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THE EFFECT OF MULTIPLE NEUROTRANSMISSION ON THE BIOMECHANICS OF THE HUMAN STOMACH

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ABSTRACT

The mathematical model of the human stomach has been used to investigate the effect of multiple neurotransmission by acetylcholine, nitric oxide and motilin on biomechanics of the human stomach (Miftahof, 2017). The results have revealed the dynamics of active and total force development at different stages of the activation of excitatory and inhibitory system. The chronotropic allosteric interaction among ACh, NO and Mot plays a pivotal role in coordinated motor activity of the organ. Abnormalities in their interplay could lead to motor dysfunction.

Keywords: biomechanics, human stomach, acetylcholine, nitric oxide, motilin.

INTRODUCTION

Cholinergic neurons are the most prominent in the ENS of the human stomach. Acetylcholine molecules, released upon stimulation by Ca^{2+}, exert postsynaptic metabotropic responses by binding to muscarinic, μ_2 and μ_3 - $G_{q/11}$, $G_{12/13}$ - protein coupled receptors linked to the phospholipase C (PLC) intracellular signaling pathway. Ionotropic effect, on the other hand, is achieved through the activation of ligand gated voltage-dependent Ca^{2+} - channels. The electrophysiological outcome is characterized normally by the generation of fast excitatory postsynaptic potentials.

The inhibitory neurotransmission in the human stomach is mediated by nitric oxide (NO). NO elicits inhibitory pre- and post-junctional effects on ganglionic neurons and smooth muscle cerlls. Intracellularly, NO activates soluble guanylate cyclase with the production of 3',5' - cyclic guanosine monophosphate which further upregulates protein kinase G, phosphorylates phospholamban on the sarcoplasmic reticulum and increases the uptake of intracellular calcium (Ca_i^{2+}). The ionotropic effects of NO include the opening of large and small conductance K^+ channels, and the possible closure of Ca^{2+}- dependent Cl^- and L- type Ca^{2+} channels.

Motilin (Mot) is a 22-amino-acid polypeptide. It is released regularly - the process is tightly regulated by the dynamics of Ca_i^{2+}. The effects of hormone on the gastric contractile activity are dose-dependent: at low concentrations, 0.03-10 (nM), Mot affects myenteric cholinergic transduction by enhancing the release of ACh, whilst at higher concentrations, 10-100 (nM), it directly evokes the mechanical reaction of smooth muscle.

The aim of the study is 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.

RESULTS AND CONCLUSION

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 (Figure 1).

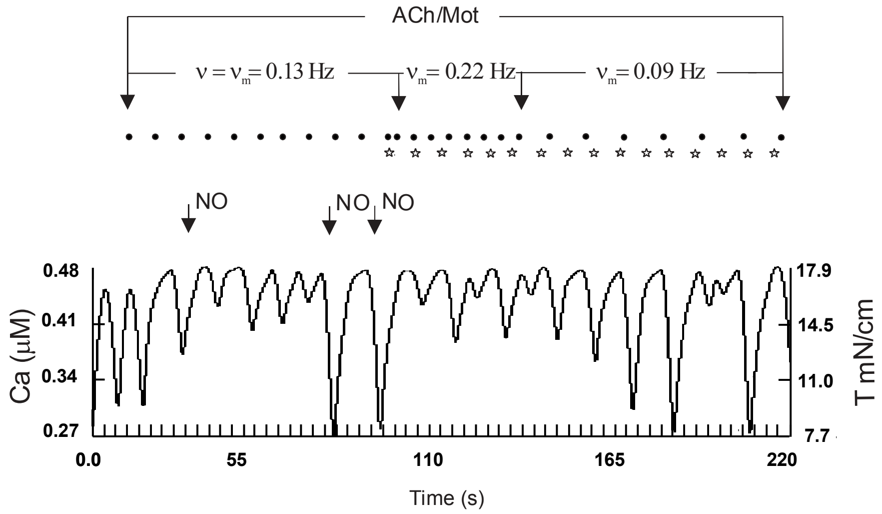

Fig. 1 - The dynamics of intracellular calcium and total force variations

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 interaction among ACh, NO and Mot plays a pivotal role in coordinated motor activity of the organ. Abnormalities in their interplay lead to motor dysfunction.

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REFERENCES

[1] Miftahof R. Biomechanics of the human stomach, 2017, Springer, Cham.