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# COMPUTER SIMULATION OF MULTIPLE NEUROTRANSMISSION IN THE HUMAN GASTRIC ANTRUM

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**The aim of the study is to analyze *in silico,* the conjoint action of acetylcholine (ACh), nitric oxide (NO) and high concentrations of motilin (Mot) on myoelectrical activity of the gastric antrum under complex physiological stimuli. Acting alone at increasing doses, Mot steadily depolarizes smooth muscle, reduces the amplitude and shortens the duration of slow waves. These changes correspond to a significant rise in the basal muscle tone and the active force, $T^a$=16.1 mN/cm. The mechanical stretching of the antrum at a high frequency and the subsequent release of Ach, results in the production of regular high amplitude spikes on the crests of slow waves. Smooth muscle responds with strong phasic contractions, $T^a$ =8.3 mN/cm. The application of Mot at 50-100 nM does not affect the cholinergically mediated myoelectrical activity, although it evokes contractions of inconsistent amplitudes: $T^a$=2.9-8.3 (mN/cm). The release of a "puff" of NO to the gastric antrum which has been exposed to ACh and Mot, fails to exert any inhibitory effect. When the addition of NO precedes ACh and Mot, acute short-lasting relaxations with min $T^a$ =7.7 mN/cm are observed. The asynchrony between the firing rate of interstitial cells of Cajal and the presence of Mot at 85 nM causes the production of active forces of wavering strength. The antrum fails to relax completely. A lower frequency of ganglionic activity allows a greater degree of relaxation, $T^a$=8 mN/cm, and contractions of larger amplitude, 9.9 mN/cm. The results have unveiled intricacies of co-transmission by multiple neurotransmitters in the antrum of the human stomach and the dynamics of active forces development. The chronotropic allosteric interaction among ACh, NO, Mot and interstitial cells of Cajal plays a pivotal role in coordinated motor activity of the organ. Abnormalities in their interplay could lead to motor dysfunction.**

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