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Aging changes agonist induced contractile responses in permeabilized rat bladder

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Aging causes changes in many organs as well as a significant decrease in filling, storage and emptying functions in bladder[1]. The symptoms like reduced voiding efficiency and bladder overactivity may bring forth a social problem such as incontinence[2,3]. Especially in women, urinary incontinence incidence increases with age and the side-effects of the present drugs unfortunately fail to carry out a radical therapy. Contractile mechanisms can be studied using chemically permeabilized smooth muscle preparations in which the plasma membrane is permeabilized[4]. The use of different permeabilizing agents can generate preparations which vary in the preservation of cellular mechanisms. The aim of this study is to examine how aging affects the intracellular calcium movements due to agonist induced contractions in permeabilized female rat bladder smooth muscle. Young (2 to 4 months old) and old (16 to 20 months old) female Sprague-Dawley rats were used in the study. Bladder detrusor smooth muscle strips (approximately 150-250 µm in diameter and 3-4 mm in length) were mounted in 1 ml organ baths containing Hepes buffered modified Krebs' solution (NaCl 126; KCl 6; $CaCl_2$ 2; $MgCl_2$ 1.2; glucose 14 and HEPES 10.5 in mM) under a resting tension of 100 mg. Tissues were permeabilized with 40 µM β-escin for 30 min. After permeabilization, all drugs were given in a solution containing (mM) K propionate 130; $MgCl_2$ 4; Na_2ATP 4; tris-maleate 20; creatine phosphate 10; EGTA 4 or 0.05 and creatine phosphokinase 3.3 units/ml; leupeptin 1 µM. Isometric contractions were recorded by sensitive transducers and expressed as % of 80 mM K^+ elicited in intact tissues. Data are expressed as mean±S.E.M. Statistics was done by ANOVA/Bonferroni. $P<0.05$ was accepted as significant. 50 µM carbachol-induced contractions in young group that is 37.14±7.0% (n=6) were significantly decreased to 20.47±2.0% in old group (n=18, $P<0.05$). These carbachol-induced contractions in young group were significantly inhibited 27% by 1 mg/ml IP_3 receptor blocker heparin (n=12, $P<0.05$) and 57% by 10 µM sarcoplasmic reticulum Ca^{2+} channel inhibitor ryanodine (n=15, $P<0.05$). However, in old group, carbachol-induced contractions were inhibited 60% by heparin (n=11, $P<0.05$), but not with ryanodine (n=15, $P>0.05$). Cumulative Ca^{2+} contractions (pCa 8-4) were significantly reduced in old group (E_{max}=12.1±3.7%, n=6, $P<0.05$) compared to young group (E_{max}=49±5.8%, n=7). 50µM IP_3-induced contractions that are 6.8±1.7% (n=17) in old group did not changed with aging (10.09±2.8% in young group, n=14, $P>0.05$). However, sarcoplasmic reticulum Ca^{2+} channel activator caffeine (10 mM) contractions were significantly decreased in older rats compared to young ones (from 11.62±2.6% to 2.6±0.8%, n=7-11, $P<0.05$). Our findings show that IP_3 induced calcium release (IICR) is primarily responsible from the contractile responses in older rats where the decrease in carbachol-induced contractions in aging may be as a result of a decrease in Ca^{2+} induced Ca^{2+} release (CICR). *This study was supported by 2012 L'Oreal Turkey "Women in Science" Grants.*

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