Different effects of ibuprofen on tactile allodynia in rat models of inflammatory pain

Thomas Pitcher, Denise Richardson, Sachi Tanimoto, Janet Nicholson. Pfizer inc, Sandwich, Kent, United Kingdom.

Inflammatory pain can be investigated pre-clinically using a variety of rodent models. However, we have limited understanding of the mechanisms underlying the development and maintenance of stimulus-evoked pain in these models, and its translation into man. In the current study, a comparison of the effects of the non-selective COX inhibitor, ibuprofen, was assessed in 3 models of inflammatory pain under fully-blinded conditions. Ultraviolet (UV) irradiation-induced skin erythema on the plantar surface of rat hind paw results in development of thermal hyperalgesia (TH), as assessed at 48h post UV. The Complete Freund's Adjuvant (CFA) model (100 μg/100 μl intraplantar injection) generates an early inflammatory response (24hrs) and injection of monoiodoacetate (MIA, 1 mg/25μl) in the rat knee is a degenerative joint model with histopathological similarities to human osteoarthritis at 14d post MIA.

The time course of development of tactile allodynia (TA), weight bearing (WB) or TH was measured and pharmacology was performed at appropriate time points. Ibuprofen (100 mg/kg, PO) reversed TA in the UV model 2hr post-dose (5.7±0.95g vs 1.9±0.4g, p<0.01, n=8) However, it did not reverse TA in the CFA or MIA models. Ibuprofen displayed efficacy against TH in CFA model (9.6±1.1sec vs 4.6±0.6sec, p<0.01, n=16) and WB in both CFA (33.19±5.53g vs -2.43±5.05g, p< 0.01, n=6) and MIA models (21.55±4.8g vs 7.72±3.77g, p<0.05, n=12).

Our data suggest a significant difference in the mechanisms underlying TA in these pain models. It is likely that the differential localization of inflammation (skin into deeper tissue) in these models triggers different nociceptive processing. We could speculate that in CFA and MIA models, where inflammation involves deep somatic tissues, TA may be maintained centrally. In contrast in the UV model where inflammation appears limited to the skin, TA may be generated by localized inflammation and is consequently sensitive to ibuprofen.