

Refinement: analgesia and clinical signs in the framework of product development



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Goal

Role of laboratory mice in research and testing

Clinical signs of disease, pain, suffering in mice

Impact of pain killers on animals' physiology and behaviour --- and on data outcome and study results

New methods for the detection of pain, suffering, or impaired wellbeing in mice

Annual usage of laboratory animals

Worldwide

~100 Million animals used in research and testing

Europe

~10 -11 Million

UK

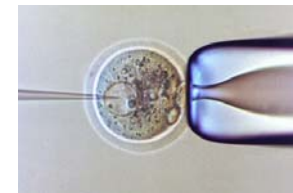
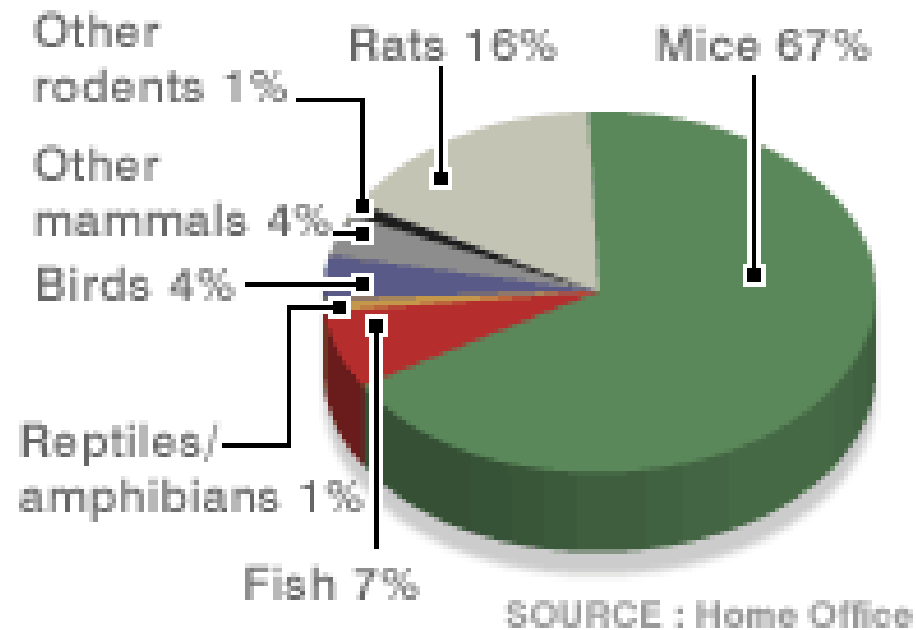
~2.85 Million animals were used in experiments in 2004

Baumans 2005

Data for UK in 2004: taken from BBC news, 8 December 2005, 4 April 2006

Annual usage of laboratory animals

PROCEDURES BY ANIMAL



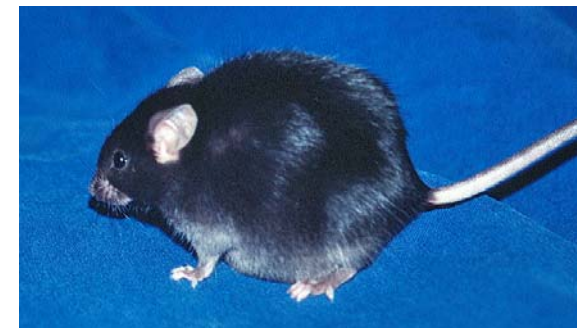
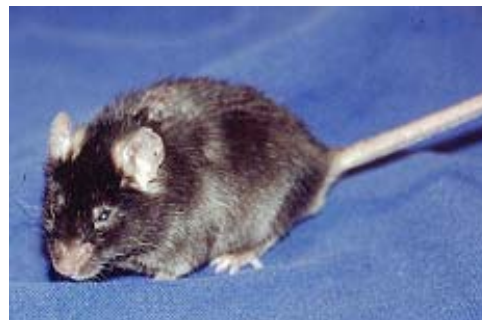
Data for UK in 2004: taken from
BBC news, 8 December 2005, 4 April 2006

