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MP17-08
NEUROGENIC BLADDER DYSFUNCTION IN A MURINE MODEL OF MULTIPLE SCLEROSIS IS CAUSED BY CORONAVIRUS-INDUCED DEMYELINATION OF THE NERVOUS SYSTEM
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INTRODUCTION AND OBJECTIVES: Neurogenic bladder dysfunction develops in patients with different neurodegenerative disorders including multiple sclerosis (MS). Lower urinary tract symptoms are reported in the majority of MS patients with the most common complaints of urinary urgency and frequency. The objective of this work was to evaluate neurogenic bladder dysfunction in a murine model of multiple sclerosis induced by a neurotrophic strain A59 of mouse hepatitis virus (MHV-A59).

METHODS: Adult mice (C57BL/6J, 8 wks of age, N=84) received single inoculation of MHV-A59 leading to the occurrence of coronavirus-induced encephalomyelitis (CIE). Animals were monitored daily for 4 wks for clinical signs of neurologic impairment. Clinical Symptom Score (CSS, 0-5) was assigned based on the level of tail toxicity, kyphosis and limb paresis/paralysis. Micturition patterns were assessed by filter paper assay and cystometric recordings in unrestrained mice. Contractile responses of the detrusor were evaluated in vitro by tension measurements in response to agonists and electric field stimulation (EFS).

RESULTS: Inoculation with MHV-A59 virus induced a significant neural deficit with average CSS of 2.6±0.5 at 2 wks post-inoculation accompanied by 25±5% of weight loss (p<0.001 to baseline). Histological analysis of spinal cord sections revealed multiple demyelinated lesions. Cystometric recordings confirmed neurogenic bladder overactivity at 4 wks post-inoculation including shortened inter-micturition interval, lower voided volume and elevated number of non-micturition contractions (p<0.05 to control group). In response to EFS, the cholinergic component of contraction was significantly reduced in mucosa intact CIE mouse bladders, while the atropine-resistant (purinergic) component was increased. Removal of the mucosa from CIE mouse bladders increased the cholinergic and decreased the purinergic components.

CONCLUSIONS: Our results suggest that coronavirus-induced demyelination of the central nervous system causes the development of neurogenic bladder dysfunction that is similar to detrusor overactivity observed in MS patients. The underlying mechanisms may include an alteration in nerve-evoked contractions mediated by a urothelium dependent suppression of muscarinic and augmentation of purinergic mediated response in the bladder detrusor.

Source of Funding: This study was supported by the NIH/NIDDK grant DK097819

Source of Funding: Deutsche Forschungsgemeinschaft (DFG)

MP17-09
EXPRESSION OF MONOACYLGLYCERASE (MAGL) IN THE HUMAN LOWER URINARY TRACT: A NEW TARGET FOR INTERVENTION INTO THE ENDOCANNABINOID SYSTEM?
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INTRODUCTION AND OBJECTIVES: Endocannabinoids (2-arachidonoylglycerol, 2-AG, and anandamide) play an important role in the control of smooth muscle tone in the lower urinary tract, and of micturition. Recent studies suggested that the endocannabinoid system may be an attractive target for therapy of lower urinary tract symptoms (LUTS). Inhibition of anandamide degradation by inhibitors of FAAH causes beneficial urodynamic effects in rats with experimental urethral obstruction. However, expression of monoacylglycerolase (MAGL), which degrades 2-AG, has not been addressed in the lower urinary tract. Objective: To examine the expression of MAGL in the human bladder and prostate.

METHODS: Prostate tissues were obtained from patients undergoing radical prostatectomy. Detrusor tissues were obtained from the trigonum of bladders from radical cystectomy. Expression of MAGL was investigated by Western blot analysis. Localization was examined by double fluorescence staining.

RESULTS: MAGL and FAAH were detected by Western blot analyses in the human prostate and trigonum. In the prostate, MAGL colocalized with calponin and pan-cytokeratin, indicating expression in smooth muscle cells and in the glandular epithelium. In smooth muscle cells of the prostate, MAGL colocalized with FAAH. In the trigonum, double labelling with calponin indicated expression of MAGL and FAAH in smooth muscle cells. However, MAGL and FAAH showed no colocalization in the trigonum, indicating expression in separate smooth muscle cells. In addition, immunoreactivity for MAGL was observed in the urothelium, being even stronger as immunoreactivity in the smooth muscle. Expression of cannabinoid receptor 1 and 2 (CB1, CB2) was observed in smooth muscle cells of the trigonum, where immunoreactivity colocalized with MAGL.

CONCLUSIONS: MAGL is expressed in the human detrusor and prostate, where it may be critical for endocannabinoid availability. While MAGL is coexpressed with FAAH in smooth muscle cells of the prostate, smooth muscle cells in the detrusor express either MAGL, or FAAH. Inclusion of MAGL into cannabinoid-based therapies may enhance urodynamic effects in experimental models or clinical studies.

Source of Funding: 

MP17-10
INHIBITORY EFFECT OF URB937, A PERIPHERALLY-RESTRICTED INHIBITOR OF FATTY ACID AMIDE HYDROLASE, ON PROSTAGLANDIN E2-INDUCED HYPERACTIVITY OF BLADDER MECHANOAFFERENT NERVE FIBERS IN RATS
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INTRODUCTION AND OBJECTIVES: The endocannabinoid-degrading enzyme fatty acid amide hydrolase (FAAH) is suggested involved in bladder sensing but it is not known if FAAH-inhibition can modify nerve-activity during bladder overactivity (BO). Prostaglandin E2 (PGE2) is implicated in human and rat BO and intravesical PGE2 increases C-fiber mechanoafferent activity in rats. We studied effects by