419

Gillespie J[1], Markerink-van Ittersum M [2], de Vente J[2]
1. School of Surgical Sciences, 2. European Graduate School of Neuroscience (EURON)

CHOLINE ACETYL TRANSFERASE EXPRESSING INTERSTITIAL CELLS IN THE OUTER MUSCLE LAYERS OF THE BLADDER

Abstract Text:

Hypothesis / aims of study

The aim was to identify cells in the detrusor muscle layer which express the enzyme responsible for the synthesis of acetylcholine (choline acetyl transferase: ChAT) and to explore the possibility that these cells may be involved in the generation of detrusor activity.

Study design, materials and methods

Sections of the lateral wall of the bladder were isolated from 6 male guinea pigs (300-400g) killed by cervical dislocation. Tissues were then incubated separately in Kreb's solution at 36^{o}C, gassed with 95% O_2 and 5% CO_2, and containing 1 mM of the phosphodiesterase inhibitor isobutyl-methyl-xanthene (IBMX). Individual pieces of tissue were then exposed to 100 micro M of the nitric oxide (NO) donor diethylaminoNONate for 10 minutes. Control tissues were kept in Kreb's solution. Samples were then fixed in 4% paraformaldehyde and processed for immunohistochemistry.

Results

The outer muscle bundles of the bladder wall are associated with cells which respond to NO with a rise in cGMP. These cells, described as interstitial cells, are found on the outer margins on the bladder wall (muscle coat interstitial cells; MC-ICs), on the surface of the muscle bundles (surface muscle interstitial cells; SM-ICs) and within the muscle bundles (intramuscular interstitial cells; IM-ICs). Staining for ChAT identified the cholinergic innervation of the muscle but also a population of cells lying within the muscle bundles similar to the IM-ICs. These cells had round cell bodies and extended processes which ran parallel to the muscle fibres. In the presence of blocking peptide no ChAT staining was seen within the muscle bundles. Two populations of nerves were found close to these cells, one containing ChAT and a smaller number containing calcetonin gene related peptide (CGRP).

Interpretation of results

Deleted: ¶

These observations suggest a complex signalling arrangement within the outer layers of the detrusor muscle. It is speculated that detrusor activation may be driven by two mechanisms: the release of acetylcholine from parasympathetic nerves or from interstitial cells. The close proximity of two types of nerves to the interstitial cells suggests that they may receive both excitatory and inhibitory neural inputs. Two forms of activity have been described in the isolated whole bladder: contractures and phasic activity. The contractures have been linked to the micturition event while the phasic activity may be associated with the generation of afferent neural activity. It is possible that these different signalling arrangements are involved in the generation of these different contractile systems. Phasic activity is inhibited by CGRP. Thus, if the IM-ICs are involved in phasic activity the CGRP nerves may be inhibitory.

Concluding message

There are cells, IM-ICs, within the outer muscle layer of the detrusor which may be capable of releasing ACh. This arrangement of nerve/interstitial cell/muscle may represent an additional mechanism contributing to detrusor activation and regulation of activity.

Supported by a Detrol LA Research Grant from Pfizer Inc.

FUNDING: **Pfizer**