Annual usage of laboratory animals

Pain and suffering must be prevented

EU directive 2010

Ethical reasons



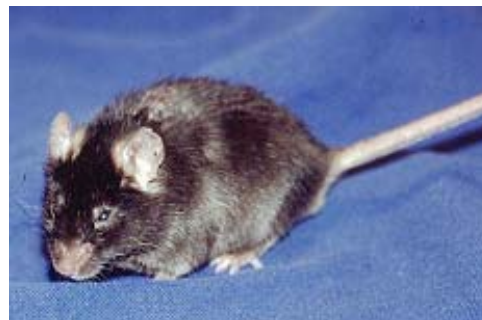
Annual usage of laboratory animals

Pain and suffering must be prevented

EU directive 2010

Ethical reasons

→ analgesia = pain killers



Annual usage of laboratory animals

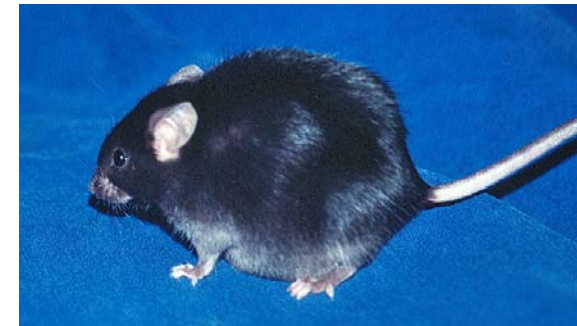
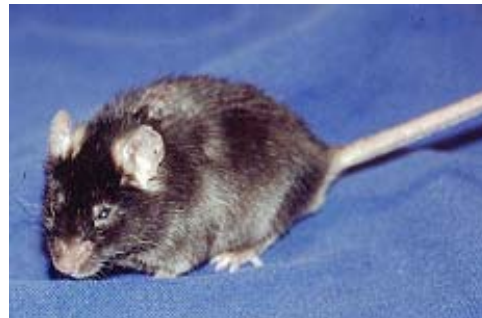
Pain and suffering must be prevented

EU directive 2010

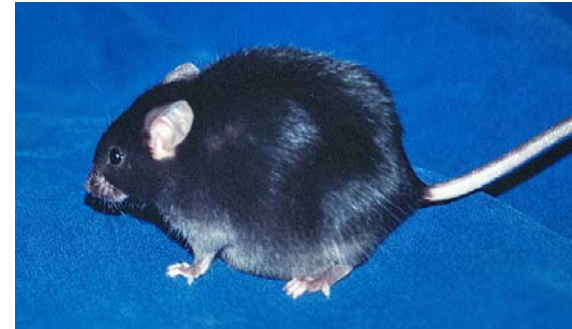
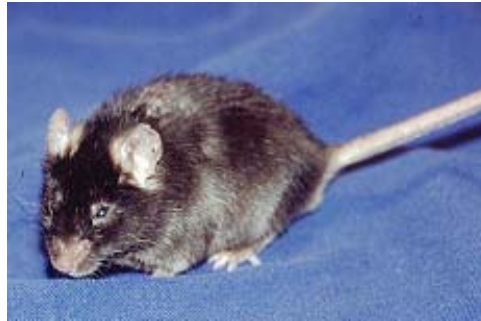
Ethical reasons

→ analgesia = pain killers

→ humane endpoints

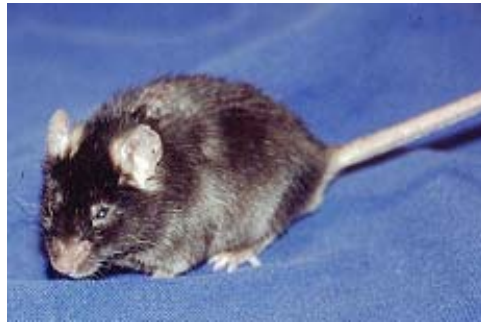


Clinical signs: appearance, posture



= implementation of humane endpoints

Clinical signs: appearance, posture

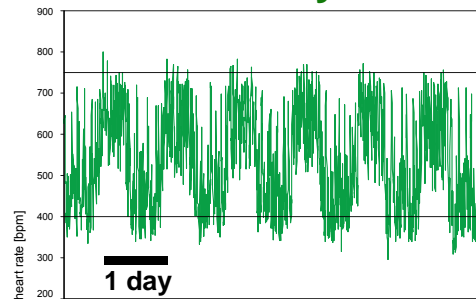


= implementation of humane endpoints
≠ starting early pain relief

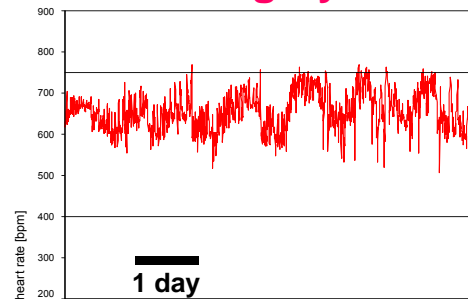
Clinical signs: Physiology

Heart
Rate
[bpm]

