	Response to 10^{-5} M Carbachol (n=29, N=4)		Response to 15Hz stimulation (n=26, N=4)	
	g/mg	% of control tissue response	g/mg	% of control tissue response
Control	2.81±0.31	100±0	1.14±0.16	100±0
1mM TEA	2.27±0.41 p<0.05	69.7±6.26 p<0.05	1.13±0.18 NS	109±11.45 NS
10mM TEA	1.93±0.40 p<0.05	56.0±7.12 p<0.05	2.06±0.37 p<0.05	221.7±28.4 p<0.05

Conclusion: The increase in spontaneous contractile activity of normal human detrusor smooth muscle upon addition of TEA suggests that spontaneous activity is an action potential mediated process. Blockade of TEA-sensitive potassium channels profoundly potentiates the effect of intrinsic nerve stimulation in the normal human detrusor, this is consistent with a large increase in transmitter release effected by blockade of potassium channels. However, in contrast, the reduction of the response to carbachol in the presence of TEA may be due to muscarinic receptor antagonism.

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AGE-RELATED CHANGES IN ACETYLCHOLINE AND ADENOSINE TRIPHOSPHATE RELEASES FROM HUMAN BLADDER SMOOTH MUSCLES

Aims of study

With regard to excitatory innervation of urinary bladder, it is generally accepted that, in addition to a cholinergic neurotransmission, an atropine-insensitive, non-adrenergic, non-cholinergic neurotransmission exists in most mammalian bladder. Adenosine triphosphate (ATP) is believed to be the neurotransmitter responsible for non-cholinergic portion of bladder contraction (1, 2). Thus, the neurogenic contraction of bladder is mainly mediated by two neurotransmitters, acetylcholine (ACh) and ATP. It is well known that the aging process affects bladder function. However, little information is as yet available on the age-related changes in neurotransmitters release from bladder smooth muscles. We reported the measurement of ACh release induced by electrical field stimulation (EFS) in rabbit bladder smooth muscles, using microdialysis method (3). In this report, we evaluated the age-related changes in the ACh and ATP releases induced by EFS in human bladder smooth muscles.

Methods

Smooth muscle strips were obtained from detrusor in 25 patients (42 - 82 years) with bladder carcinoma. The strip was suspended in a 20 ml muscle bath filled with Krebs-Henseleit solution, was connected to an isometric force displacement transducer, and an isometric tension development was recorded. The contractions induc by EFS (duration; 0.2 msec, frequency; 5 - 50 Hz and 2 sec train) were constructed. The microdialysis probe (O-P-100-10, Eikom, Kyoto, Japan) was inserted into the strip. Ringer solution was perfused into the probe at a rate of 2 μl/min. The dialysate during EFS (0.2 msec pulse duration, 20 Hz, 2 sec train and 2 min interval for 10 min) was collected. A volume of 10 μl of the each sample was injected into ACh and ATP assay systems, and the amount of ACh and ATP released in the dialysate was measured by HPLC.

Results

Contractile responses induced by 80 mM KCl and the frequency-response curves to EFS did not significantly change with age. In this assay system, the detection limits of ATP and ACh were 0.1 and 0.02 pmol/injection,

respectively. The contractile responses and releases of ACh and ATP induced by EFS were significantly inhibited by the pretreatment with tetrodotoxin (1 μM). ATP release during EFS increased with age, and ACh release decreased with age. There was a significant positive correlation between age and ATP release, and there was a significant negative correlation between age and ACh release (figure).

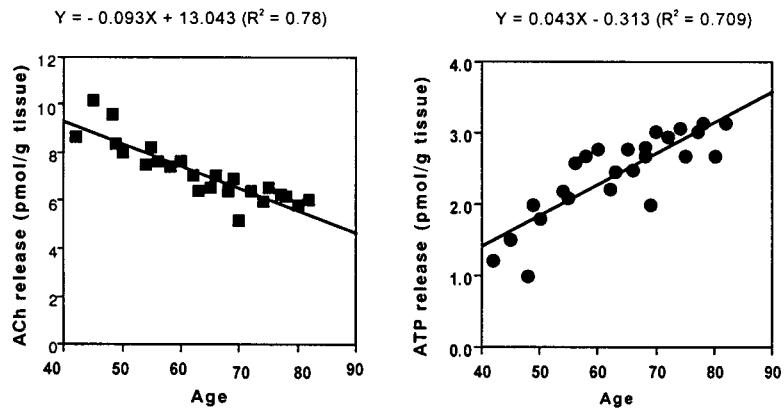

Figure: Correlation between age and ACh release (left) and ATP release (right) in human bladder

Conclusions

The present data suggest that there are age-related increase in ATP release and decrease in ACh release during EFS. This may contribute to age-related functional changes in human bladder smooth muscles.

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VOLTAGE GATED POTASSIUM CHANNELS IN DETRUSOR MUSCLE

AIMS OF STUDY: The aetiology of detrusor instability remains unknown, but myogenic change is thought to be important (1). Voltage-gated potassium channels (K_V channels) are important in the repolarising phase of action potentials and in the control of membrane potential. Potassium channel dysfunction may have an aetiological role in detrusor instability and may offer the possibility of a new pharmacological target in the treatment of detrusor instability.We have investigated the function of K_V channels and the expression of six subunits from the *Shaker*-related K_V1 family in bladder smooth muscle.

METHODS: The expression of the six K_V1 channel subunits was investigated in stable human detrusor using tissue obtained from cystectomy specimens. Slices of detrusor were labelled with channel-specific polyclonal antibodies and a double labelling immunofluoresence protocol was used to compare channel localisation with that of smooth muscle α-actin. Images were collected using a cooled CCD camera and processed using Improvision Openlab software. The specificity of the antibodies was confirmed by Western blotting. The functional