CAPSAICIN-INDUCED VASOCONSTRICTION OF THE MOUSE KNEE JOINT:
INVolVEMENT OF TRPV1 RECEPTORS

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Capsaicin is the pungent component of chilli peppers that concomitantly activates and desensitizes C-fibre and Aδ fibres sensory nerves. Stimulation causes an acute neurogenic response including vasodilation, plasma extravasation and hypersensitivity. However, in the present study we have shown that capsaicin produces a vasoconstrictor effect in the mouse knee joint via Transient Receptor Potential Vanilloid 1 (TRPV1) receptor activation.

Female C57BL6/129SVJ mice (25-30 g), either genetically unaltered wild type (WT) or knockout mice lacking the gene for the TRPV1 receptor (TRPV1KO), were bred in house from mice donated by S Boyce (Merck, Sharp & Dohme, UK). Mice were anaesthetised with urethane (2.5 mg/g i.p.) and 30 G needles were used for all intra-articular injections. 125I-albumin (45 kBq, ICN, UK) was administered intravenously via the tail vein and allowed to re-circulate. Mice then received intra-articular injections of capsaicin (100 nM; 10 µl) and vehicle (80 % saline, 10 % ethanol, 10 % Tween 80; 10 µl; contralateral joint) into the knee joint. For 30 min thereafter, 125I-albumin levels in the joint were determined using a collimated gamma probe (Europrobe, Bright Technologies, UK). The 125I-albumin accumulation was expressed as a percentage of counts/min detected in the agent-treated joint compared to the vehicle-treated joint. A percentage of >100 shows that more 125I-albumin is present in the test joint compared to the control joint. Vice versa, a percentage of <100 shows that less 125I-albumin is present in the test joint compared to the control joint. The vasoconstrictor effect of capsaicin was confirmed using a Laser Doppler blood flow Imager (IDI; Moor Instruments, UK).

Capsaicin (100 moles) caused a significant decrease (p<0.01) in 125I-albumin accumulation in WT mice within 2 min of injection that was sustained until > 30 min (0 min, 97.3 ± 1.8 %; 2 min, 75.1 ± 4.4 %; 30 min, 75.1 ± 5.1 %, n = 4-5). This response was completely abolished (p<0.01) in TRPV1KO mice (0 min, 99.9 ± 1.1 %; 2 min, 100.9 ± 0.2 %; 30 min, 101.6 ± 1.0 %, n = 3). The present study has confirmed studies previously performed in rats showing that administration of a single dose of capsaicin elicits an acute vasoconstriction in the mouse knee joint. The study by Cambridge & Brain (1993) showed that capsaicin causes a significant decrease in blood flow following intra-articular injection into the rat knee joint at doses lower than those required for increased vascular permeability. The authors suggested that locally injected capsaicin has non-specific actions on synovial blood vessels in addition, or further, to those induced by release of vasodilator neuropeptides. However, the use of TRPV1 knockout mice in the present study has demonstrated that capsaicin produces this effect via the TRPV1 receptor and, therefore, that capsaicin is probably acting via C fibre and/or Aδ fibre activation.


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