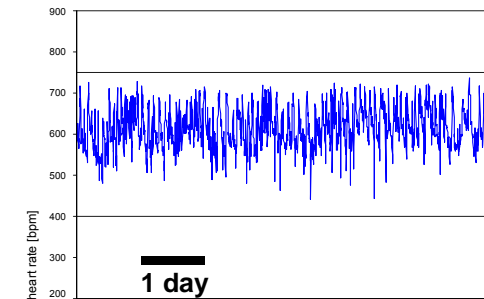
healthy



surgery



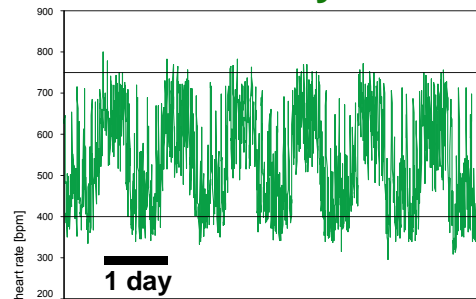
tumor disease



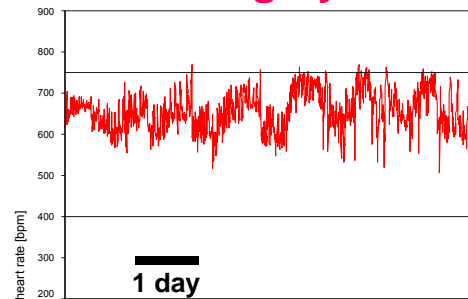
Clinical signs: Physiology

Heart
Rate
[bpm]

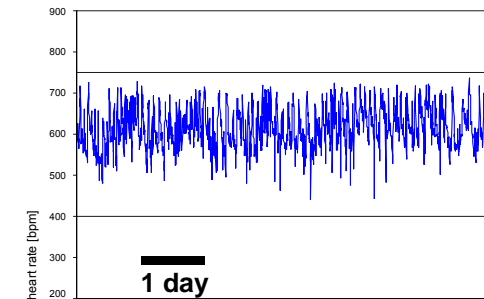
healthy



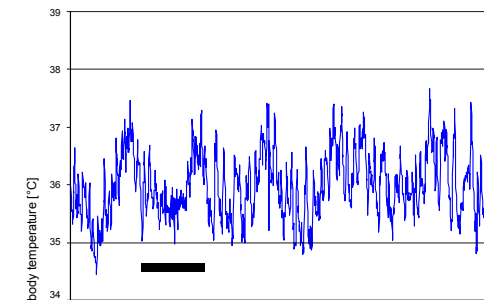
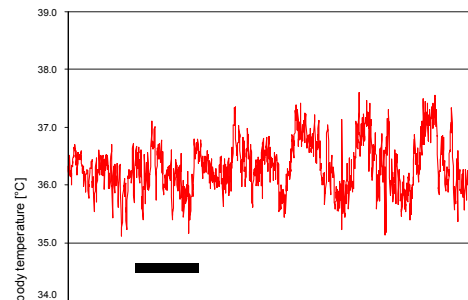
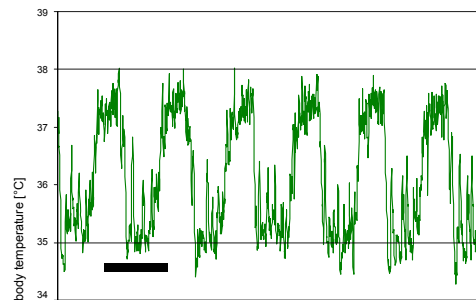
surgery



tumor disease

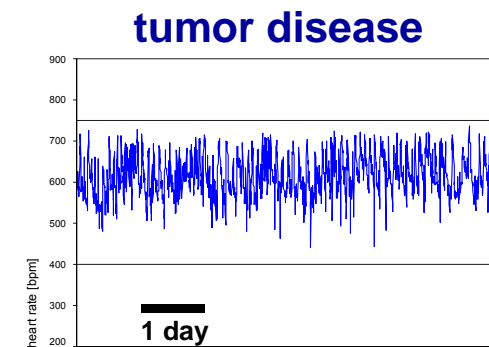
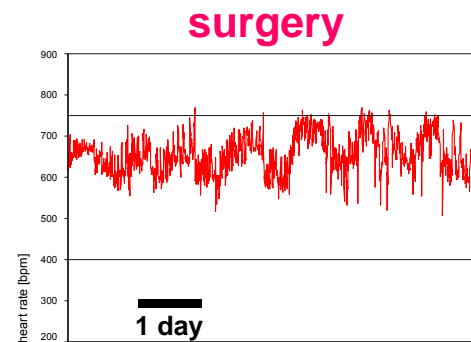
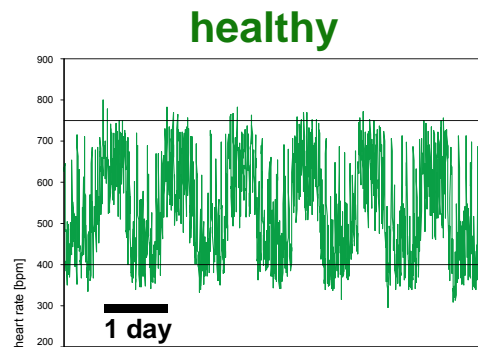


Body
temp.
[°C]

