

Relaxin increases contractile activity and neuronal Nitric Oxide Synthase (nNOS) expression in the muscle coat of mouse colon

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Since the first observations, many actions have been attributed to Relaxin (RLX), so that it has been defined a pleiotropic hormone. This peptide of 6000 Da is synthesized by reproductive organs both in females and males. In particular, in females RLX is produced by corpus luteum (30-150 pg/ml) and its highest plasma levels (900 pg/ml) are reached during pregnancy, when RLX is also released by the decidua and placenta. In pregnancy, RLX plays its traditional role as inhibitor of spontaneous myometrial contractions and maintains uterine quiescence. Recently, RLX has shown to affect the smooth muscle of mouse gastric fundus and small intestine, depressing its motility through a nitric oxide (NO)-mediated mechanism.

In this study, we investigate the functional role of RLX in the muscle coat of female mouse colon. In the presence of 50 nmol/l RLX, continuous recordings of isometric tension showed a fast reduction of circular muscle tone, followed by a stable increase of contraction amplitude. This double effect was mimicked by the application of 40 μ mol/l NaNO₂, a NO donor, and completely blocked by 1 μ mol/l ODQ, an inhibitor of cyclic GMP which represents the main intracellular mediator of NO actions. The treatment of the tissue with 1 μ mol/l TTX prevented the decrease of muscle tone caused by RLX, indicating that this specific effect was neuronally triggered. To clarify the underlying cellular mechanism, the neuronal Nitric Oxide Synthase (nNOS) expression was evaluated in colonic segments treated with (50 nmol/l) RLX for 10 min or 40 min. In particular, two different antibodies able to recognize respectively the neurogenic and the myogenic nNOS were used. Interestingly, at both times of treatment, we observed an increase of neurogenic nNOS immunoreactivity (IR) and a decrease in myogenic nNOS-IR. These two opposite effects result statistically significant.

Present functional and morphological findings demonstrate that RLX produces a paradoxical effect in the colonic muscle coat which likely represents the final result of an interaction between the two splice variants of the nNOS enzyme.

Keywords: Relaxin, mice, colon, NO, NO synthase