

Validation of the RatMet electronic von Frey for measurement of mechanical nociceptive thresholds in rats

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Background & Aim

- Von Frey (VF) filaments are the “gold standard” for mechanical threshold (MNT) testing in rodents¹ despite a number of disadvantages.
- In traditional VF assessments tactile stimuli are applied in progressively increasing non-linear steps with separate filaments of changing cross-sectional area. With this approach the relationship between force and nociceptive receptive field varies uncontrollably and the resulting data are non-parametric.
- We evaluated the RatMet² (fig.1), a novel electronic VF system with a unique filament coupled to a soft force transducer. The RatMet electronic VF (eVF) has a force range of 0-100gF.

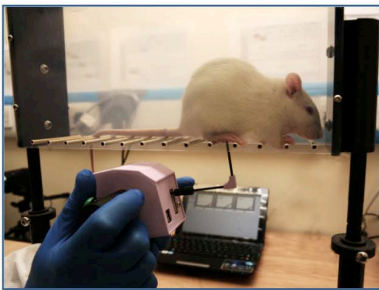


Figure 1: RatMet electronic Von Frey

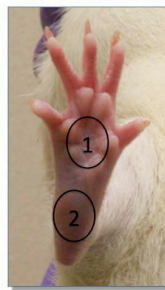


Figure 2: Target area for eVF filament application (1) and plantar Cg injection (2).

Material & Methods

- All procedures were carried out under project licence (60/3793) under the Animals (Scientific Procedures) Act (1986) and Newcastle University's Animal Welfare and Ethical Review Body (AWERB).
- Female Wistar rats (n=22, 234 ± 8g).
- Study 1: Positive control**
→ Buprenorphine (0.05mg.kg⁻¹, SC) vs 0.9% NaCl (n=6, cross-over) MNT measured before (T₀), & 1, 2, 4, 8h post-injection (T₁-T₈).
- Study 2: Negative control**
→ [Carrageenan (Cg) + buprenorphine] vs [Cg + 0.9% NaCl] (n=16, randomized controlled)
Cg injected (1 mg.kg⁻¹) subcutaneously, in the plantar aspect of the left metatarsus (fig. 2) followed after 3h by buprenorphine (0.05mg.kg⁻¹, SC). MNT measured before (T₀), & 1, 2, 4, 8h post plantar Cg injection (T₁-T₈).
- In both studies:** RatMet was used for MNTs on both pelvic paws (fig. 2), using the mean of the 3 middle of 5 tests.
Statistical analysis: general linear model for repeated measurement, and *post-hoc* Bonferoni test. Significance: P < 0.05.

Results

- Baseline MNTs were 33 ± 3gF in study 1, 44 ± 19gF in study 2.
- Study 1 (fig. 3):** MNT decreased over time in the NaCl group (P > 0.05) and increased in the buprenorphine group (P < 0.05 at T₁, not significant at other time points).
- Study 2 (fig. 4):** MNT decreased after carrageenan injection by 82% at T₈ (P < 0.05) and increased after buprenorphine to 73 ± 20gF (T₄, P < 0.05).

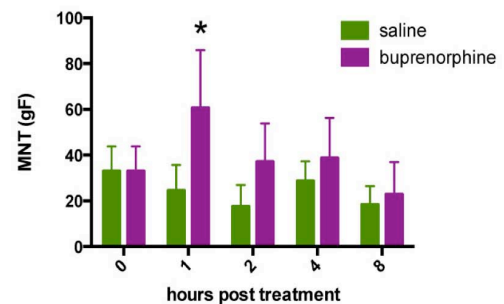


Figure 3: Mechanical thresholds (mean ± SD) measured by the RatMet on the left pelvic paw (eVFL) expressed in gF, before and after subcutaneous injection of NaCl or buprenorphine. * indicates a significant difference in MNTs between NaCl and buprenorphine treated animals.

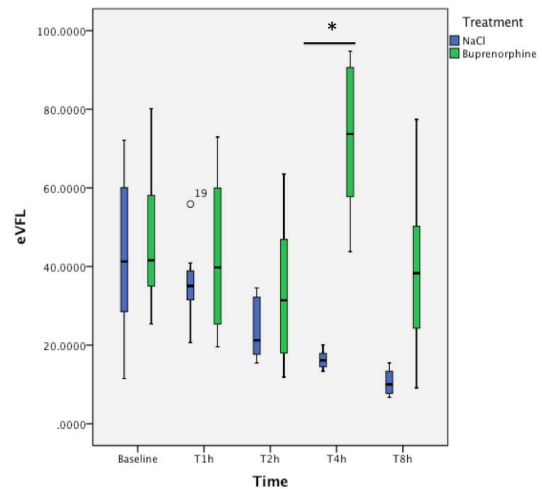


Figure 4: Mechanical thresholds measured by the RatMet on the left pelvic paw (eVFL) expressed in gF. Carrageenan injection in the left paw after baseline measurements, NaCl or buprenorphine injection (SC) 3h after carrageenan. * indicates a significant difference in MNTs between NaCl and buprenorphine treated animals.

Discussion & Conclusions

- The difference in baseline between the 2 studies was unexpected as the strain, sex and origin of the rats were identical and the husbandry conditions, operator and time of day of the measurements were consistent. Further studies are needed to investigate the origin of this difference and establish the baseline mechanical threshold of pain-free rats.
- The RatMet detected expected hyperalgesia and antinociception after treatments: MNT increased after buprenorphine administration in pain-free rats; decreased after carrageenan injection; and increased in rats subsequently given buprenorphine.
- The force range of 0-100 gF was adequate for testing rats in both studies.
- A single treatment-blinded operator performed all the measurements; further studies are required to evaluate inter-operator reproducibility.
- The RatMet appears suitable for analgesiometric studies in rats and has substantial advantages compared to traditional VF testing.

References:

- Bove G (2006) Mechanical sensory threshold testing using nylon monofilaments: the pain field's "tin standard". Pain 124: 13-17
- TopCat Metrology Ltd, Ely, UK. www.topcatmetrology.co.uk

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