

NEUREGULIN1 (NRG1) REGULATES MUSCARINIC RECEPTOR IN THE BLADDER OF RATS WITH DETRUSOR OVERACTIVITY INDUCED BY BLADDER OUTLET OBSTRUCTION

Hypothesis / aims of study

Neuregulin1 (NRG1) is a growth and differentiation factor which plays critical roles in development, and plasticity of the nervous system. Binding of NRG1 results in tyrosine phosphorylation of ErbB receptors which initiates multiple downstream signals including PI3 kinase, MAP kinase, and cyclin-dependent kinase to modulate expression and activity of different functional proteins such as ion channels and neurotransmitter receptors. Several studies have shown that NRG1 are involved in regulation of neuronal nicotinic acetylcholine receptors. But the role for NRG1/ErbB2 signaling in regulating bladder muscarinic receptor is not well understood. The aim of this study is to determine the expression of muscarinic and NRG1/ErbB2 receptor in rat bladder, and changes in their distribution and expression following detrusor overactivity (DO) induced by bladder outlet obstruction (BOO).

Study design, materials and methods

The study was conducted using 40 male Sprague-Dawley rats (body weight 250–300 g), subdivided into control (n=20) and BOO groups (n=20). Partial BOO was induced for 3 weeks and DO was confirmed with measuring intravesical pressure and intraabdominal pressure. A portion of the bladder was dissected into bladder urothelium and the smooth muscle layer, and the expression of receptors was detected by RT-PCR and Western blotting.

Results

Cystometry showed a significant decrease in contraction interval and increase in contraction pressure in the BOO group. On RT-PCR and Western blotting, the expression of M₂, M₃ receptors was increased in the urothelium of the BOO group, and there was increased M₃ receptor expression in the muscle layer of the BOO group. The expression of NRG1/ErbB2 receptors was only increased in the urothelium of the BOO group; there was a smaller increase in the muscle layer.

Interpretation of results

The NRG1 may up-regulate M3 receptor via multiple binding profiles such as PI3K/MAPK signal cascades to affect the ErbB2 receptor and thus enhanced DO.

Concluding message

There were detectable changes in Neuregulin1, muscarinic and ErbB receptors with DO induced by BOO. Our results suggest that the changes of NRG1 expression could have a role in mediating the afferent sensory responses in the urinary bladder.

References

1. J Neuropathol Exp Neurol. 2012 Feb;71(2):104-15
2. Handb Exp Pharmacol. 2011;(202):15-43
3. Neurourol Urodyn. 2012 Jan;31(1):178-84

Disclosures

Funding: none **Clinical Trial:** No **Subjects:** ANIMAL **Species:** Sprague-Dawley rats **Ethics Committee:** All animal experiments followed a protocol approved by ethics committee on animal research at Chungnam National University Hospital.