The vasoactive potential of kisspeptin-10 in the peripheral vasculature

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Splice products of the Kiss1 protein (kisspeptins) have been shown to be involved in a diverse range of functions; these include puberty, cancer metastasis and reproduction, as well as constriction of large human arteries (Mead et al., 2007). Circulating kisspeptin plasma levels are low in normal individuals but are elevated during various disease states, as well as pregnancy. Here, we investigated the potential of kisspeptin-10, the shortest biologically active kisspeptin, to influence microvascular effects, concentrating on the cutaneous vasculature.

Female and male CD1 and C57BL/6 mice (8–12 weeks old) were obtained from Charles River (Kent, U.K.). Mice were anaesthetised with urethane (25% w/vol; 2.5 g/kg i.p.), and the dorsal skin was shaved. Plasma extravasation was used as an indication of oedema formation and assessed using an Evans blue accumulation assay in skin, as described by Cao et al (1999). Blood flow was measured using a $^{99m}$technetium clearance technique in skin, as described by Schmidhuber et al (2007).

Kisspeptin-10 (0.3-10nmol/injection site) caused a dose-dependent increase in Evans blue extravasation, indicating oedema formation. Extravasation was shown to be inhibited by the histamine H$_1$ receptor antagonist mepyramine (5nmol/site, co-injected). The extravasation response was characterised by a ring of pallor at the injection site, suggesting vasoconstrictor activity. Therefore, changes in dorsal skin blood flow were assessed by clearance of intradermally injected $^{99m}$technetium. Kisspeptin-10 (10nmol/site) was found to significantly reduce clearance (p<0.05), in keeping with a decreased blood flow and providing further evidence for vasoconstrictor activity. The decreased clearance was partially inhibited by co-treatment with the cyclooxygenase inhibitor indomethacin (3nmol/site).

Two peripheral vasoactive roles for kisspeptin-10 are suggested. Firstly, plasma extravasation indicative of oedema formation, and secondly, decreased peripheral blood flow, indicating microvascular constriction. Thus kisspeptin-10 may have vasoactive properties in the murine peripheral microvasculature.


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