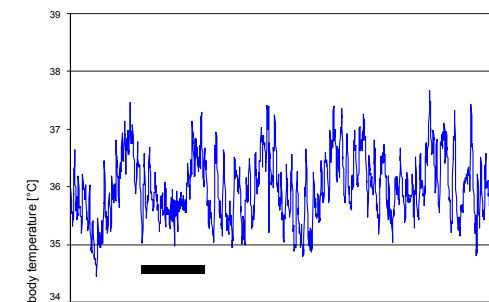
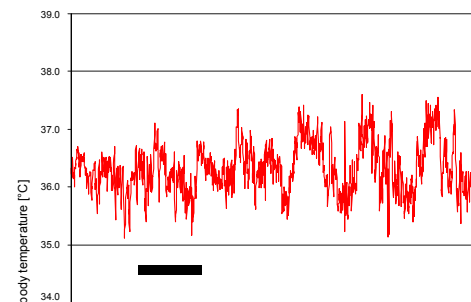
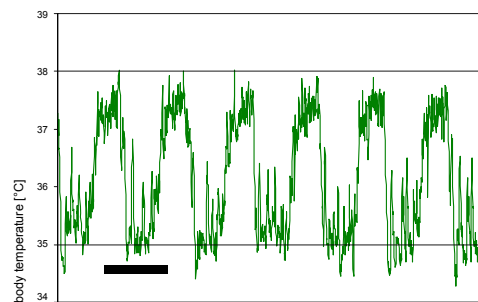


Clinical signs: Physiology

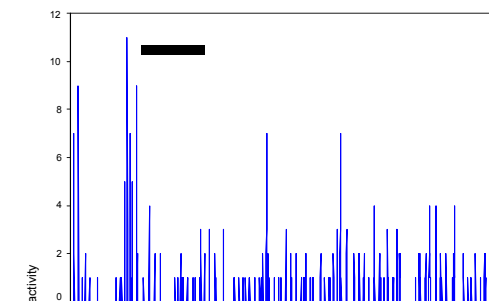
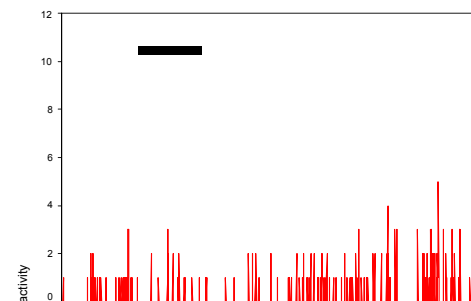
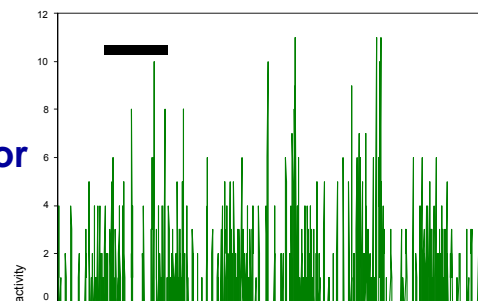
Heart
Rate
[bpm]



Body
temp.
[°C]



Locomotor
activity
[counts]



