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Refinement of stress models of BPS/IC-related to better reproduce urinary bladder changes and pain.

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HYPOTHESIS / AIMS OF STUDY

Stress has been suggested to play a pivotal role in the initiation, maintenance, and episodic aggravation of BPS/IC symptoms in numerous patients. In order to investigate the pathophysiological mechanism of pain, several models of stress have been used, among which the maternal deprivation model (MDM) and the water-avoidance stress test (WAS) are the most used. Previous preclinical studies using stress models demonstrated that an excess of norepinephrine plays a fundamental role in these processes through the activation of alpha-1A adrenoceptors.

WAS is based on stressful event applied during a limited period resulting in effects with unknown duration, while MDM tend to cause effects that are long-lasting.

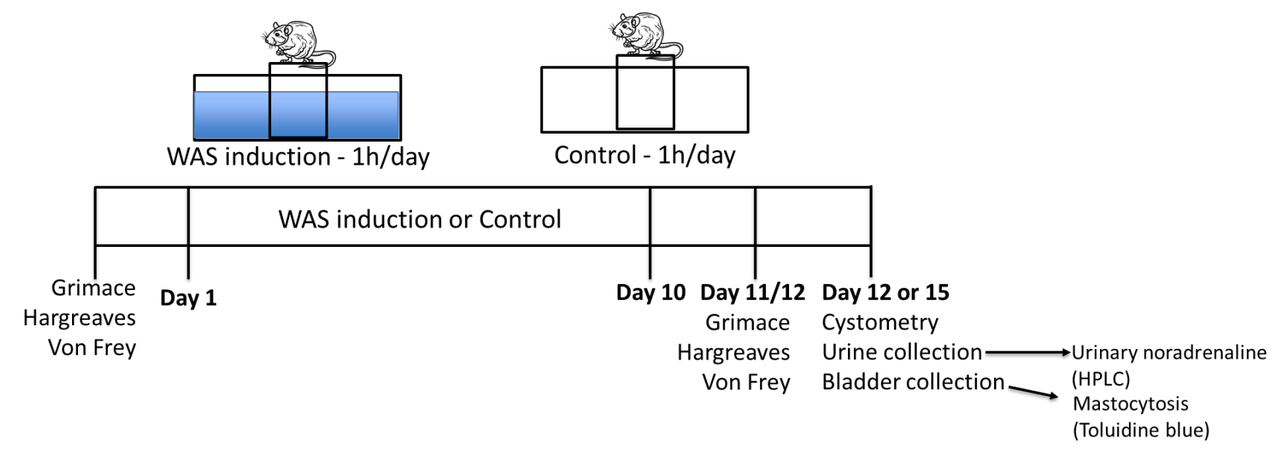
The aim of the present study was to further refine the WAS and MDM stress models. We expect that repeated stressful events aggravate bladder function and induce sensory changes in rodents.

STUDY DESIGN, MATERIALS AND METHODS

<u>Experimental design 1 (ED1)</u>:

Adult (6M) female Wistar groups:

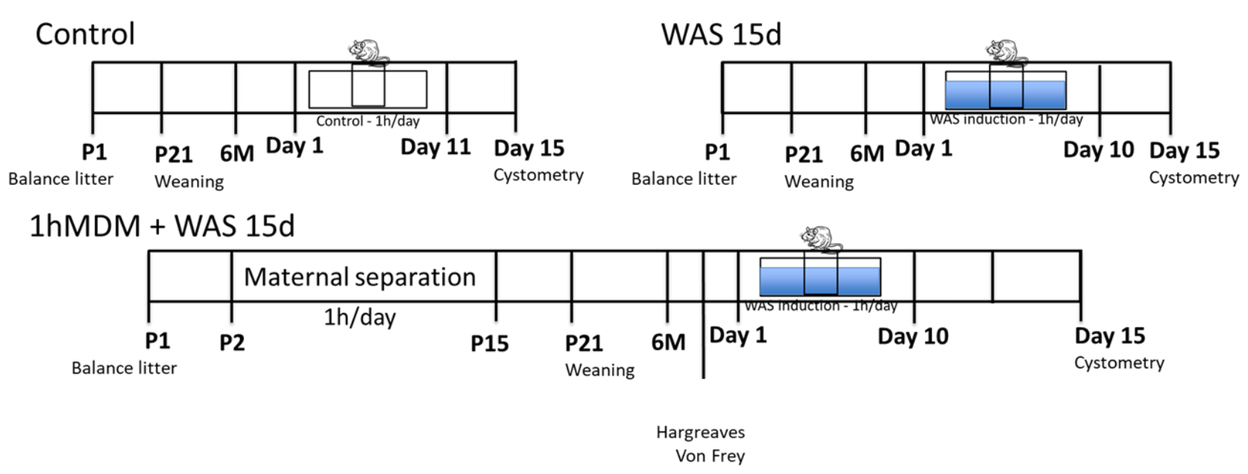
- control 12d
- control 15d
- WAS 12d
- WAS 15d



