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THE EFFECT OF AGE ON CONTRACTILE RESPONSES OF THE PORCINE URETER

Hypothesis / aims of study

Ageing has been reported to increase the risk of ureteral calculus development [1]. This condition is frequently accompanied with ureteral colic which is understood to be caused by constriction of the ureteric tube, initiated by smooth muscle contractions. The cholinergic, α-adrenergic, and 5-hydroxytryptamine (5-HT) systems have been shown to increase ureteric contraction and hence, have a significant role in ureteral obstruction [2]. The aim of this study was to compare the effects of various agonists (phenylephrine, carbachol and 5-HT) in ureteral tissues from old and young pigs.

Study design, materials and methods

Contractile responses of isolated smooth muscle strips suspended longitudinally to phenylephrine, carbachol and 5-HT were examined in distal ureteral tissues from young (20 weeks) and old (56 weeks) pigs. Tissues developed spontaneous contractile activity and responses were expressed as area under the curve (AUC) (g^{-1} s) and frequenzy (Hz) normalised to tissue weights.

Results

When subjected to increasing concentrations of phenylephrine and 5-HT, porcine ureteral tissues from both age groups developed bursts of phasic contractions and increasing concentrations caused increased frequency of phasic activity. In response to carbachol, this similar pattern of contractions was observed in tissues from the older animals, but tissues from the younger animals did not exhibit any response to carbachol.

The potency (pEC_{50}) values of agonists were similar for tissues from both age groups, where comparison was possible (young vs old: 4.42±0.18 vs 4.83±1.43 for phenylephrine, 5.16±0.09 vs 5.43±0.16 for 5-HT). However, the maximum contractile responses expressed as AUC to phenylephrine were significantly enhanced in tissues from the older group (Figure 1a, $p<0.001$). Phenylephrine-induced frequency of contractions was also greater in older animals (young vs old: 0.1478±0.0149Hz vs 0.1478±0.0340Hz respectively). Tissues from younger animals failed to respond to carbachol, but in older animals, ureteral strips developed contractile activity (Figure 1b) and the maximum frequency of contractions was 0.031±0.002Hz. In contrast, for 5-HT, maximum AUC contractile responses were depressed in tissues from older animals (Figure 1c, $p<0.001$). However, the maximum frequency response was similar in tissues from both age groups (young vs old, 0.193±0.009 vs 0.212±0.014Hz).

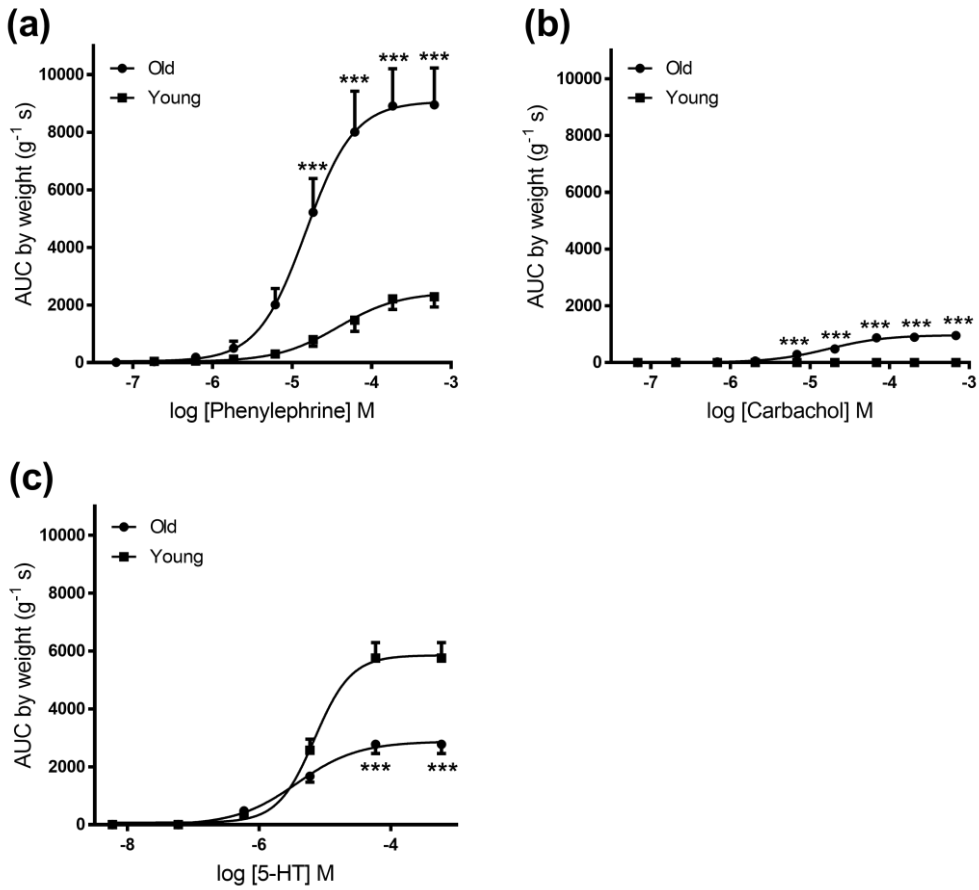

Figure 1: Concentration-response curves for (a) phenylephrine, (b) carbachol and (c) 5-HT in distal ureteral tissues from old and young pigs. Responses are expressed as AUC by weight in g^{-1} s as mean±SEM of 8 preparations for each group.

Interpretation of results

Maximal contractile responses to the α-adrenoceptor agonist phenylephrine and the muscarinic receptor agonist carbachol were greater in older animals, whereas contractile responses to 5-HT were greater in younger animals. There were no changes in potency for phenylephrine and 5-HT. Therefore, changes observed in the maximal contractions are unlikely to be caused by changes in the density or affinity of functional receptors expressed with age as this would have produced a rightward shift of concentration curves. Additionally, it is also unlikely that these age-related changes are due to a general modification of smooth muscle contraction capability with age, since phenylephrine induced greater contractions with age whilst 5-HT-stimulated contractions were reduced with age. It is suggested that these age-related modifications in adrenergic and 5-HT responses may be due to changes in the intracellular signalling pathways stimulated by receptor activation, while in muscarinic receptor mediated contractions, the alterations may be due to changes in receptor expression.

Concluding message

These results suggest that there are age-related changes in the contractile responsiveness of the ureter which may affect the effectiveness of agents used to cause uretral relaxation.

References

1. Canda et al (2007) Urol Int 78:289-298.
2. Costa-Bauza et al (2007) World J Urol 25:415-421.

Disclosures

Funding: Pro-Vice Chancellor Scholarship, Bond University **Clinical Trial:** No **Subjects:** ANIMAL **Species:** Pig **Ethics Committee:** Bond University Ethics Committee