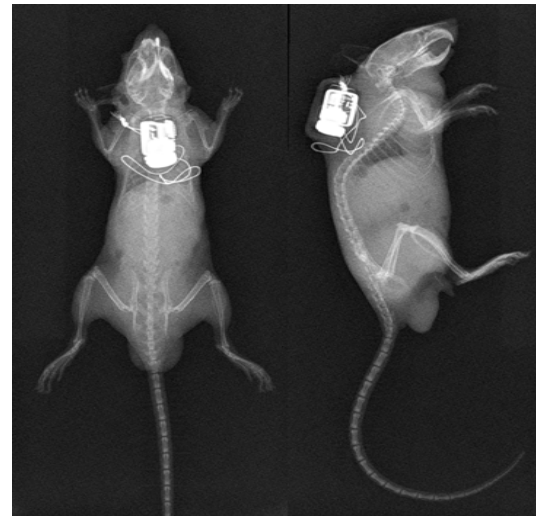
6d, tumor disease

Clinical signs: Physiology

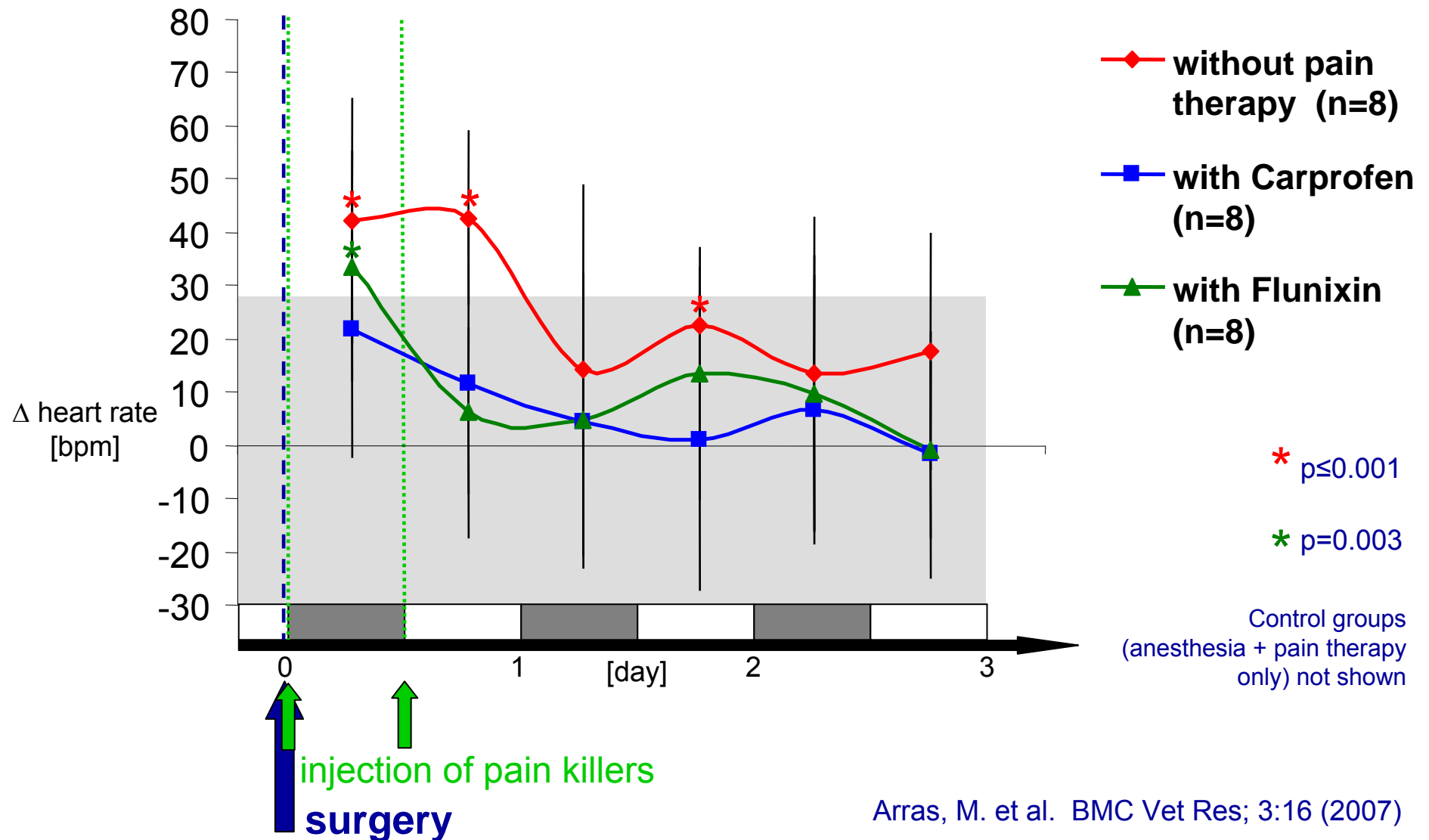
Telemetric measurements

→ preliminary implantation of transmitters

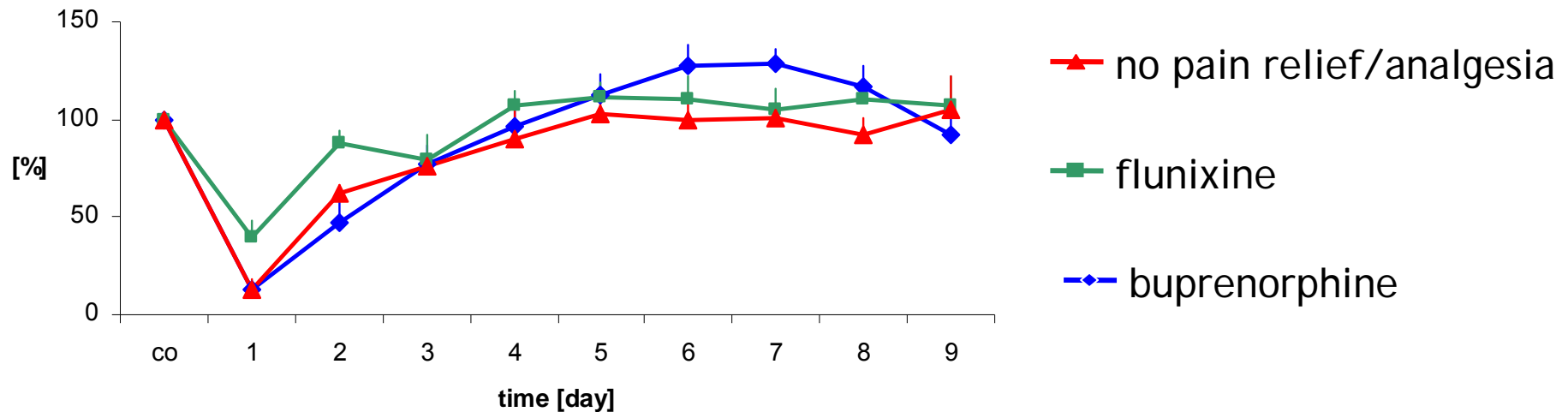
≠ laboratory routine



Impact of pain killers on physiology



Impact of pain killers on clinical signs and/or behaviour



Decrease of food consumption after surgery

Alteration of body weight, water intake, wheel running activity

Adamson 2010, Bourque 2010, Arras 2007, Bomzon 2006

Side-effects of pain killers

Side-effects

- distort clinical signs, physiology and behaviour
- are mostly unknown or neglected
- interfere with data outcome
- impair reproducibility and reliability of results