<u>Experimental design 2 (ED2)</u>:

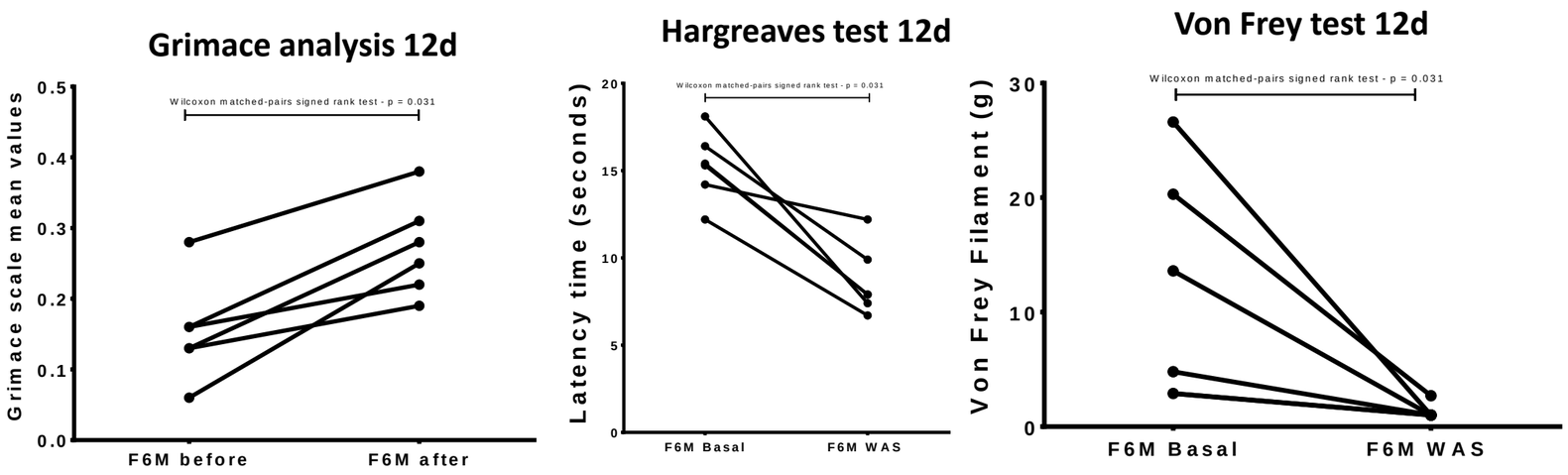
Female Wistar groups:

