DOI 10.1007/s11062-015-9504-3
Neurophysiology, Vol. 47, No. 2, April, 2015

Excitability Characteristics of a Urinary Bladder Detrusor Smooth Muscle Cell as a Basis for Choosing Parameters of Rehabilitation Electrostimulation: A Simulation Study

A. V. Kochenov,[1,3] Ye. P. Poddubnaya,[2,3] I. A. Makedonsky,[2] and S. M. Korogod[1]

Received February 25, 2014

Electrical stimulation targeted at smooth muscle cells (SMCs) of the urinary bladder detrusor (UBD) is used in a complex of rehabilitation procedures performed during treatment of neurourological diseases, in particular of those associated with the deficiency of M2/M3 acetylcholine receptors modifying the efficacy of parasympathetic innervation of these cells. The choice of parameters of such stimulation meets difficulties because of limited knowledge about biophysical and physiological processes induced in the stimulated cells. Certain information about such processes can be obtained with the use of a UBD SMC computer model built according to the data of biological experiments characterizing ion channels, ion exchangers, and other mechanisms regulating the intracellular calcium concentration ($[Ca^{2+}]_i$) typical of the prototype. We explored the standard characteristics of the electrical excitability of the model SMC ("strength – duration" relationship for the threshold current and dynamics of the refractoriness following generation of action potentials, APs), as well as coupled changes in the membrane potential, partial transmembrane currents, and $[Ca^{2+}]_i$ values evoked by depolarizing current pulses. In some computational experiments, such stimulation was performed under conditions of a higher conductivity of purinergic ionotropic receptor channels, thereby mimicking the action of purinomimetics. The model UBD SMC generated APs with parameters close to those of the prototype; AP generation was accompanied by long periods of absolute and relative refractoriness (up to 30 and 600 msec, respectively). The relative refractoriness period included an early phase (AP half-recovery lasting about 220 msec) and a late phase; each of these phases included "fast" and "slow" components with the time constants differing from each other by an order of magnitude. These time characteristics of the refractoriness were determined by the kinetic characteristics of the processes of activation/inactivation of voltage- and calcium-dependent ion channels and by those of the $[Ca^{2+}]_i$ return to the basal level under the action of a set of Ca^{2+} extrusion mechanisms. An important UBD SMC biophysical parameter was also the reversal potential (E_{Cl}) for calcium-dependent chloride current (which is activated, in particular, due to the parasympathetic action on M2/M3 receptors). This current changed its main "depolarizing" direction to the hyperpolarizing one when the membrane potential exceeded the E_{Cl} level.

Keywords: mathematical model, smooth muscle cell (SMC), urinary bladder detrusor (UBD), electrostimulation, ion channels, M2/M3 cholinoreceptors, purinoreceptors.

INTRODUCTION

At present, electrical stimulation of organs and tissues is rather widely used during surgical interventions. Such stimulation allows one to reveal sites of location of nerve fibers in the operated tissue and, thereby, helps to prevent denervation of the organs and severe negative functional consequences related to such denervation. Exploratory intra-operative electrostimulation (IES) is used during organ- and nerve-sparing prostatectomy [1] and during surgery for rectal [2–5] and uterine [6] cancer. In recent years, IES has been used successfully for surgical correction of congenital anorectal (rectal atresia, RA) and urological (bladder exstrophy–total epispadias, BETE) malformations in children [7, 8]. After surgery for these malformations, cross-tissue electrical stimulation of the muscles of the pelvic

[1]Dnipropetrovsk division of the International Center for Molecular Physiology, National academy of Sciences of Ukraine, Dnipropetrovsk, Ukraine.
[2] Rudnev Dnipropetrovsk Specialized Clinical Medical Center of Mother and Child, Dnipropetrovsk Regional Council, Dnipropetrovsk, Ukraine.
[3] Dnipropetrovsk Medical Academy, Ministry of Public Health of Ukraine, Dnipropetrovsk, Ukraine.
Correspondence should be addressed to:
A. V. Kochenov (kochenov_artem@yahoo.com);
Ye. P. Poddubnaya (piddubna.olena@gmail.com);
I. O. Mekedonsky (igor_makedonsky@yahoo.com);
S. M. Korogod (dnipro@biph.kiev.ua).