Quantifying detrusor smooth muscle electrophysiology from calcium transient images to understand urinary incontinence

Chitaranjan Mahapatra*[1], Rohit Manchanda , and Keith L Brain

[1]Chitaranjan Mahapatra – University of Paris-Saclay, Centre National de la Recherche Scientifique - CNRS – Campus CEA Sacla, 151 route de la Rotonde,Bâtiment 151, France

Résumé

Urinary incontinence also known as urine leakage is associated with enhanced spontaneous phasic contractions of the detrusor smooth muscle (DSM). Membrane electrical activity in terms of synaptic potential and action potential (AP) plays a key role in initiating DSM contraction by developing transient (Ca2+)i elevations due to the influx of Ca2+ through voltage-gated Ca2+ channels. Information on how all ionic currents interplay in order to modulate the shape and time course of the calcium transient is sparse. The objective of this study to quantify the contribution of ionic currents in shaping experimental calcium transient profile using computational modeling.
The simultaneous experimental recording of AP and intracellular calcium transient images from the mouse urinary bladder are obtained. The individual membrane current components are modeled and validated. To generate a calcium transient, this model also incorporates a calcium dynamic based on the exponential function. In order to describe the calcium-dependent gating of Ca2+-dependent potassium channels and to update the equilibrium potential of the Ca2+ ion, the intracellular Ca2+ concentration is updated during the simulation period.
Simulation of simultaneous recordings of AP and cytosolic calcium (Ca2+)i are done on the NEURON software platform. The model shows (Ca2+)i as a function of synaptic input induced AP to simulate extracted experimental data, where Ca2+ transient is recorded simultaneously during AP in mouse DSM cell. In our model, the radius "r" and time constant

tau of the shell influence the Ca2+ transient profile. In the DSM cell model, the submembrane calcium transient occurs from a depth of 0.1 μm to a depth of 0.6 μm. We have investigated whether Ca2+ current via the L-type Ca2+ channel is responsible for the firing of APs with fast upstroke generation. It is found that inhibition of the L-type Ca2+ channel not only prevented AP generation, it also reduced the cytosolic Ca2+ transient. This study supports the application of L-type Ca2+ channel inhibitor as a potential drug for UI.

*Intervenant