.edu

Two types of research can benefit laboratory animals. A substantial body of pain research is performed on animals as models for humans to guide pharmaceutical development and investigate mechanisms. Clinical research specifically examines pain control for the sake of the animal itself, but the volume of this research is still small, particularly for rodents and rabbits. Believing that information to support effective mitigation of pain in laboratory animals can be gleaned from both primary and clinical literature, we have undertaken to create an evidence-based web resource for information regarding treatment of pain in laboratory animals. The concept was inspired by a well-known procedure-specific resource for guidance of physicians on pain management (<http://www.postoppain.org/>). Review and interpretation of the pain literature can benefit labo-

ratory animal veterinarians and researchers by guiding them in what is currently known about efficacy, safety and other effects of pain control in laboratory animals. Use of a method to sort through previously conducted studies is also a form of Reduction, in that with this information, future studies can be targeted more specifically, using fewer animals overall. There is also a need to begin to recognize when use of certain analgesic types, or the presence of pain itself, may affect a study outcome or the success of peer review. It is therefore important to determine whether pain and analgesic criteria are being uniformly applied to animal models by examining the published literature. This presentation will describe our web resource, the ATLAS (Analgesic Therapy in Laboratory Animal Species) Database.

Session IV-5: Poster presentations

IV-5-401

Investigation about anesthesia of rodent fetuses with transplacental pentobarbital administration

M. Senuma¹, H. Takashima¹, M. Kuwagata¹, Y. Yoshida¹ and K. Imai²

¹Hatano Research Institute, FDSC, Hadano, Kanagawa, Japan; ²Osaka Dental University, Osaka, Japan

takashima.h@fdsc.or.jp

Correct anesthesia or euthanasia is an essential factor for making specimens of late stage rodent fetuses. We examined the conditions required to anesthetize rodent fetuses by pentobarbital administration to dams. CrI:CD(SD) rats were anesthetized with sodium pentobarbital intravenously 20 minutes before caesarean sections on day 21 of gestation, and Crj:CD-1(ICR) mice were treated on day 18 of gestation. The doses were 5, 10, 20, 30 or 50 mg/kg of body weight at the time of the caesarean section. Six fetuses from each dam were examined for responses to pain stimulation and their physical responses were scored 60 minutes after the caesarean section. In rat fetuses, the 10 mg/kg or more

dose groups showed deep anesthesia during the 60 minutes, but fetuses of the 5 mg/kg group awoke after 40 minutes. In the 50 or 30 mg/kg groups of mice fetuses, locomotor activity and response to stimulation decreased soon after the caesarean section, and the fetuses were anesthetized for 60 minutes. In the 20 mg/kg group, response to stimulation disappeared but aroused fetuses were observed 20 minutes after the caesarean section. The mortality of fetuses at the time of the caesarean section did not increase in any dose group for both species. These results suggest that pentobarbital administration to the dam is able to anesthetize rodent fetuses for 1 hour.