New methods for detection of pain

Behavioural assessment

- Twitching, flinching

Wright Williams 2007

- Mouse pain face scale

Langford 2010



Ear position



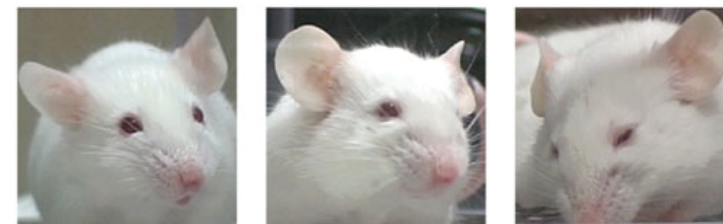
Whisker change



Orbital tightening



Nose bulge



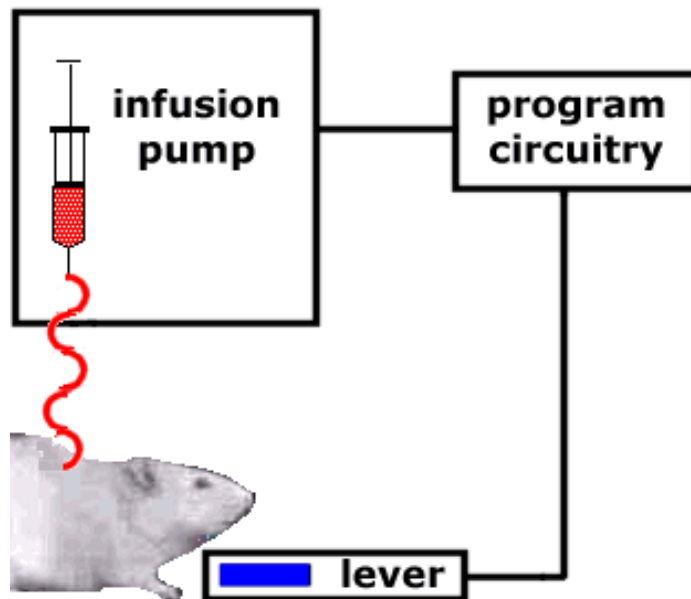
Cheek bulge

New methods for detection of pain

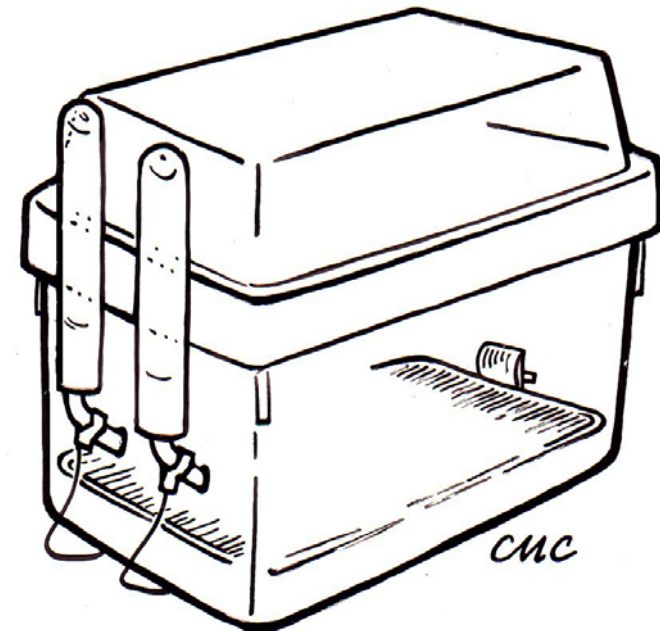
Behavioural assessment

- Analgesia self administration

Pham 2010



copyright Claire Cannon
