Facilitation of murine enteric cholinergic neurotransmission by 5-HT₄ receptor activation: control by phosphodiesterases

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BACKGROUND

Man, dog, pig:
- 5-HT₄ receptors present on enteric cholinergic neurons innervating smooth muscle cells
- activation of those 5-HT₄ receptors by a 5-HT₄ receptor agonist (e.g. prucalopride) => ongoing acetylcholine release => smooth muscle contraction

Pig:
- 5-HT₄ receptor pathway in enteric cholinergic neurons is controlled by phosphodiesterase (PDE) 4
- PDE4 inhibition => contractions, facilitated by prucalopride, are further enhanced

ORGANISM

Aim:
Mouse: 5-HT₄ receptors on enteric cholinergic neurons innervating smooth muscle cells + control by phosphodiesterases?

RESULTS

1. PRUCALOPRIDE = 5-HT₄ receptor agonist

fundus

jejunum

IBMX = non-selective phosphodiesterase inhibitor

fundus

jejenum

IBMX + PRUCALOPRIDE

fundus

jejenum

CONCLUSION

In murine fundus, jejunum and colon:
- 5-HT₄ receptors
  - are present on cholinergic neurons innervating circular smooth muscle cells
  - activation enhances electrically induced cholinergic contractions
- phosphodiesterases (PDEs)
  - are present in circular smooth muscle cells
  - PDE inhibition induces relaxation

In murine fundus:
- 5-HT₄ receptor pathway in enteric cholinergic neurons is controlled by PDEs
- mild PDE inhibition enhances the facilitating effect of prucalopride

In murine jejunum and colon:
- no evidence for PDE-mediated control of the 5-HT₄ receptor pathway in enteric cholinergic neurons was yet obtained
- further investigation with selective PDE inhibitors is necessary