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Induction of oxidative stress causes functional alterations in mouse urothelium via a TRPM8-mediated mechanism: implications for aging

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Summary

The incidence of bladder conditions such as overactive bladder syndrome and its associated urinary incontinence is highly prevalent in the elderly. However, the mechanisms underlying these disorders are unclear. Studies suggest that the urothelium forms a ‘sensory network’ with the underlying innervation, alterations in which, could compromise bladder function. As the accumulation of reactive oxygen species can cause functional alterations with age, the aim of this study was to investigate whether oxidative stress alters urothelial sensory signalling and whether the mechanism underlying the effect of oxidative stress on the urothelium plays a role in aging. Five-month-old(young) and 24-month-old (aged) mice were used. H_2O_2, used to induce oxidative stress, resulted in an increase in bladder afferent nerve activity and urothelial intracellular calcium in preparations from young mice. These functional changes were concurrent with upregulation of TRPM8 in the urothelium. Moreover, application of a TRPM8 antagonist significantly attenuated the H_2O_2-induced calcium responses. Interestingly, an upregulation of TRPM8 was also found in the urothelium from aged mice, where high oxidative stress levels were observed, together with a greater calcium response to the TRPM8 agonist WS12. Furthermore, these calcium responses were attenuated by pretreatment with the antioxidant N-acetyl-cysteine. This study shows that oxidative stress affects urothelial function involving a TRPM8-mediated