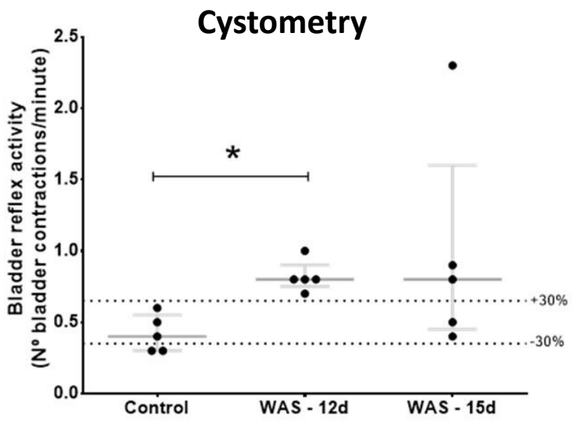
- Control
- WAS 15d
- 1hMDM + WAS 15d

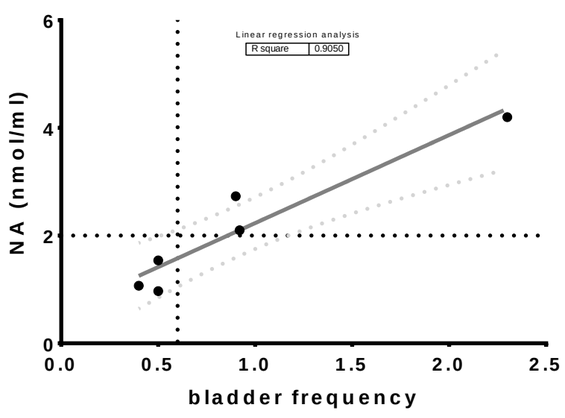


RESULTS

<u>ED1 results</u>:



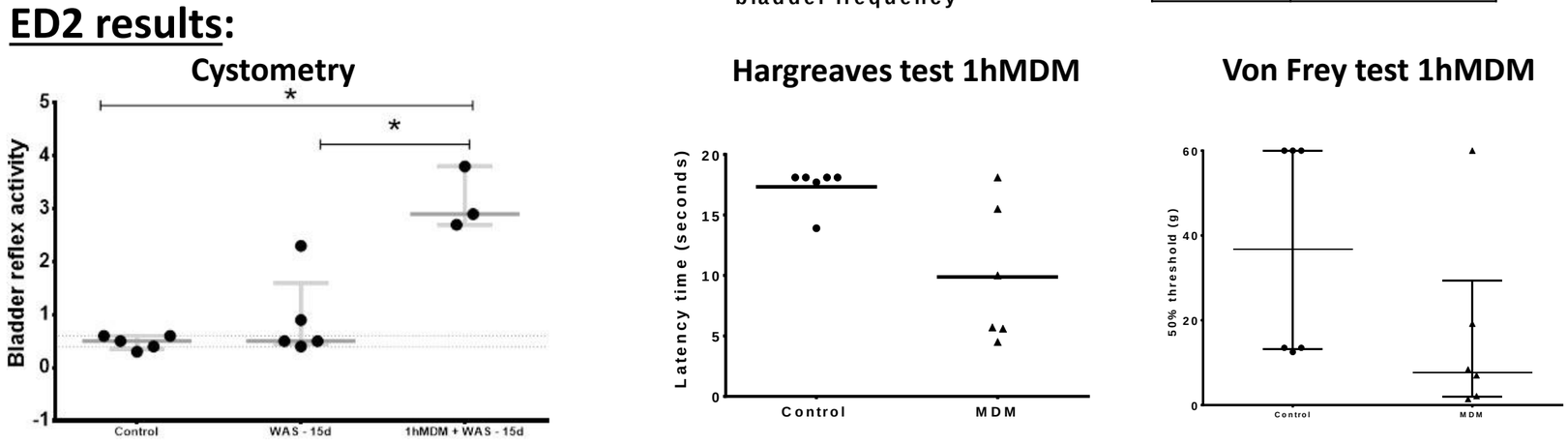




	[NA] nmol/ml
Control	0,2
WAS 12d	4,5
WAS 15d	2,1

	Mast cells/mm²
Control	15 ± 4
WAS 12d	32 ± 3 * p < 0.05
WAS 15d	7 ± 2

<u>ED2 results</u>:



INTERPRETATION OF RESULTS

Animals submitted to WAS present transient signs of pain, bladder hyperactivity and inflammation.

Urinary noradrenaline seem to predict the outcome of bladder activity in the WAS model.

1h MDM+WAS paradigm may be appropriated for long-term studies of bladder function and to investigate the possible origin of flare-ups.

CONCLUDING MESSAGE

The choice an animal model and timepoint for analysis should be a matter of carefully refinement. Repeated stressful events seems to be a good paradigm to mimic BPS/IC stress phenotype in what concerns bladder symptoms and pain.

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Funding This project has received funding from the Innovative Medicines Initiative2 Joint Undertaking under grant agreement No777500. This Joint Undertaking receives support from the European Union's Horizon2020 research and innovation programme and EFPIA. The statements and opinions presented here reflect the authors' view and neither IMI nor the EU, EFPIA, nor any Associated Partners are responsible for any use that may be made of the information contained herein. www.imi.europa.eu www.imi-paincare.eu