Refinement of animal models of pain:

Establishment of strategies to alleviate avoidable pain in rat models for pain and inflammation

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Effect of analgesic treatment on experiments

Analgesic drugs may affect several systems in the organism, and consequently the experimental data

- However, this is not necessarily always the case
- and we don’t really know until we have investigated it
What about pain models?

- Can we treat against pain where pain is a part of the model?

- We should at least, if possible, treat against avoidable and unnecessary pain
  - Post-operative pain
  - When relevant pain is not tested

Says who?

✓ Our morality says we should
✓ Our legislation says we should (*EU Directive 2010/63/EU, Article 15 §2*)
✓ Our scientific data may say we should
  - Dougherty et al, *Differential influence of local anesthetic upon two models of experimentally induced peripheral mononeuropathy in the rat*, Brain Res. 570, 1992
  - Hestehave et al, *Is there a reasonable excuse for not providing post-operative analgesia when using animal models of peripheral neuropathic pain for research purposes?* Manuscript, 2016
The hypothesis

- Control
- Negative control: Arthritis without pain relief
- Positive control: Arthritis with anti-inflammatory pain relief
- Arthritis with pain relief expected not to interfere with model parameters

Parameters for animal welfare:
- Welfare score
- Pain relief
- Stress reduction

Parameters relevant for the model:
- Arthritis score
- Cytokines
- Histopathologi

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Results – parameters relevant for model

- Analgesic treatments had only minor impact on the clinical and pathological development on the arthritis parameters.

- The anti-inflammatory compound carprofen (positive control) appeared to have a more pronounced effect on the joint swelling than the opioid buprenorphine, as expected.

- Histopathological changes seemed not to be altered by analgesic treatment.

- Cytokine analysis inconclusive.
Results

- The differences between groups on pain, stress and wellbeing parameters were only subtle.
- The most notable finding was a decreased hyperalgesia in one of the buprenorphine groups.
Conclusions

- Data indicate that there is no immediate justification to withhold buprenorphine analgesia to rats subjected to the applied monoarthritis model, in the present setup.

- More studies are needed, to further improve the wellbeing of the animals.

- More studies needed to improve the actual model, in order to focus the inflammation to the joint and avoid infiltration into surrounding tissue.
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