<http://cmccannon.net>



New methods for detection of pain

Behavioural assessment

- Nest building behaviour

Arras 2007



with analgesia after surgery



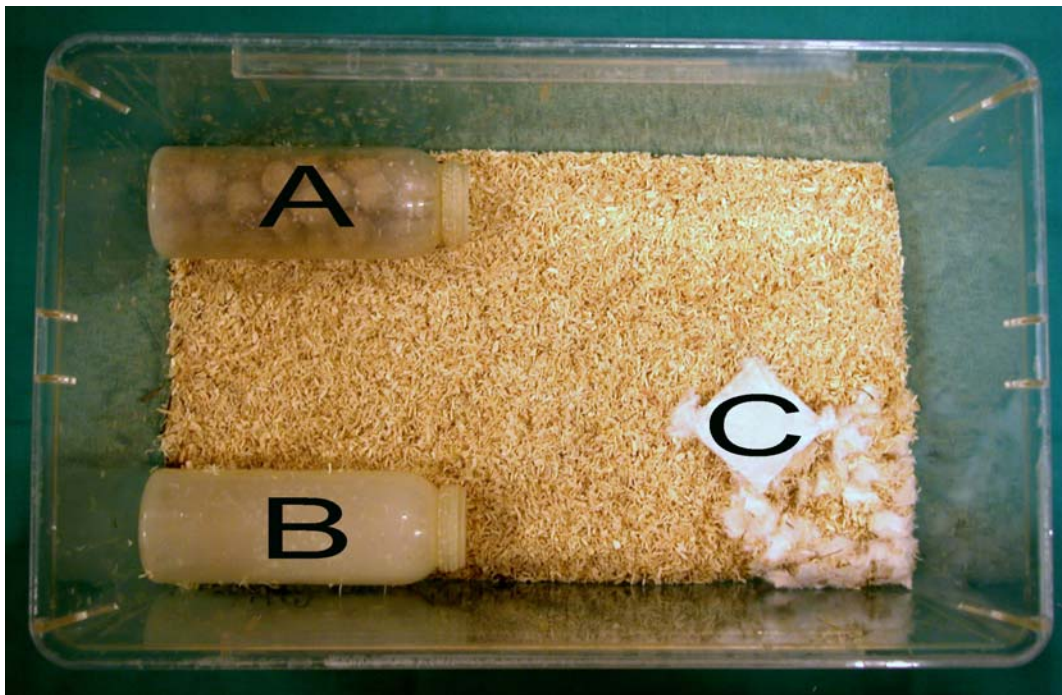
without analgesia after surgery

New methods for detection of pain

Behavioural assessment

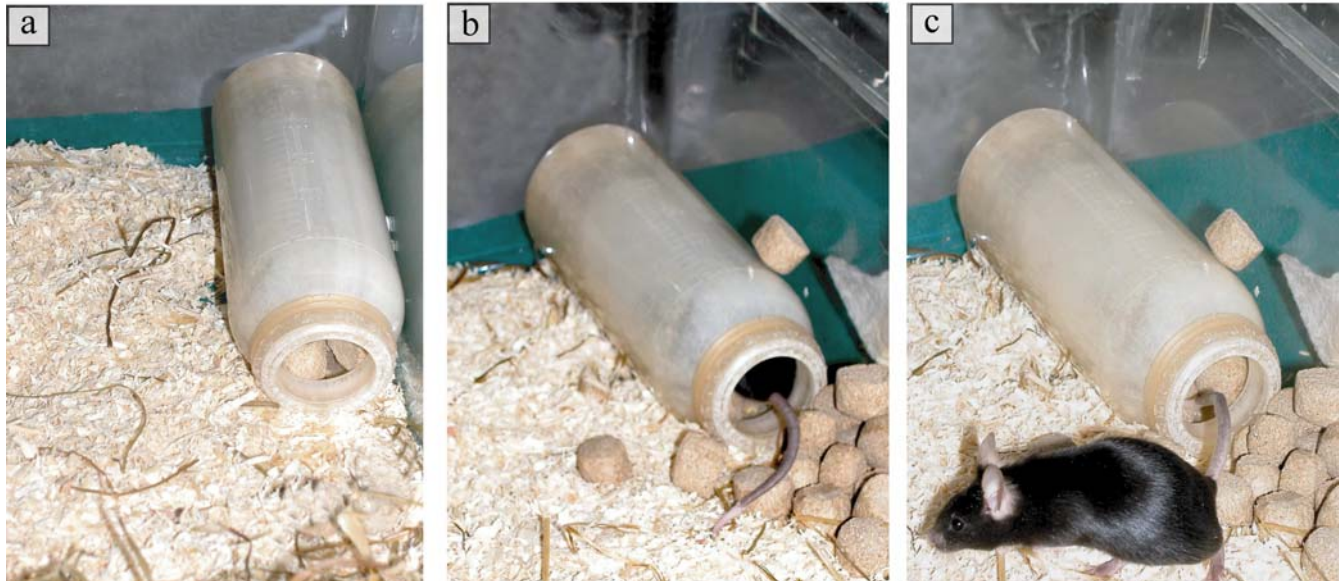
- Burrowing behaviour

Jirkof 2010



Experimental Setup.
Burrowing test
apparatus (A),
shelter (B)
and nesting material (C)
in home cage.

