P3J-18-7 Region-related contractile response to tetrodotoxin in mouse gastrointestinal tract

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Tetrodotoxin (TTX) is an useful pharmacological tool to distinguish between neurogenic and myogenic responses of drugs in visceral smooth muscle organs. Although TTX generally does not affect muscle tonus, we found that TTX caused contraction of mouse colon. Aim of the present study is to characterize the TTX-induced contraction in the mouse gastrointestinal strips. Longitudinal muscle strips from stomach, small intestine and caecum were ineffective to TTX. However, TTX caused contraction of colonic strips in a concentration-dependent manner. Other Na^+ channel blockers (QX-222, lidocaine) also contracted the colonic strips. Ranking order of the contraction is consistent with that of Na^+ channel blocking activity. Treatment with TTX, L-NAME or ODQ significantly decreased the TTX-induced responses. Both L-NAME and ODQ caused the contraction of colon but not in the gastric and small intestinal strips. Region-dependency of L-NAME- and ODQ-induced contractions correlated with that of TTX-induced responses. Sodium nitroprusside caused marked relaxation of colonic strips compared with muscle strips from other regions. In conclusion, TTX causes contraction of mouse colonic strips through blockade of the potent and tonic nitrergic inhibitory innervation.