ACETYLCHOLINE RELEASED FROM SUDOMOTOR NERVES IS CAPABLE OF CONTRIBUTING TO CUTANEOUS VASODILATION DURING HEATING IN HUMANS

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Inhibition of nitric oxide synthase (NOS) reduces the magnitude of cutaneous vasodilation during a heat stress in humans. Given that acetylcholine is released from sudomotor nerves during whole-body heating, coupled with the observation that acetylcholine stimulates nitric oxide production leading to vasodilation, it is possible that acetylcholine released from sudomotor nerves is capable of contributing to cutaneous vasodilation during a heat stress via nitric oxide related mechanisms. To test this hypothesis, in seven subjects skin blood flow and sweating rate were simultaneously monitored over three microdialysis membranes placed in the dermal space of forearm skin. One membrane was perfused with the acetylcholinesterase inhibitor neostigmine (10 μM), the second membrane was perfused with the NOS inhibitor N^G-nitro-L-arginine methyl ester (L-NAME; 10 mM) dissolved in the aforementioned neostigmine solution, while the third membrane was perfused with Ringer's solution (vehicle). Each subject was exposure to a minimum of 20 minutes of whole-body heating via a water-perfused suit. This perturbation increased average skin temperature from 34.6±0.1 to 38.6±0.2°C ($P<0.05$) and sublingual temperature from 36.9±0.1 to 37.3±0.1°C ($P<0.05$). Following the heat stress maximal skin blood flow at each site was identified via administration of 28 mM sodium nitroprusside through the microdialysis membranes. Skin blood flow was then normalized relative to maximal skin blood flow for that site.

Unit (% maximum SkBF)	Rest	ΔSkBF (I)	ΔSkBF (II)
SkBF (NEO)	29.2 ± 4.7*#	12.8 ± 3.2*#	40.0 ± 4.3#
SkBF (control)	19.5 ± 3.1	7.6 ± 2.7	39.4 ± 2.9#
SkBF (L-NAME + NEO)	13.0 ± 1.5	3.6 ± 1.0	20.3 ± 2.1

SkBF: skin blood flow; NEO: neostigmine; ΔSkBF (I): increase in SkBF from rest to a period early in the heat stress (i.e. prior to clear increases in SkBF at L-NAME site); ΔSkBF(II): increase in SkBF from the rest to the end of heating. * significantly different from control site, # significantly different from L-NAME+NEO site. ($P<0.05$ for both).

The observation that the increase in skin blood flow early in the heat stress [i.e. ΔSkBF (I)] at the neostigmine treated site was significantly greater than at the control site suggests that acetylcholine released from sudomotor nerves is capable of modulating cutaneous vasodilation early in the heat stress. Moreover, the observation that early in the heat stress skin blood flow at the L-NAME + neostigmine treated site was significantly less than skin blood flow at the neostigmine treated site suggests that the elevation in skin blood flow at the neostigmine treated site was NOS dependent. In contrast, the lack of difference in skin blood flow between the neostigmine and control sites at the end of heating suggests that acetylcholine released from cholinergic nerves does not contribute to cutaneous vasodilation during moderate whole-body heating.

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