Role of mitochondrial and IP_3 dependent Ca^{2+} release in the generation of slow wave activity in the guinea-pig prostate

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With increasing age males are likely to develop benign prostatic hyperplasia (BPH), a condition of urethral obstruction characterised by proliferation of prostatic stromal tissue as well as increased prostatic contractility. We have recently demonstrated that spontaneous electrical activity can be recorded in the stromal layer of the guinea-pig prostate (1). In this study, t he role of mitochondria and internal Ca^{2+} stores in the generation of slow wave activity in the guinea-pig prostate was examined using intracellular microelectrodes. Prostates were removed from guinea-pigs (250-350g) killed humanely by stunning and exsanguination. Saccular glands were pinned to the bottom of an organ bath, which was subsequently mounted on an inverted microscope stage and perfused with physiological saline solution (35°C). Two distinctly different types of spontaneous electrical recordings were recorded in the guinea pig prostate. The majority (85%) of impaled cells (n=143) displayed ‘slow wave’ activity which consisted of a depolarizing transient (14 mV in amplitude) with a 1-6 nifedipine-sensitive spikes superimposed while 15% of cells displayed a simple ‘pacemaker’ biphasic depolarization (37 mV in amplitude) which was unaffected by nifedipine (1 μM). Both electrical waveforms occurred at a frequency of 5-6 min^{-1}. In the presence of nifedipine, application of the mitochondrial uncouplers, FCCP or CCCP (1-3 μM) depolarised the membrane (8-10mV) before abolishing electrical activity. Blockade of inositol trisphosphate (IP_3)-mediated Ca^{2+} release with 2-aminoethoxy-diphenylborate (2-APB 60 μM) or phospholipase C and IP_3 formation using U73122 (5 μM) or neomycin (1 and 4 mM) significantly reduced slow wave frequency, amplitude and duration. These results suggest that mitochondrial or IP_3-dependent release of Ca^{2+} from intracellular stores is likely to have a modulatory role in the regulation of the frequency and time-course of slow wave activity in the guinea-pig prostate.

(1) Exintaris, B., M.F. Klemm, and R.J. Lang, J Urol, 2002. 168(1): 315-22.