WATER AVOIDANCE STRESS INDUCED BLADDER OVERACTIVITY IN MICE IS ASSOCIATED WITH ENHANCED CONTRACTILE BLADDER RESPONSES

INTRODUCTION

Bladder dysfunction such as overactive bladder, incontinence and interstitial cystitis are common in the general population and even more common with age (Telegman et al., 2004). A body of clinical evidence exists linking bladder disorders with stress, anxiety and depression, including witness trauma (Lai, 2015). Stress appears to greatly influence the development of bladder symptoms, or worsen symptoms (Minassian, Devore, Hagan, & Grodstein, 2013). In spite of this, there is little research on the precise mechanisms. This study investigates the hypothesis that water avoidance stress in mice causes bladder dysfunction and an overactive bladder phenotype via mechanisms including altered detrusor responses.

METHODS

Female C57BL/6J mice (12-14 weeks) were randomly allocated to Control (n=5) or Water Avoidance Stress (WAS) (Stress) (n=5) experimental groups. WAS mice were placed on a central pedestal surrounded by room temperature distilled water for 1hr/day for 10 days. Controls were age-matched and housed normally without environmental stress exposure. Voiding pattern analysis was performed prior to (Day 0) and on days 1, 3, 5, 7 and 10 of the stress protocol. Mice were euthanised 24 hours after the final stress exposure and bladders were removed and an isolated bladder preparation methodology was taken from previous studies by our group (West et al., 2018).

RESULTS

Stress induced an overactive bladder phenotype in mice with a significant increase in the number of voiding events observed at all time points tested (Figure 2). Urinary frequency doubled by 24-hours following the first stress exposure (p<0.05) and increased 7-fold (p<0.001) following 10-days WAS. This increase in frequency was associated with a significant decrease in void size but no change in total voided volume (data not shown).

Contractile responses to the muscarinic agonist carbachol (p<0.05) (Figure 3A), and purinergic agonists ATP (p<0.05) and alpha,beta-mATP (p<0.05) (Figure 3B) were significantly increased in bladders from WAS mice, with no significant change in response to KCl (data not shown).

CONCLUSIONS

Repeated exposure to environmental stress through water avoidance altered voiding behaviour and enhanced contractile bladder responses to muscarinic and purinergic stimulation. In addition, the contribution of neuronal ATP to effenter nerve evoked contractile responses increased respectively in bladders from WAS mice. Environmental stress causes an overactive bladder phenotype. The mechanism involved appears to include enhanced responsiveness of the detrusor muscle to muscarinic and purinergic stimulation.

REFERENCES