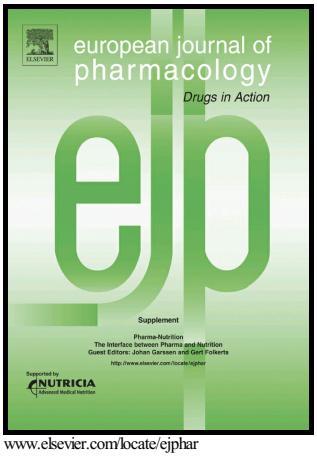

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Inhalation anaesthetic isoflurane inhibits the muscarinic cation current and carbachol-induced gastrointestinal smooth muscle contractions

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Abstract

Gastrointestinal tract motility may be demoted significantly after surgery operations at least in part due to anaesthetic agents, but there is no comprehensive explanation of the molecular mechanism(s) of such adverse effects. Anesthetics are known to interact with various receptors and ion channels including several subtypes of transient receptor potential (TRP) channels. Two members of the canonical subfamily of TRP channels (TRPC), TRPC4 and TRPC6 are Ca^{2+}-permeable cation channels involved in visceral smooth muscle contractility induced by acetylcholine, the primary excitatory neurotransmitter in the gut. In the present study, we aimed to study the effect of anesthetics on muscarinic receptor-mediated excitation and contraction of intestinal smooth muscle. Here we show that muscarinic cation current (mI_{CAT}) mediated by TRPC4 and TRPC6 channels in mouse ileal myocytes was strongly inhibited by isoflurane (0.5 mM), one of the most commonly used inhalation anaesthetics. Carbachol-activated mI_{CAT} was reduced by 63 ± 11 % (n=5), while GTPγS-induced (to bypass muscarinic receptors) current was inhibited by 44 ± 9 % (n=6). Furthermore, carbachol-induced ileum and colon contractions were inhibited by isoflurane by about 30%. We discuss the main sites of isoflurane action, which appear to be G-proteins and muscarinic receptors, rather than TRPC4/6 channels. These results contribute to our better understanding of the signalling pathways affected by inhalation anaesthetics,