Burrowing Test

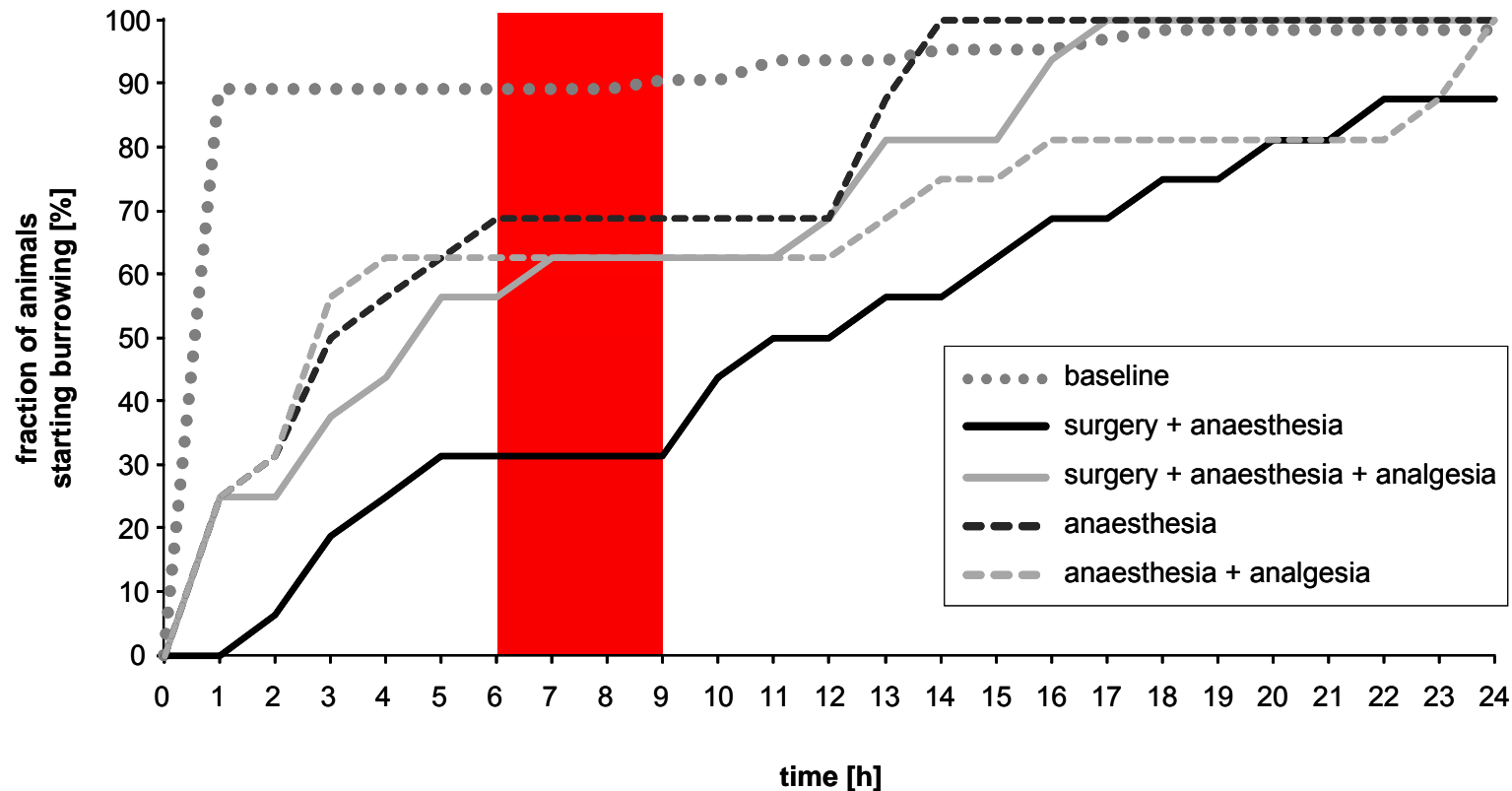


Burrowing: Species-specific, spontaneously occurring behaviour

High motivation to dig burrows persists during domestication

Use as indicator for impaired wellbeing

Burrowing Test



Burrowing performance was inhibited after surgery without pain relief.

The impact of analgesia is reflected in burrowing behaviour.

Jirkof 2010

Summary

Actual status

Easy-to-use, sensitive methods of analyses of spontaneous, home cage based behaviours for assessment of pain and suffering were currently developed

Ongoing work

Validation of such methods in the laboratory routine

- evaluation of currently used but not validated pain relief regimens
- evaluation of new pain treatment protocols and pain killers

Final goal

Establishing standardized pain treatment protocols

- proven analgesic efficacy
- well-defined side-effects

Conclusion

Standardized pain treatment protocols

- assure early and efficient alleviation of pain and suffering in mice
- provide reliability and reproducibility of results!



Conclusion

Standardized pain treatment protocols

- assure early and efficient alleviation of pain and suffering in mice
- provide reliability and reproducibility of results!

Further research is necessary to determine the impact of pain killers on animal wellbeing and data outcome.

Funds for such refinement are urgently needed.



Thank you for your attention

Andreas Rettich
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Robin Schneider

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Obstacles in pain relief regimens and detection of pain

Dosage recommendations for pain killers rely on analgesiometry and anecdotal evidence \neq clinical situation

Richardson 2005, Mogil 2009

Detection of early-stage pain and suffering

