Validation of a novel electronic von Frey system for use in rodents: MouseMet and RatMet

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Background

Mechanical nociceptive threshold (MNT) testing using von Frey filaments is still the "gold standard" method for testing nociceptive thresholds in rodents used in pain research. However, this method has a number of disadvantages (1):

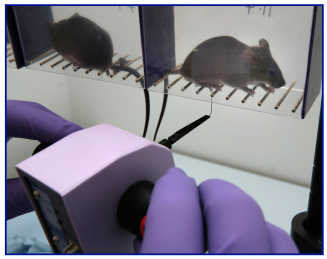
Each von Frey filament provides a constant force once it has buckled

Most notably, increasing forces are applied in discrete, non-linear steps, so that repeated stimuli are required for one MNT data point. Only an approximation of the MNT is achieved and the data are non-parametric. In addition, the cross sectional area of each filament is different, and the contact area changes during testing, so the relationship between force and compressive stimulus is largely unknown

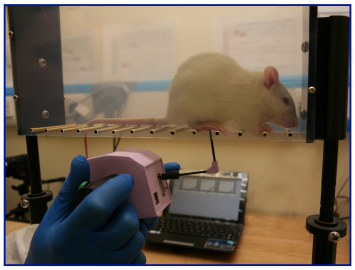
Electronic ramped force systems produce continuous data and reduce the number of stimuli required, but those using stiff force transducers are difficult to use consistently and low forces are dwarfed by hand tremor and side load, which is a particular problem in mice

A novel electronic system unaffected by hand tremor and side load has been developed by utilising a soft spring (MouseMet; Topcat Metrology Ltd)

The system also incorporates a one dimensional cage system of adjustable height which encourages the animal to stay sideways on to the tester, maximising the foot area for testing and minimising operator discomfort during prolonged testing



The MouseMet electronic von Frey has a 0.1-7 gF range designed specifically for mice



The RatMet electronic von Frey has a 1-80 gF range suitable for rats

We have evaluated the MouseMet and the RatMet in the appropriate species in a number of different laboratories in the UK and Australia

Methods

MNT were measured in mice in four independent laboratories during studies expected to produce hypersensitivity, analgesia or both (2,3):

(A) 24 adult female B6 mice in an investigation into the effects of a novel analgesic on complete Freund's adjuvant (CFA)-induced hypersensitivity (n=8 per treatment)

(B) 8 male 10-12 week old 129OlaHsd mice with nerve injury-induced hypersensitivity (n=8 per treatment)

(C) 27 C57BL/6 mice during an investigation to characterize mechanisms of oxaliplatin-induced cold allodynia (n=4-5 per treatment)

(D) 22 Wistar rats in an investigation into buprenorphine analgesia (0.05 mg/kg) after carageenan-induced hypersensitivity (n=6-8 per treatment)

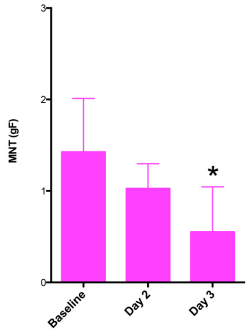
All animals were allowed to acclimatize in individual runs for at least 10 minutes prior to 3-5 measurements of MNT in a hind foot, with at least 2 minutes between tests at the same site

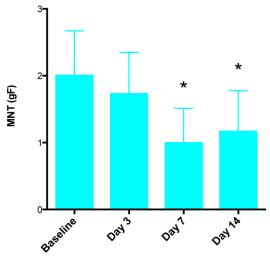
Data were analysed using one way ANOVA (* = P<0.05)

Results

All treatments expected to cause hypersensitivity reduced MNT and analgesic treatment either restored baseline values or increased MNT

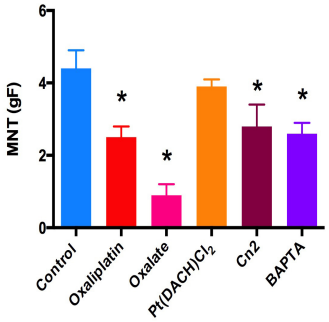
(A) MNT (mean±SD) in control mice (hind paw) before and after CFA injection (n=12)
** indicates significantly lower than control.*

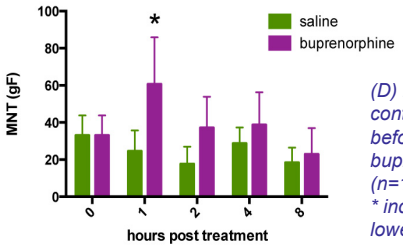




(B) MNT (mean±SD) before and after nerve injury (n=8)
** indicates significantly lower than control*

(C) MNT (mean±SE) 1 hour after hind paw SC injection of 5% glucose (control) or substances expected to induce hypersensitivity (n=4-5)
** indicates significantly lower than control*





(D) MNT (mean±SD) in control rats (hind paw) before and after SC buprenorphine injection (n=12)
** indicates significantly lower than control*

Conclusions

The MouseMet and RatMet systems produced repeatable data in control animals and detected hypersensitivity or antinociception after a variety of treatments expected to cause allodynia or analgesia respectively. This demonstrates both face and construct validity, reliability and responsiveness of the measurement instrument (4).

References

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(4) Reid J et al (2013) Pain assessment in animals. In Practice 35:51-56