

PAIN AND INFLAMMATION

Thermal hyperalgesia - Hargreaves test

In the preclinical studies of pain and analgesics development, the thermal stimulus is one of the main noxious stimuli modalities that induces reflexive behaviors (e.g. guarding, avoidance, withdrawals, flinches) indicative of pain¹. The Hargreaves test is a sensitive method that uses radiant heat as a thermal stimulus and automatically determines nociceptive threshold². Hargreaves test presents sensitivity for measuring hyperalgesia following administration of proinflammatory or algesic agents and is responsive to many classes of analgesic drugs².

Test System: *Rattus norvegicus* (Sprague-Dawley).

Reference Item: Morphine (10 mg/Kg s.c.)

Number of animal per group: 6 animals.

Main read-outs: Paw withdrawal latency upon thermal stimulus.

Route of administration: upon request.

Treatment mode: upon request.

Validation Data

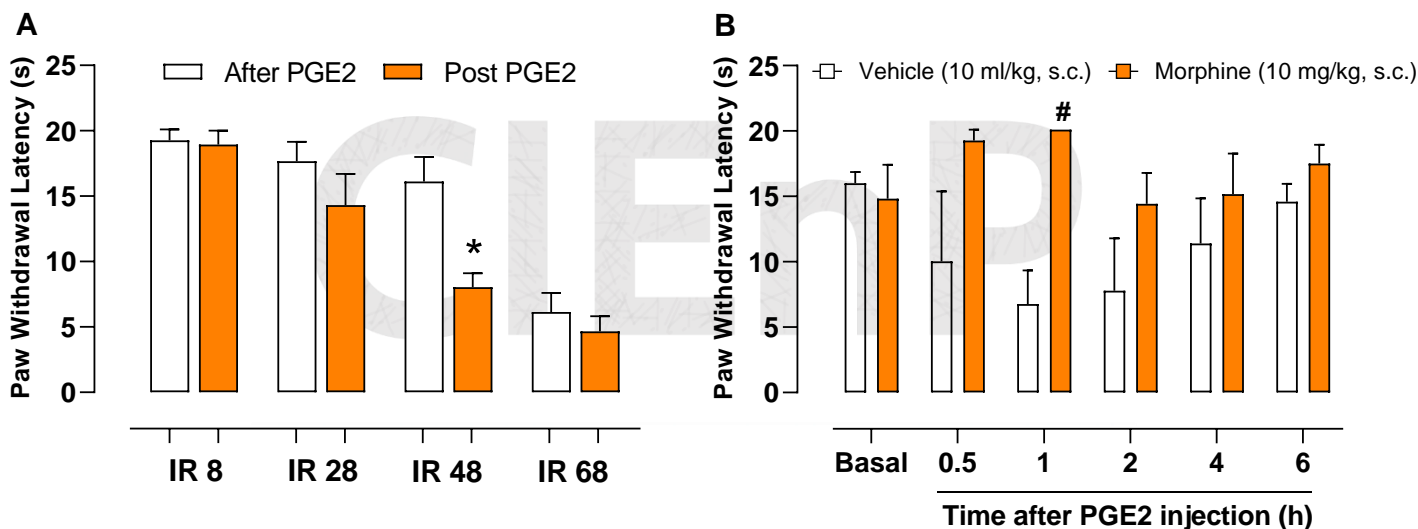


Figure 1. Thermal hyperalgesia (Hargreaves test) in Sprague-Dawley rats. (A) Effect of different infrared (IR) intensities on rats paw withdrawal latency before and after PGE2 (100 ng/paw) injection into the paw; (B) Paw Withdrawal Latency before and after treatments. On panel B, firstly, it was obtained the basal values. After, rats were treated with vehicle (saline, 10 ml/kg, s.c.) or morphine (10 mg/kg, s.c.). 1 hour after treatments PGE2 (100 ng/paw) was injected into rats paw and the paw withdrawal latency were evaluated 0.5, 1, 2, 4 and 6 hours after PGE2 administration. Results are expressed as mean \pm S.E.M. Two-way ANOVA followed by Bonferroni post hoc test. * indicates significantly statistic difference compared with after PGE2 group. # indicates significantly statistic difference compared with vehicle group. PGE2: prostaglandin E2; s.c.: subcutaneous.

To avoid bias and to allow reproducibility all *in vivo* experiments follow the ARRIVE guidances³. Mouse colony from Charles River Laboratories are breed and maintained in SPF conditions. The project includes study plan and final report. Raw data are inspected by quality assurance unity. The experimental procedures was previously approved by the CIEnP Committee on the Ethical Use of Animals.

References:

- 1 Armendariz A and Nazarian A., 2018. C Morphine antinociception on thermal sensitivity and place conditioning in male and female rats treated with intraplantar complete freund's adjuvant. *Behav Brain Res.* 343, 21–27.
- 2 Hargreaves K, Dubner R, Brown F, Flores C, Joris J. 1987. A new and sensitive method for measuring thermal nociception in cutaneous hyperalgesia. *Pain* 32, 77–88.
- 3 Kilkenny C, Browne WJ, Cuthill IC, Emerson M, Altman DG. Animal research: reporting in vivo experiments: The ARRIVE guidelines. *PLoS Biol.* 8 (6): e1000412, 2010.