CAPSAICIN-MEDIATED NEUROGENIC VASODILATATION IN NEUROKININ-1, NK₁, RECEPTOR KNOCKOUT MICE

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Capsaicin induces tachykinin NK₁ receptor-dependent neurogenic oedema in the mouse ear and this model has been used to determine the absence of NK₁ receptors in NK₁ knockout (NK₁^{-/-}) mice[1]. We have now simultaneously measured neurogenic vasodilatation and oedema in the ear.

Wild-type and NK₁^{-/-} Sv129+C57BL/6 mice were used in this study. Anaesthesia (urethane, 25% w/v; 100ml/10g) was induced. Oedema was assessed by the accumulation of ¹²⁵I-albumin, and blood flow by laser Doppler flowmetry. Responses were measured for 1 h after topical application of capsaicin to one ear and vehicle to the contralateral ear. Capsaicin induced oedema in wild-type Sv129+C57BL/6 mice ($p < 0.001$), but not in NK₁^{-/-} mice, as expected[2]. However, neurogenic vasodilatation ($p < 0.05$) was observed in both wild-type and NK₁^{-/-} mice, and remained in wild-type mice in the presence of the NK₁ antagonist SR140333 (480 nmol/kg). Interestingly, increased blood flow in the NK₁^{-/-} mice was significantly ($p < 0.05$) greater than that in the wild-type mice. It was substantially blocked in NK₁^{-/-} mice pretreated with the CGRP antagonist CGRP₈₋₃₇ (400nmol/kg), or wild-type mice treated with both SR140333 and CGRP₈₋₃₇, but not in wild-type mice treated with CGRP₈₋₃₇ alone.

The results suggest that neurogenic vasodilatation is a consequence of CGRP and NK₁ receptor mediated responses in the mouse. They also indicate that some form of interaction between functional CGRP and NK₁ receptors may occur.

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REFERENCES

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2. Cao, T., Gerard, N.P., and Brain, S.D. (1999) *Am. J. Physiol.* 277, 476–481.