Dissociation between Sympathetic Purinergic Response and ATP Response in the Mesenteric Artery of the Dog

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Abstract—In the presence of prazosin and propranolol, electrical transmural stimulation of isolated dog mesenteric artery produced a sympathetic purinergic contraction, which was followed by a relaxation in PGF₂α-contracted arteries. Such purinergic responses were mimicked by brief exposure to α,β-methylene ATP (α,β-Me ATP) and were completely inhibited after desensitization of P₂X-purinergic receptors. However, exogenous ATP predominantly evoked a relaxation in PGF₂α-contracted artery. These results suggest that the sympathetic purinergic response may be caused by a P₂X-purinergic receptor-selective mechanism or substance, rather than ATP.
results out of 10 preparations. These responses to electrical stimulation were completely inhibited after treatment with guanethidine (3 μM, n=3) or α,β-Me ATP (10 μM) (n=5, Fig. 1C) suggesting that the responses are sympathetic and are mediated through P_{2X}-purinergic receptors (4-6). In fact, the sympathetic purinergic responses were mimicked by brief exposure to α,β-Me ATP, a P_{2X}-purinergic receptor selective agent (9). For example, brief application (for 30 sec) of α,β-Me ATP (0.1-1 μM) produced a contraction, which was followed by a relaxation upon removal of the drug in PGF_{2α}-contracted arteries (Fig. 1B). On the other hand, exogenous ATP at concentrations ranging from 10 to 1000 nM elicited only a relaxation. At higher concentrations, a transient contraction preceded the sustained relaxation (Fig. 1B). When a single concentration of ATP (10 μM) was non-cumulatively applied for 30 sec, a small contraction and a subsequent relaxation were produced during the exposure to ATP. Removal of ATP further developed a relaxation. The amplitude of the initial contraction induced by 10 μM ATP was approximately equal to those induced by electrical stimulation at 1 or 3 Hz (n=5). Treatment with α,β-Me ATP (10 μM) abolished the contractile response to ATP, while the relaxing response remained without inhibition (n=5, Fig. 1C). These results suggest that only the contractile response is mediated through P_{2X}-purinergic receptors.

If ATP is involved in the purinergic response, some relaxing response could be evoked during the stimulation at low frequencies or after desensitization of P_{2X}-purinergic receptors, because the predominant action of ATP was a relaxation in this artery. However, no relaxation was elicited by electrical stimulation under such conditions (Fig. 1C). Thus, the present results suggest that the sympathetic purinergic responses of
the dog mesenteric artery may be caused by an unknown substance selective to P2X-purinergic receptors (designated as substance P2X), rather than ATP. Alternatively, neurogenically released ATP may act on only the P2X-purinergic receptors, unlike exogenous ATP.

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References