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## Altered contractility of circular and longitudinal smooth muscle in trinitrobenzenesulfonic acid-induced ileitis in guinea pigs

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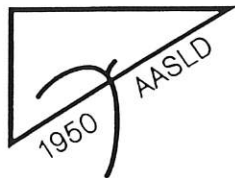
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ALTERED CONTRACTILITY OF CIRCULAR AND LONGITUDINAL SMOOTH MUSCLE IN TRINITROBENZENESULFONIC ACID-INDUCED ILEITIS IN GUINEA PIGS. **R. Garcia-Villar**, J.P. Martinolle, P.G. McLean, J. Fioramonti, L. Buéno. INRA, Pharmacology Unit, Toulouse, France.

Altered gastrointestinal motility is a common feature of gut inflammation which may result from changes in intrinsic nervous system and/or myocyte responses to transmitters. Intraluminal trinitrobenzenesulfonic (TNBS) acid is an established model of chronic ileitis in the guinea-pig. This study was aimed at determining the *in vitro* contractile responsiveness of both circular and longitudinal muscle of TNBS-inflamed vs healthy guinea-pig ileum.

**Methods:** Guinea-pigs were given an intrajejunal injection (0.3 ml) of either saline (controls; n=24) or TNBS in 50% ethanol (80 mg/kg; n=24), and sacrificed 6 days later. Ileum strips (longitudinal and circular; 8x2 mm) were placed in a superfusion system (Krebs; 37°C; 2 ml/min; O<sub>2</sub>/CO<sub>2</sub> 95/5%). Concentration-response curves (CRCs) to KCl (n=4), carbachol (n=8), histamine (n=6), serotonin (5-HT; n=12) and epinephrine were constructed (0.1nM-0.1mM). Epinephrine was superfused with 1μM alprenolol (β-adrenoceptor antagonist) plus yohimbine (α<sub>2</sub>-antagonist, 1μM, n=6) or prazosin (α<sub>1</sub>-antagonist, 1μM, n=6). Isometric contractions were recorded and quantified. For each agent, maximal effect (E<sub>max</sub>) was expressed as contractile force per mm<sup>2</sup> of tissue cross-section area (mN/mm<sup>2</sup>; mean±SEM) and potency as EC<sub>50</sub> (μM; mean±SEM).

**Results:** Longitudinal strips from controls were contracted in a concentration-dependent manner by carbachol (E<sub>max</sub>: 4.2±1.2 mN/mm<sup>2</sup>), histamine (2.7±0.6), 5-HT (6.1±0.8), epinephrine+yohimbine (3.0±0.5) and epinephrine+prazosin (2.4±0.4); corresponding EC<sub>50</sub>s (μM) were 0.14±0.04, 0.61±0.17, 1.88±0.33, 16.3±5.3 and 41.8±13.4, respectively. In longitudinal strips from TNBS-treated animals, E<sub>max</sub> for carbachol (7.5±1.1) and histamine (5.3±0.7) were increased compared to controls (p<0.05) without changes in EC<sub>50</sub>s (0.23±0.06 and 1.61±0.15); no changes were observed for 5-HT (E<sub>max</sub> 6.2±0.7; EC<sub>50</sub> 2.01±0.51); in contrast, α<sub>1</sub>- or α<sub>2</sub>-adrenoceptor stimulation did not contract these inflamed strips. Circular strips from controls were concentration-dependently contracted by carbachol (E<sub>max</sub>: 12.9±0.15), histamine (7.5±1.6) and 5-HT (12.2±1.6) with EC<sub>50</sub>s of 0.23±0.03, 0.56±0.07 and 3.01±0.71, but not by epinephrine. In circular strips from TNBS-treated animals, E<sub>max</sub> for carbachol (10.0±1.5) and histamine (5.4±1.0) were not different from controls, but EC<sub>50</sub>s were increased: 7.67±2.54 (p<0.05) and 5.19±1.24 (p<0.05) respectively; E<sub>max</sub> for 5-HT was decreased (6.9±1.8; p<0.05) without change in EC<sub>50</sub> (3.24±0.69); epinephrine had no effect. Finally, CRCs to KCl in longitudinal and circular strips were not different in TNBS-treated tissues and in controls.

**Conclusion:** In TNBS-induced ileitis the contractile responses of the guinea-pig ileum to receptor agonists are differentially altered: circular muscle tends to become less responsive, and longitudinal muscle more responsive, than in controls. In contrast, nonreceptor-mediated KCl contraction is not modified.

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