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**21**OCT  
2022

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## Neural control of the lower urinary tract during hydrocephalus

MARTA LOUÇANO<sup>1,2,3,4</sup>, ANA COELHO<sup>1,2,3</sup>, SÍLVIA CHAMBEL<sup>1,2,3</sup>, CÉLIA DUARTE CRUZ<sup>1,2,3</sup>, ISAURA TAVARES<sup>1,2,3</sup>

1. Department of Biomedicine, Unit of Experimental Biology, Faculty of Medicine, University of Porto, Portugal; 2. IBMC-Institute of Molecular and Cell Biology, University of Porto, Portugal; 3. I3S-Institute of Investigation and Innovation in Health, University of Porto, Portugal; 4. Chemical and Biomolecule Sciences, School of Health, Polytechnic of Porto, Portugal

Neurological impairments may affect the neural control of the Lower Urinary Tract (LUT), due to structural and functional changes. Hydrocephalic patients usually present a triad of symptoms, which include gait disturbances, dementia and urinary incontinence. The consequences of hydrocephalus in brain structures, namely those involved in neural control of micturition remain mostly unknown. We used a validated animal model of hydrocephalus (rats injected in the cisterna magna with kaolin) to study the neuronal control of the LUT in hydrocephalus, focusing on two circumventricular areas: the Locus Coeruleus (LC) and the Periaqueductal grey (PAG). Studying neuronal activation of the PAG, a decrease in the number of fos-immunoreactive IR cells in the group of hydrocephalic animals was observed. Analysing the different column of the PAG separately, it was observed that this reduction was statistically significant only in ventrolateral PAG (VLPAG).

During hydrocephalus the levels of tyrosine hydroxylase (TH, enzyme involved in noradrenaline biosynthesis) increase in the LC, which may affect surrounding areas, namely the Pontine Micturition Center (PMC). To analyse if hydrocephalic animals present changes in noradrenaline levels at the spinal cord which may affect micturition, the expression of dopamine beta-hydroxylase (DBH), another enzyme involved in noradrenaline biosynthesis, in L6 spinal cord sections, was evaluated by immunohistochemistry. Hydrocephalic animals showed a higher number of fibres immunoreactive to DBH. Cystometric analysis of hydrocephalic animals, 8 weeks after induction, was used to evaluate the bladder's function. It was found that hydrocephalic animals show an increase both in the number of bladder contractions and of minimum pressure.

These results suggest alterations in the brain-bladder control network leading to an exaggerated micturition reflex. Considering the significant role of PAG in the voiding reflex, its lower activation may lead to miscommunication with other areas involved in the network, namely the PMC or LC.

Noradrenergic projections from the LC are responsible for the coordination between bladder contractions and EUS relaxation during voiding. Our study shows an increase in the levels of DBH in the Onuf's nucleus. It is possible that the increased availability of the limiting enzyme in the synthesis of noradrenaline contributes to the increased number of bladder contractions during hydrocephalus.

**Keywords:** hydrocephalus, urinary incontinence, Periaqueductal Gray, Locus Coeruleus