Bovine Adrenal Medulla 8-22, a Model of Non-histaminergic Itch

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Introduction

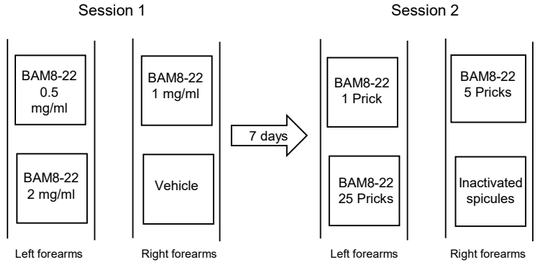
- Itch is transmitted by two parallel nociceptive pathways: a subgroup of mechano-insensitive c-fibers transmitting histaminergic itch and a subgroup of polymodal c-fibers transmitting non-histaminergic itch [1].
- The activation of non-histaminergic pathway is mediated by the binding to protease-activated receptors (PAR2 and PAR4) activated by cowhage, the most used model for non-histaminergic itch, or to mas related G protein-coupled receptors (Mrgprs) [2].
- Bovine adrenal medulla 8-22 is an endogenous peptide derived from the hormone proenkephalin. It is able to activate MrgprX1 and induces itch via the G protein-q/11 α-subunit (Gαq/11) pathway [3].

Aim

The aim of this study is to design a model of non-histaminergic itch by using Bovine adrenal medulla (BAM)8-22.

Methods

- 22 healthy subjects were recruited for this study.



- Session 1: BAM8-22 solution (2, 1, 0.5 mg/ml) and vehicle were applied (standard allergy skin prick test, SPT).
- Session 2: BAM8-22 (1mg/ml) by SPT lancets with 1, 5 and 25 pricks and inactivated cowhage spicules soaked in 1 mg/ml BAM822 solution.
- 9-minute visual analog scale-scores of itch and pain intensity (the values of peak itch intensity and area under the curve (AUC) were subsequently extracted);
- Measurements of mechanically evoked itch (MEI), mechanical pain sensitivity and threshold (MPS and MPT), cold detection and pain threshold (CDT and CPT), warm detection threshold (WDT), heat pain threshold (HPT), and supra-threshold heat sensitivity (SHTS).

Results

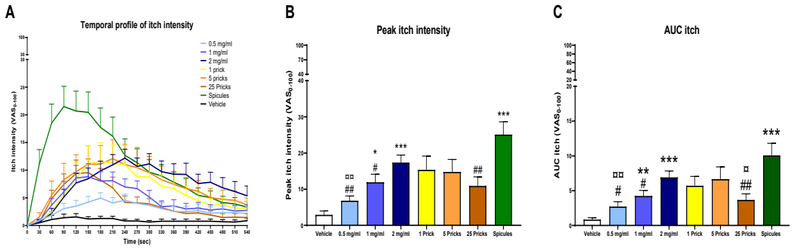


Figure 1: Itch Profile
A) Temporal profile of itch; B) Peak itch intensity; C) AUC itch

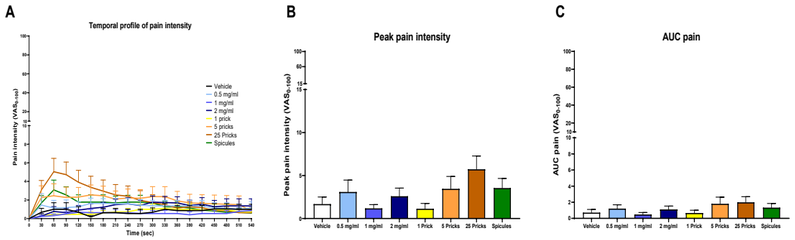


Figure 2: Pain Profile
A) Temporal profile of pain; B) Peak pain intensity; C) AUC pain

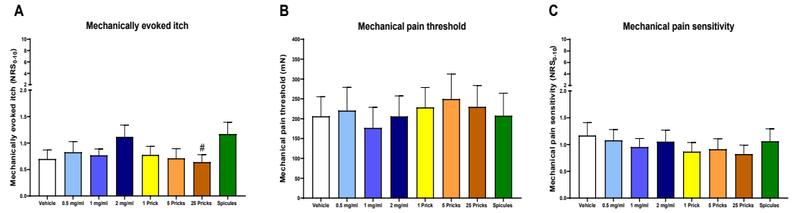


Figure 3: Mechanical sensitivity
A) Mechanically evoked itch; B) Mechanical pain threshold; C) Mechanical pain sensitivity

Results (cont.)

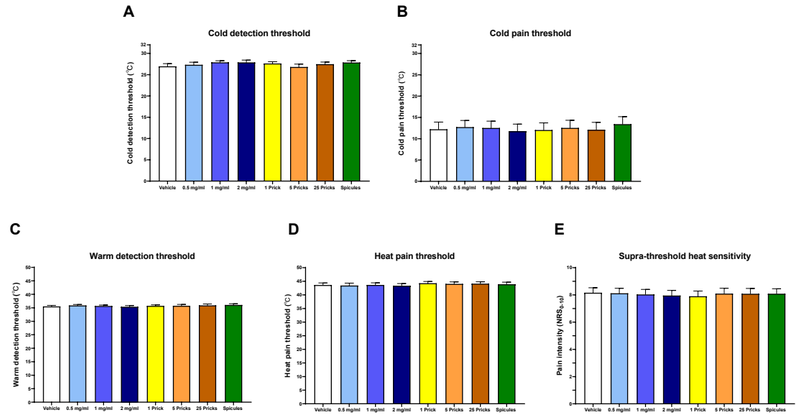


Figure 4: Thermal sensitivity
A) cold detection threshold; B) cold pain threshold; C) warm detection threshold; D) heat pain threshold; E) supra-threshold heat sensitivity.

Conclusions

BAM8-22 represents an experimental model of non-histaminergic itch, using inactivated cowhage spicules as delivery method. The model induces a moderate itch intensity without concurrent pain. BAM8-22 and active cowhage both induce non-histaminergic itch, but medieted by different receptor populations (MrgprX1 vs PAR2-4).

References

[1] Andersen, H. H., van Laarhoven, A. I. M., Elberling, J. & Arendt-Nielsen, L. Modulation of itch by conditioning itch and pain stimulation in healthy humans. J. Pain 18, 1437–1450 (2017).
[2] Akiyama, T. et al. Cross-sensitization of histamine-independent itch in mouse primary sensory neurons. Neuroscience 226, 305–312 (2012).
[3] Sikand, P., Dong, X. & LaMotte, R. H. BAM8–22 peptide produces itch and nociceptive sensations in humans independent of histamine release. J. Neurosci. 31, 7563–7567 (2011).

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