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Prostacyclin, but not nitric oxide, is the major mediator of acetylcholine-induced vasodilatation in the isolated mouse heart

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Abstract:
In many species, acetylcholine (Ach) induces coronary vasodilatation *via* endothelium-derived nitric oxide (NO). The aim of the present study was to examine if this rule pertains also to the coronary circulation of the mouse. We examined the involvement of NO and prostacyclin (PGI_2) in the coronary flow response to Ach as compared to response to bradykinin (Bk) in hearts isolated from FVB or C57Bl/6 mice and perfused according to the Langendorff technique.
In the isolated mouse heart, response to Ach consisted of two distinct phases: immediate, transient vasodilatation/vasoconstriction (less than 1 min) that differed between FVB and C57Bl/6 mice; and delayed sustained vasodilatation (up to 8 min) that was similar in FVB and C57Bl/6 mice. In FVB mice, the immediate phase of the Ach response consisted of a short-lasting vasodilatation followed by a vasoconstriction. In contrast, in C57Bl/6 mice, the immediate phase of the Ach response consisted exclusively of a short-lasting vasoconstriction. However, both in FVB and C57Bl/6 mice, the delayed vasodilatation was a major part of the coronary flow response to Ach and it was associated with an increase in 6-keto-$PGF_{1\alpha}$ concentration in the effluent. L-NAME (5×10^{-4} M) displayed a minor effect on the delayed phase of the Ach response in either mice strain. In turn, indomethacin (10^{-6} M), but not rofecoxib (5×10^{-6} M), completely inhibited the delayed phase of the Ach response and the concomitant PGI_2 release. On the other hand, vasodilatation induced by Bk was markedly inhibited by L-NAME, while it was unaffected by indomethacin in FVB as well as in C57Bl/6 mice.
In summary, in the isolated mouse heart, Ach-induced coronary flow response displays an unusual biphasic nature and is mediated in major part by PGI_2, but not by NO. Thus, in the isolated mouse heart, in parallel to Bk or other agents that are suited for the functional assessment of NO-dependent endothelial function, Ach should be used to assess PGI_2-dependent endothelial function.

Key words:
acetylcholine, prostacyclin, nitric oxide, isolated mouse heart, coronary vessels, endothelium